Interplay between migraine and pregnancy outcomes

By

Katherine Gwyneth Phillips

A thesis submitted to the University of Birmingham for the degree of

DOCTOR OF PHILOSOPHY

Institute of Applied Health Research
College of Medical and Dental Sciences
University of Birmingham
April 2024

Abstract

Background: Migraine is highly prevalent in women of reproductive age and there is evidence to suggest that it impacts on the risk of adverse pregnancy outcomes. In particular, an association between migraine and pre-eclampsia has been well described. Links between migraine and other pregnancy outcomes such as miscarriage and preterm birth have been investigated, but findings have been less conclusive. Migraine often requires pharmacological therapy to manage symptoms and prevent episodes, but information about the safety of some migraine medication during pregnancy is lacking. This thesis aims to describe the epidemiology of migraine in pregnancy, determine its associated outcomes, and assess the safety of migraine medication during pregnancy.

Methods: An epidemiological study was carried out using and electronic primary care record database to describe the annual prevalence of migraine in pregnancy and the medications commonly prescribed amongst pregnant women with migraine. An umbrella review was conducted of literature comparing pregnancy outcomes in i) women with migraine to women without migraine ii) women with migraine who were treated to women with migraine who were not treated during pregnancy. A retrospective matched cohort study using the CPRD pregnancy register was conducted to compare the risk of miscarriage in women with migraine to those without migraine. Within the migraine cohort, a nested case-control study was conducted to compare the odds of miscarriage in those exposed to migraine medication in pregnancy compared to women with migraine who were not exposed to medication. Finally, a retrospective cohort study using delivery records from the Hospital Episode Statistics (HES) maternity tail was conducted to compare delivery outcomes (preterm birth, low birth weight, small for gestational age, mode of delivery and stillbirth) in women with migraine to those without migraine.

Results: The age-adjusted prevalence of migraine in pregnancy increased from 11.4% (95% CI 10.3%-12.4%) in 2000 to 17.2% (95% CI 16.7%-17.5%) in 2018. Over the same period, there was an increase in the rates of prescription for numerous medications for the management of migraine, notably, triptans, antidepressants (including amitriptyline) and beta blockers. In the umbrella review, migraine was associated with a higher odds of pre-eclampsia (pooled OR 2.05 (1.47-2.84), peripartum mental illness (pooled OR = 1.75 (1.20-2.54)) and preterm birth (pooled OR 1.26 (1.21-1.32)). Triptan-exposed women had increased odds of miscarriage compared to women without migraine (pooled OR 3.54 (2.24-5.59)). In the matched cohort study, migraine was associated with a 6% higher risk of miscarriage (aRR 1.06 95% CI (1.04-1.08)). Results from the nested case-control study showed that in pregnancies of women with migraine, exposure to triptans, amitriptyline and NSAIDs were associated with a significantly higher odds of miscarriage (aORs 1.24 (1.11-1.38), 1.25 (1.08-1.45) and 1.74 (1.57-1.93), respectively). Migraine was associated with an higher risk of extremely preterm (aRR 1.18 (95% CI 1.01-1.37) and medically-indicated preterm delivery (aRR 1.11 (95% CI 1.02-1.20)) in the matched delivery record cohort.

Conclusion: Prevalence of recorded migraine during pregnancy has increased over the past few decades, as have rates of prescriptions for migraine medications during pregnancy. Migraine was associated with pregnancy complications such as pre-eclampsia, peripartum mental illness, miscarriage and preterm birth (potentially driven by medically indicated preterm birth). Exposure to triptans, NSAIDs and amitriptyline in pregnant women with migraine was associated with miscarriage. Future work should focus on how migraine type and severity impact these outcomes, the associations of migraine drugs with other pregnancy outcomes and potential underlying causative mechanisms.

Acknowledgements

The work in this thesis was funded by the National Institute for Health and Care Research (NIHR) Academic Clinical Fellowship and the Strategic Priority Fund "Tackling multimorbidity at scale" programme (grant numbers MR/V005243/1 and MR/W014432/1) delivered by the Medical Research Council and the National Institute for Health Research in partnership with the Economic and Social Research Council and in collaboration with the Engineering and Physical Sciences Research Council. This work was also supported by Health Data Research UK (HDRUK2023.0030), which is funded by UK Research and Innovation, the Medical Research Council, the British Heart Foundation, Cancer Research UK, the National Institute for Health and Care Research, the Economic and Social Research Council, the Engineering and Physical Sciences Research Council, Health and Care Research Wales, Health and Social Care Research and Development Division (Public Health Agency, Northern Ireland), Chief Scientist Office of the Scottish Government Health and Social Care Directorates.

The views expressed are those of the author and not necessarily those of the funders, the NIHR or the United Kingdom Department of Health and Social Care. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

I would like to thank my supervisors, Dr Francesca Crowe, Professor Krishnarajah Nirantharakumar and Dr Benjamin Wakerley for their support and guidance throughout my PhD and for the opportunity to undertake this work.

I would like to thank and acknowledge the co-authors who helped me prepare several manuscripts that arose from this thesis for publication.

Many thanks to my University of Birmingham colleagues for their guidance and expertise in data extraction, statistical analysis, epidemiology and clinical coding.

Thank you to the members of the MuM-PreDiCT consortium for the opportunity to undertake this PhD and to learn from their wealth of knowledge, expertise and lived experience in the field of maternal health.

Finally, thank you to my parents, Jackie and John, and my husband, Conor, who have supported and encouraged me throughout my PhD and career.

List of manuscripts arising from PhD thesis

Published manuscripts

Phillips K, Nirantharakumar K, Wakerley BR, Crowe FL. Trends in the prevalence and pharmacological management of migraine during pregnancy in the UK, 2000–2018. Journal of Neurology, Neurosurgery & Psychiatry 2024;:jnnp-2024-33353.

Phillips K, Clerkin-Oliver C, Nirantharakumar K, Crowe FL, Wakerley BR. How migraine and its associated treatment impact on pregnancy outcomes: Umbrella review with updated systematic review and meta-analysis. Cephalalgia. 2024;44(2)

Manuscript in submission to peer reviewed journal

Phillips K, Gokhale K, Damase-Michel C et al. Migraine, associated treatments and risk of miscarriage: a matched cohort study and nested case-control study using the CPRD pregnancy register. Journal of Neurology, Neurosurgery & Psychiatry: under review

Other related manuscripts published during this PhD

Subramanian A, Lee SI, Hemali Sudasinghe SPB, Wambua S, Phillips K, et al Detection and evaluation of signals associated with exposure to individual and combination of medications in pregnancy: a signal detection study protocol BMJ Open 2023;13:e073162. doi: 10.1136/bmjopen-2023-073162

Anand A, Phillips K, Subramanian A on behalf of the MuM-PreDiCT Group, et al Prevalence of polypharmacy in pregnancy: a systematic review BMJ Open 2023;13:e067585. doi: 10.1136/bmjopen-2022-067585

Lee SI, Hope H, O'Reilly D, Kent L, Santorelli G, Subramanian A, Moss N, Azcoaga-Lorenzo A, Fagbamigbe AF, Nelson-Piercy C, Yau C, McCowan C, Kennedy JI, Phillips K, et al. Maternal and child outcomes for pregnant women with pre-existing multiple

long-term conditions: protocol for an observational study in the UK. BMJ Open 2023;13(2):e068718.

Sumbramanian A, Azcoaga-Lorenzo, A, Anand, A, Phillips K et al. Polypharmacy during pregnancy and associated risk factors: a retrospective analysis of 577 medication exposures among 1.5 million pregnancies in the UK, 2000-2019. BMC Med 21, 21 (2023). https://doi.org/10.1186/s12916-022-02722-5

Singh M, Crowe F, Thangaratinam S, Abel KM, Black M, Kelvin Okoth, Richard D Riley, Eastwood KA, Hope H, Wambua S, Healey J, Lee SI, Phillips K et al Association of pregnancy complications/risk factors with the development of future long-term health conditions in women: overarching protocol for umbrella reviews BMJ Open 2022;12:e066476.

Phillips K, Davison J, Wakerley B. Headache in pregnancy: a brief practical guide. British Journal of General Practice 2022;72(725):593–4.

Table of contents

List of tables

List of figures

Chapter 1 : Introduction

1.1 Introduction

This chapter covers the definition of migraine, including its clinical features, diagnosis, management and epidemiology. The pathophysiology of migraine, including how it relates to cardiovascular risk will be described. What is already known about the associations between migraine and pregnancy outcomes will be summarised. The pharmacological management of migraine during pregnancy and what is already known about safety of migraine drugs during pregnancy will be described. Finally, the aims and objectives of the thesis will be laid out.

1.2 Definition

Migraine is a primary headache disorder characterised by attacks of moderate to severe headaches and associated with symptoms such as photophobia (sensitivity to light), phonophobia (sensitivity to sound), nausea or vomiting.

1.3 Clinical features

Migraine is characterised by moderate to severe headache, which typically lasts for more than four hours when treated (1, 2). Other diagnostic features include nausea, vomiting, photophobia and phonophobia. Approximately a third of patients with migraine also experience aura(3), transient visual or sensory symptoms, which occur before the onset of headache(4). Migraine is further classified as episodic, where headaches occur on fewer than fifteen days per month; or chronic, where headaches occur on fifteen or more days per month(1, 2).

Migraine is diagnosed on clinical grounds. Table 1.1 summarises the diagnostic criteria used to diagnose migraine in the UK.

Table 1.1: Diagnostic criteria (from NICE CG150 and International Headache Society: The International Classification of Headache Disorders 2018)

Migraine without aura	At least 5 attacks. Headaches fulfil the following criteria:
	• Lasting 4-72 hours in adults or 2-72 hours in adolescents
	• At least two of the following characteristics:
	  o Unilateral location (more commonly bilateral in children)
	  o Pulsating quality
	  o Moderate to severe pain
	  o Aggravated by or causing avoidance of, routine activities of daily life
	• Associated with at least one of the following symptoms:
	  o Nausea and/or vomiting
	  o Photophobia and phonophobia
	• Headache must not be better accounted for by another diagnosis

Migraine with aura	At least 2 attacks fulfilling the following criteria:
	• One or more typical, fully reversible symptom:
	  o Visual symptoms such as zigzag lines or scotoma
	  o Sensory symptoms such as unilateral pins and needles or numbness
	  o Speech and/or language symptoms such as dysphasia
	• At least three of the following:

	○ At least one aura symptom spreads gradually over at least 5 minutes ○ Two or more aura symptoms occur in succession ○ Each individual aura symptom lasts 5-60 minutes ○ At least one aura symptom is unilateral ○ At least one aura symptom is positive ○ The aura is accompanied, or followed by, a headache • Headache must not be better accounted for by another diagnosis

1.4 Management of Migraine

Migraine can be precipitated by a number of internal and external triggers. These commonly include disturbed sleep, irregular or missed meals, dehydration, lack of exercise and menstruation(5).

It is recommended that people with migraine keep a headache diary to help identify triggers and monitor response to treatment. Lifestyle management of migraine includes the avoidance of triggers, management of stress, good sleep hygiene, staying hydrated, regular meals, exercise and weight management (5).

In the majority of patients with migraine, headache frequency and severity can be managed with appropriate medication. (see below).

1.5 Migraine Prevalence and Burden

Migraine is the second most common primary headache disorder after tension-type headache and is estimated to affect about 1 in 7 people worldwide(6). It is two to three times more common in women and prevalence peaks in people aged 35-39 years, meaning it is of particular importance for women of reproductive age (7).

Migraine is the leading cause of disability amongst people under 50 years, contributing to 45.1 million years lived with disability to the global disease burden. A 2013 US survey found people living with migraine report a negative impact on their education, employment and family relationships (8). A 2011 study into the costs of headache disorders in Europe estimated that the annual cost for migraine was €111 billion. Direct costs of migraine included outpatient care, investigations, medications and hospitalisation. Indirect costs included lost productivity and work absenteeism (9). In the UK, migraine and other headaches are among the most common neurological presentations to A&E and account for around 2.5 million GP appointments per year(10).

A 2018 report into the socioeconomic impact of migraine in the UK found that migraine-related absenteeism and presenteeism were associated with 55-86 million workdays lost, accounting for £5.6-8.8 billion in lost productivity. This is not including the more difficult to measure costs associated with “interictal anxiety” (worry about the next migraine episode and avoidance of perceived triggers) and the negative impact on career advancement and related loss in earnings(11).

1.6 Pathophysiology

There is evidence for a strong genetic component to migraine. A 40% risk has been reported in those with one parent with migraine, rising to 75% if both parents have

migraine(12). More than 180 gene variants have been identified that each result in a small increase in overall migraine risk(13).

The pathogenesis of migraine is still not fully understood, but it is now thought to primarily be neuronal changes that lead to migraine through the activation of branches of the trigeminal nerve which leads to the release of pro-inflammatory mediators. This inflammation affects the pain-sensitive meninges resulting in headache(12). A wave of excitation followed by inhibition of neurones in the cortex are what is thought to lead to aura (14). Calcitonin gene-related peptide (CGRP), a neuropeptide involved in the regulation of cardiovascular and pain mechanisms, is thought to play an important role in the pathophysiology of migraine. High levels of CGRP are found in the central nervous system during migraine episodes. These are believed to cause dilation of cerebral and dural blood vessels, release of inflammatory mediators from mast cells, and transmission of nociceptive information from intracranial blood vessels to the nervous system, all of which play a role in the pathophysiology of migraine (15). Newer medications which target CGRP, or its receptor, have been found to provide effective relief from symptoms (13).

1.7 Migraine and vascular risk

Migraine is not a benign neurological disorder as it may increase the risk of developing other long-term health conditions. Associations have been described between migraine and stroke and cardiovascular disease. A meta-analysis showed a risk ratio (RR) of 1.55 (95% 1.38-1.75) for the association between migraine and stroke(16). In women, the RR was 2.08 (95% CI 1.13-3.84), with women under the age of 45 at particular risk (RR 3.65 (2.21-6.04)) (17). Migraine with aura is associated with around a twofold risk of stroke compared to migraine without aura (18).

A systematic review and meta-analysis of 15 observational studies found that migraine is also associated with an increased risk of angina (overall pooled adjusted effect estimate 1.29 (1.17-1.43) and myocardial infarction (pooled effect estimate 1.33 (1.08-1.64)). The associated risk is higher in women (MI: pooled effect estimate 1.67 (1.36-2.06), angina: pooled effect estimate: 1.38 (1.17-1.63). A particular association was found in migraine with aura (MI: pooled effect estimate 2.61 (1.86-3.65), angina: pooled effect estimate: 2.94 (1.59-5.43) (19).

Potential underlying mechanisms include dysfunction of the endothelium, which impairs the ability of the blood vessels to contract and relax appropriately as well as the clotting function of the blood (20). In addition, genetic abnormalities of the coagulation system and increased platelet activity have been described in migraine patients, which lead to a prothrombotic state (21). Finally, migraine has been found to be associated with an increased burden of conventional cardiovascular risk factors, such as hypertension and hypercholesterolaemia, although it is unclear whether migraine increased the likelihood of these conditions, or whether lifestyle factors, such as BMI, play a role(22). All of these factors, in turn, predispose to atherosclerosis and cardiovascular disease.

1.8 Migraine and pregnancy

According to the Global Burden of Disease study 2019, migraine affects 18.6% of women aged between 20 and 64(23), making it an important condition during pregnancy. Similar results were found in a 2003 UK survey of women aged 16-65 which reported a prevalence of 18.3%(24). The prevalence of migraine during pregnancy has not been described in the UK population.

A review of observational studies found the majority of women (60-70%) report that migraine resolves during pregnancy, with rates of remission highest in the second and third trimesters(25). This is thought to be because oestrogen and endogenous opioids rise during pregnancy, raising the pain threshold. In addition, there are no longer menstruation-related hormonal fluctuations, which are a major trigger for migraine attacks (26). Less often, migraines can occur for the first time during pregnancy (27).

However, there is increasing evidence to suggest migraine impacts on pregnancy outcomes. In particular, a link between migraine and pre-eclampsia, a disorder of the placenta characterised by new-onset hypertension and end-organ damage(28), has been well described. A 2019 meta-analysis found a two-fold increase in the risk of pre-eclampsia in women with migraine when pooling the results of nine observational studies(29). There is a suggestion that there are similar mechanisms underlying this association as were discussed above in cardiovascular disease. Migraine and pre-eclampsia share common pathophysiological mechanisms including a pro-inflammatory state, endothelial dysfunction and hypercoagulability. It is therefore suggested that women with migraine have poor vascular compensatory mechanisms to stressors such as pregnancy, meaning complications such as pre-eclampsia are more likely (30). This is supported by the fact these are also features of pre-eclampsia (31-34). Other conditions related to the placenta have similar underlying pathophysiology. Preterm birth has been associated with a pro-inflammatory state(35) and miscarriage with endothelial dysfunction(36). Links between migraine and these conditions have been investigated (37), but findings have been less conclusive.

This has motivated the thesis objectives to study the adverse pregnancy outcomes through an umbrella review of the literature (chapter 4) and analysis of large pregnancy cohorts (chapter 3, 5 and 6).

1.9 Specific Pregnancy Outcomes

1.9.1 Miscarriage

Miscarriage is broadly defined as a loss of intrauterine pregnancy before viability. The definition of viability varies, but it is often determined by gestational age, with the threshold ranging from 20 to 28 weeks (38). Conversely, the World Health Organisation (WHO) defines miscarriage as the loss of a fetus weighing less than 500g (39). The denominator for miscarriage rate is also variable, with some definitions considering only pregnancies confirmed clinically by ultrasonography (38).

Miscarriage is thought to affect 15.3% of clinically recognised pregnancies. The impacts of miscarriage are wide-ranging. Immediate physical impacts can include bleeding and infection and psychological impacts can include anxiety, depression, and, in some cases, post-traumatic stress disorder and suicide(38). There are also broader societal impacts, miscarriage is estimated to cost the UK £471 million per year(40, 41). Risk factors for miscarriage include chromosomal abnormalities; endometrial defects; uterine abnormalities; increasing maternal and paternal age; maternal BMI, smoking and high alcohol use; maternal health conditions such as antiphospholipid antibodies, hypothyroidism and infections. Recurrent miscarriage is associated with a higher risk of future obstetric complications such as preterm birth, fetal growth restriction and stillbirth (38).

1.9.2 Preterm Birth

Preterm birth is defined as a viable birth occurring before 37 weeks complete gestation (42). It is further classified as extremely preterm (less than 28 weeks), very preterm (28 to 32 weeks) and moderate to late preterm (32-37 weeks). Preterm birth can also be classified by the mode of birth, spontaneous (preterm labour or preterm prelabour

rupture of membranes (PPROM) occurring spontaneously) or medically indicated (preterm delivery by caesarean section or following induction of labour) (42). Risk factors for spontaneous preterm delivery include short interpregnancy intervals, low body mass index (BMI), nutrient deficiency, previous preterm birth, intrauterine infection, and maternal disorders such as hypertension, diabetes, asthma, systematic lupus erythematous (SLE), hyperthyroidism and chronic kidney disease (CKD) (43) (44). Indications for preterm delivery may be maternal such as pre-eclampsia or placental abruption; or foetal such as intra-uterine growth restriction or foetal distress (45). It occurs in about 11% of births worldwide. Preterm birth is one of the leading causes of neonatal death(42). Although the aetiology of preterm birth is not fully understood, risk factors for preterm birth include low and high maternal age; previous preterm birth; male babies; short inter-pregnancy interval; smoking; maternal infections; nutrient deficiency; pregnancy complications such as pre-eclampsia and gestational diabetes and maternal health conditions such as diabetes, systemic lupus erythematous and polycystic ovarian syndrome. It is associated with a number of short-term complications for the baby, including respiratory distress, sepsis, neurological conditions and hearing and vision impairment. Longer term it is associated with poorer neurodevelopmental outcomes(42).

1.9.3 Low birth weight and small for gestational age

Low birth weight (LBW) babies are defined as those who are liveborn and weigh less than 2500g. It is further classified as very low birth weight (VLBW) (<1500g) and extremely low birth weight (ELBW) (<1000g) (46). LBW affects approximately 15-20% of births worldwide(47). Babies may be low birth weight because they are preterm (but an appropriate weight for their gestational age), because their growth is restricted in utero. Babies whose weight is below the 10^{th} percentile for their gestational age are

defined as small for gestational age (SGA) (48). Risk factors for LBW and SGA include extremes of maternal age; smoking; multiple pregnancy; pregnancy complications such as pre-eclampsia; maternal long-term conditions such as hypertension or hypertension; anaemia and infections. Complications of LBW and SGA include an increased risk of neonatal death, impaired neurodevelopment, and risk of long-term conditions for the child such as diabetes and cardiovascular disease(49).

1.10 Medications and pregnancy

Exclusion of pregnant women from clinical trials has meant that there is a lack of information for the safety of medications during pregnancy (50, 51). This, in addition to the legacy of incidents such as thalidomide (52), has led to a cautious approach to the use of medications in pregnancy. While some medications are known to be unsafe for the developing fetus, stopping medication during pregnancy could also harm the mother and baby. For instance, stopping anti-epileptics could result in seizures, and stopping psychiatric medications could increase the risk of self-harm or suicide, both major causes of indirect maternal mortality in the UK (53).

Observational studies provide valuable evidence about the risks and benefits to medication use in pregnancy without having to overcome the ethical barriers that preclude interventional studies in this population.

1.11 Pharmacological Management of Migraine

Pharmacological therapy is often required in the management of migraine. For the management of pain and nausea during acute episodes, it is recommended that patients are offered triptans and simple analgesia (paracetamol or NSAIDs), and anti-emetics respectively. Depending on the frequency and severity of attacks, impact on quality of life and patient preference, prophylactic treatment may be offered to prevent attacks.

First line options include propranolol, topiramate, amitriptyline, candesartan, or pizotifen. Those requiring specialist treatment in secondary care may be offered flunarizine, botulinum toxin A, calcitonin gene-related peptide (CGRP) inhibitors or Gepants(1) (54).

1.12 Migraine Medications and Pregnancy

Medication use is common during pregnancy in women with migraine. A US study of a large (n=859,501), administrative database found that a third of women were prescribed multiple medication during pregnancy (55).

Despite this apparent need for pharmacological therapy, safety information for migraine drugs is generally lacking. Some drugs, such as the anti-epileptics sodium valproate and topiramate, are contra-indicated due to an increased risk of congenital anomalies (56-58). Caution has been advised with the use of CGRP inhibitors, relatively new medications for the management of migraine. CGRP is hypothesised to play a role in the maintenance of normal pregnancy (59) . CGRP blockade has found to cause an increase in systolic blood pressure and fetal mortality in pregnant animal models (60) (59). Although such risks have not been reported in humans exposed to CGRP inhibitors during pregnancy, further pharmacovigilance studies are required(61) (62).

Other drugs may be used with caution during pregnancy. It is recommended acute attacks be managed with pain relief (triptans, paracetamol and NSAIDs) and anti-emetics (prochlorperazine, cyclizine, domperidone, ondansetron and metoclopramide). Aspirin, propranolol and amitriptyline can be used for prophylaxis(5). This is despite there being a limited amount of evidence for their safety in pregnancy.

The most studied drug class in the migraine population is triptans, which act by selectively binding to serotonin receptors. This relieves pain by causing

vasoconstriction of the cranial arteries, blocking pain signals within the brain and inhibiting the release of vasoactive peptides in the trigeminal nerve (63).

A 2015 meta-analysis found no increase in the rate of major congenital malformations (MCMs) (OR 0.84 (95% CI 0.61-1.16), 3 studies) or preterm birth (OR 0.90 (95% CI 0.35-2.30), 3 studies) associated with triptans, but an increase in the rate of miscarriage compared to general population (OR 3.54 (95% CI 2.24-5.59), 2 studies) (64). A 2021 systematic review attempted to look at other migraine medications but was only able to perform meta-analyses for triptans. This confirmed the lack of association with MCMs (OR 1.07 (95% CI 0.83-1.39), 2 studies) and preterm birth (1.49 (95% CI 0.37-6.08), 2 studies) and found no association with low birth weight (LBW) (1.18 (95% CI 0.94-1.48)) (65).

Other medications have indications other than migraine and their impacts on pregnancy outcomes have been studied more generally in patients with conditions other than migraine.

Paracetamol appears to have no association with adverse pregnancy outcomes in humans (66) (although testicular abnormalities have been demonstrated in the male fetuses of pregnant rats exposed to paracetamol (67)), NSAIDs are associated with a potential risk of miscarriage if taken around conception(68). Due to a risk of premature closure of ductus arteriosus (69), NSAIDs are advised against in the third trimester (70-72).

Data are limited and conflicting for propranolol, but there is no strong evidence that beta blockers are associated with congenital anomalies, preterm delivery, LBW or miscarriage(73).

For amitriptyline, studies have reported an increased risk of miscarriage, but there is no robust evidence linking amitriptyline with congenital anomalies or small for gestational age (SGA). There is conflicting evidence for the risk of preterm delivery (74).

The burden of medication use in the pregnant migraine population is described in chapter 3

The literature is formally reviewed and described in chapter 4

The associations between migraine medications and miscarriage is described in chapter 5.

1.13 The MuM-PreDiCT project

As noted in the acknowledgement section of the thesis, the work in this thesis was, in part, funded by the Strategic Priority Fund "Tackling multimorbidity at scale" programme (grant numbers MR/V005243/1 and MR/W014432/1) delivered by the Medical Research Council and the National Institute for Health Research in partnership with the Economic and Social Research Council and in collaboration with the Engineering and Physical Sciences Research Council. The project, Multimorbidity in Pregnancy: Determinant, Consequences, Clusters and Trajectories (MuM-PreDiCT) is a collaborative of 8 universities examining the causes and consequences of multimorbidity in reproductive aged women. Alongside my PhD I have been part of the MuM-PreDiCT team. As this thesis focussed on a single condition, not multimorbidity, it was not a direct output of the MuM-PreDiCT project. However, I have been part of the team that developed codelists and Stata scripts for analyses undertaken in the MuM-PreDiCT project and I was able to use or adapt these for the work undertaken in this thesis. As mentioned in the acknowledgement section, I sought expert advice from clinicians, epidemiologists, statisticians, pharmacologists and PPI representatives in the

team around the design, analysis and interpretation of the results of the studies described.

1.14 Research hypothesis, aims and objectives

1. Research hypothesis

It is hypothesised that migraine and its associated treatments increase the risk of adverse pregnancy outcomes.

2. Research aim(s)

To describe the epidemiology of migraine in pregnancy, determine its associated outcomes, and assess the safety of migraine medication during pregnancy.

3. Research objectives

- To carry out epidemiological studies using the Clinical Practice Research Datalink (CPRD) Gold pregnancy register to describe the annual prevalence of migraine in pregnancy and the medications commonly prescribed amongst pregnant women with migraine between 2000 and 2018 (Chapter 3)
- To conduct an umbrella review of the literature comparing outcomes of pregnancy in i) women with and without migraine ii) women with migraine who are treated and untreated during pregnancy (Chapter 4)
- To describe the risk of adverse pregnancy outcomes, comparing i) women with and without migraine ii) women with migraine who are treated and untreated during pregnancy using the CPRD Gold pregnancy register and Hospital Episode Statistics (HES) maternity tail (Chapters 5 and 6)

Chapter 2 : General Methods

2.1 Chapter overview

This chapter outlines the rationale for the methods used in this thesis to address the research objectives. Routinely collected healthcare data was analysed for the studies comprising chapter 3, 5 and 6 of this thesis. I will start by outlining the rationale for using this type of data and describing the specific datasets used along with their strengths and limitations. I will then describe two of the specific methods used in chapters 4 and 5 respectively: umbrella review and nested case-control.

2.2 Justification for using routinely collected healthcare data for studies of migraine in pregnancy

Chapters 3, 5 and 6 describe the epidemiology of migraine in pregnancy, determine its associated outcomes, and assess the safety of migraine medication during pregnancy. A summary of alternative methods that could have been used is given below followed by a rationale for using routinely collected healthcare data.

2.2.1 Cross sectional surveys

Cross sectional surveys could have been utilised to address the thesis aims. This would have involved recruiting a nationally representative sample of women with a history of pregnancy and surveying them on migraine history, medication use and pregnancy outcomes. Advantages of this method are that it would potentially identify more cases of migraine as those who self-manage their condition without presenting the general practice would be captured. On the other hand, compared to objective diagnoses, self-reported medical history may be less reliable (75). Another advantage would be that more detailed information about medication use (for example over-the-counter medication taken, adherence and timings of medication use) may be obtained in comparison to using prescription data. However, patient recall of prescribed medication

taken can be variable (76). There may be recall bias if a woman has attributed an adverse pregnancy outcome to medications taken during her pregnancy.

Other limitations to this methodology include a likely smaller sample size, cost of conducting the survey and potential for responder bias, whereby having had a negative pregnancy experience may influence the likelihood of responding to a survey.

2.2.2 Prospective pregnancy cohorts

The thesis aims could be addressed by establishing a prospective cohort of women prior to, or during pregnancy. Information about migraine type, severity, symptoms and medication use could be collected at baseline and prospectively during pregnancy. These could be validated using objective measures such as the International Classification of Headache Disorders (ICHD) criteria(2) or using patient records (75). This type of study has the advantage of systematically collecting data from participants over a long period. However, this would be costly and time-consuming to conduct. An alternative would be to use mothers from an established birth cohort(77), but this would be reliant on relevant exposures and outcomes having been collected.

Birth cohorts also tend not to capture outcomes such as miscarriage, which was an important outcome studies in this thesis. This outcome has been previously studied prospectively using cohorts of pregnancy planners (78). However, as a third to a half of pregnancies are unplanned(79) (80) , these may not be representative of pregnant women generally.

2.2.3 Routinely collected healthcare data

Data from routinely collected electronic health records were chosen to address the aims of this thesis. The reasons for this include that they contain contemporaneous data and offer large sample sizes (relative to cross-sectional surveys and prospective cohorts).

They are relatively low-cost and can be rapidly conducted (81). The characteristics, strengths and limitations of the specific datasets are described in detail below.

2.3 Data sources used in this thesis

2.3.1 CPRD Gold Pregnancy Register: Overview, Strengths and Limitations

Electronic health records (EHRs) have been used in UK primary practice since the 1990s. The main software systems are EMIS Health, Vision and SystmOne (82). These systems are primarily used by clinicians during consultations with patients to record information about symptoms, diagnoses, investigations and prescriptions. However, they also provide a rich source of data for research.

The Clinical Practice Research Datalink (CPRD) is a service provided by the UK Medicines and Healthcare products Regulatory Agency (MHRA) as part of the Department of Health and Social care with support from the National Institute of Health Research (NIHR). They provide anonymised longitudinal EHR data to researchers from over 2,400 general practices using Vision or EMIS. This is presented as two separate databases, GOLD and Aurum respectively. Altogether, they include over 60 million patient lives of which 18 million are currently registered and active. Linkages are available to other datasets including, secondary care data and Office for National Statistics (ONS) death registrations (83). The two databases differ in several ways, including coverage (Aurum contains more patients, primarily from England, GOLD contains more practices in Wales and Scotland) and extent of linkage to other databases (HES and ONS linkage are only available for practices in England, so linkage is more complete for Aurum) (84). CPRD has been shown to be representative of the UK population, with patient demographics being comparable to the UK census in terms of age, sex and ethnicity, However, due to geographic variation in GP practice participation

in CPRD, the dataset may not be geographically representative (83). Data from CPRD GOLD were used in this thesis as, at the time of analysis, the pregnancy register was only available in GOLD.

Within this dataset, an algorithm has been developed by the CPRD team and the London School of Hygiene and Tropical Medicine to capture all documented pregnancies using over 4000 Read and entity codes. Read codes are a hierarchical clinical coding system used to document patient symptoms, diagnoses and referrals (85). From this, a pregnancy register has been established(86).

The strengths of the pregnancy register include its large size (over 1.5 million pregnancies meeting data quality standards). Many pregnancy cohorts are limited to pregnancies resulting in a birth, meaning that important outcomes such as miscarriages, terminations and ectopic pregnancies are missed. The CPRD GOLD pregnancy register was validated by the team that developed the algorithm. When comparing the register against secondary care records of deliveries, high concordance was found (8% of deliveries recorded in the register could not be found in HES, 9% of deliveries recorded in HES had no match in the pregnancy register) (86). Rates of miscarriage within the pregnancy register were similar to those found in other UK studies (87).

However, there are limitations to this dataset. Firstly, the median gestational age at first antenatal contact was 7.6 weeks, meaning early miscarriages might not be captured. For some pregnancies, it is not possible to distinguish between types of early pregnancy loss (meaning miscarriage, termination or ectopic pregnancy), meaning they were categorised as “unspecified loss” (86).

Another limitation of the pregnancy register is that by using all pregnancy data in CPRD GOLD, the algorithm has created a number of so-called “uncertain” pregnancy

episodes (88). Specifically, around 16% of pregnancies have no recorded outcome and around 8% of pregnancy episodes conflict with another pregnancy in the same woman. According to a paper by the team responsible for developing the pregnancy register, most overlapping episodes are likely to represent a true pregnancy. Often the reason for this overlap is that the general practitioner records an event from a previous pregnancy (eg previous caesarean section) during a consultation which results in the algorithm creating a second pregnancy episode. Other reasons include two pregnancies occurring close together having been combined or one pregnancy being split into two episodes due to the late recording of an outcome. The paper suggests that women with a history of pregnancy complications or more complex pregnancies are more likely to result in uncertain pregnancy episodes, so excluding all these pregnancies may result in an unrepresentative cohort(88). How uncertain pregnancy episodes were handled is described in chapter 5 of this thesis.

A final limitation is that, as many as 47% of women access pregnancy care directly through midwifery services (89) meaning they will not have an initial booking appointment with their GP and, if they do not attend for any consultations with their GP during the antenatal period, their pregnancy may go unrecorded in the primary care system. While pregnancy information should be fed back to the GP, this may not always get recorded in the coded data, meaning that not all pregnancies are captured in the pregnancy register (88). It could be that lower risk women, who do not need to attend their GP for pregnancy-related presentations or management of other conditions, are more likely to be missed. This therefore affect how representative the dataset is of pregnancies in the UK.

2.3.2 Hospital Episode Statistics (HES) Admitted Patient Care & HES maternity tail

Data are collected on all admissions to National Health Service (NHS) hospitals in England and form the Hospital Episode Statistics Admitted Patient Care (HES APC) dataset. An estimated 98-99% of all hospital activity is funded by the NHS, meaning the majority of hospital admissions will be captured. The primary purpose of this data collection is to inform the planning and management of services and to form the basis of the pay-for-performance (Payment by Results (PbR)) system of secondary care imbursement(90). However, HES APC is also a valuable resource for research and service evaluation due to its longitudinal nature and almost universal coverage.

Specific to maternal health research, delivery episodes are generated in mother's record following a birth event. These episodes include a "maternity tail" which includes information about obstetric outcomes. This is based on information entered via local maternity databases (90). As the vast majority of births take place in NHS hospitals (97.5% in 2019) (91), this is a highly representative cohort. The maternity tail contains valuable information not available in primary care records such as method of onset of labour, live and still birth, length of gestation and birth weight(90) making it useful for epidemiological research on a population scale(92). However, there are issues to consider when using HES maternity data. Namely, the data do not form part of a mandatory return, meaning that completeness and data quality vary between trusts(90). For the analysis in chapter 6 of this thesis, missing of birthweight and gestational age was a particular limitation. How this was handled is described in more detail in chapter 6.

Linkage of CPRD primary care data with HES data is available for English practices that have provided consent to participate in a linkage scheme. Linkage is carried out

externally to CPRD by NHS England who link primary care records with hospital records using personal identifiers (NHS number, gender, date of birth and postcode). NHS England then remove these identifiers and provide CPRD with pseudonymised patient IDs that allow linkage between datasets without allowing individual patients to be identified (93).

2.4 Justification for specific methodologies used in this thesis

2.4.1 Umbrella review

A large number of systematic reviews are published every year(94), which means there are often several reviews on the same topic, which can be of varying quality. This can create a challenge for clinicians and policymakers using these sources of evidence to inform their decisions. Umbrella reviews are a way of addressing this by synthesising all existing systemic reviews on a broad topic into one document(94). This was the rationale for conducting an umbrella review as part of this thesis. A scoping review found that several reviews had been conducted on the topic of migraine and pregnancy outcomes, but not all of these had been carried out in line with established systematic methodology. In addition, reviews tended to be focussed on either migraine or drugs as an exposure or specific types pregnancy complications as an outcome meaning an overarching review would be a useful addition to the literature.

Some elements are of umbrella review methodology are shared with systematic review methods. A reproducible, systematic search of the literature is performed, reviews are selected based on a pre-defined inclusion criteria, these are critically appraised, and data are extracted and synthesised from them (94).

Two key additional challenges to conducting umbrella reviews include handling overlapping systematic reviews and the inclusion of out-of-date systematic reviews.

Reviews are considered to overlap if they evaluate the same outcomes and include the same primary studies. Overlap can be assessed graphically using a citation matrix which maps systematic reviews against primary studies. Overlap can then be quantified using corrected cover area, and rated as slight (0-5), moderate (6-10), high (11-15) and very high (>15). If there is high or very high overlap, one study is selected for inclusion. Previous studies have used the following criteria for determining which study is included: quality rating, year of publication, whether meta-analyses are reported and the number of participants(95). This method was followed in the umbrella review chapter of this thesis

Eligible reviews may also be out of date, meaning that newly published primary studies may change their results. In this case, the review can be updated, which avoids duplicating the whole systematic review process from the start. An established framework was used in this thesis to determine whether systematic reviews were eligible for update. These criteria were: i) the key search terms from the review's search strategy identified new studies which met the review inclusion criteria, ii) the findings of the new studies would have potentially changed the conclusion of the review, iii) reviews must be of high or moderate quality(96). One systematic review was updated as part of the umbrella review chapter of this thesis.

2.4.2 Rationale for using nested case-control for pharmacoepidemiology study

Chapter 5 of this thesis reports the results of a nested-case control study examining the association between drugs for the treatment of migraine and miscarriage. A rationale for using this study design is given below.

2.4.3 Other study designs considered

Prospective cohort studies are often used to examine the association between exposures and outcomes. A potential design for this study would have been to select cases of women with migraine in pregnancy who were exposed to the medications of interest, match them to women who were not exposed and compare the risk of miscarriage. However, this would have resulted in time-window bias (97), whereby those women who did not have a miscarriage, and therefore had a gestation of 24 weeks or longer (assuming terminations were excluded from the analysis), would have a longer time window during which to be exposed to the medications of interest. This could potentially move the effect estimate towards the null. Figure 2.1 illustrates this concept.

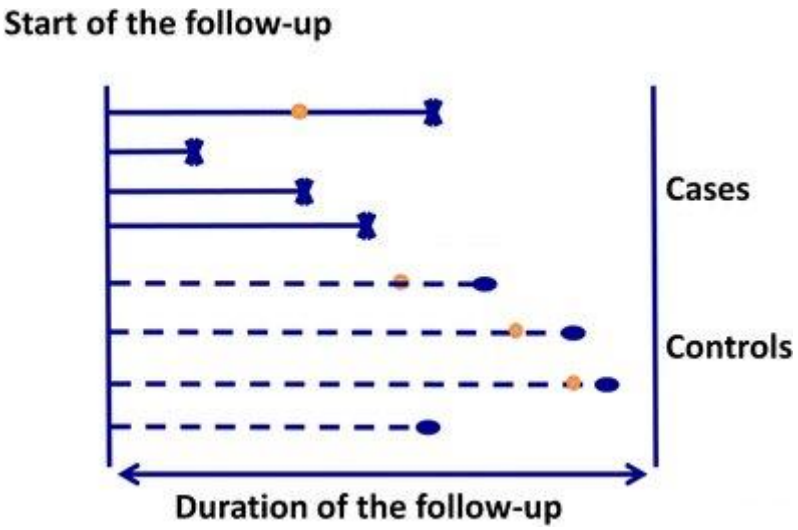


Figure 2.1 Time window bias.

The blue circles represent the end of follow up for those who did not have the outcomes of interest (controls). The blue crosses represent the outcome of interest (cases). The orange circles represent the exposure. The follow up time was longer in the controls, resulting in a higher likelihood of having the exposure. (Di Martino M, Kirchmayer U, Agabiti N, et al The impact of time-window bias on the assessment of the long-term

effect of medication adherence: the case of secondary prevention after myocardial infarction BMJ Open 2015;5:e007866. doi: 10.1136/bmjopen-2015-007866)

An alternative study design would have been a survival analysis comparing those exposed and unexposed to the drugs of interest. This has been used in previous studies examining miscarriage as an outcome (98). However, these have tended to be studying exposures that are present from the start of pregnancy, such as age or use of assisted reproductive technology, and are, therefore, not suitable for exposures occurring during pregnancy.

2.4.4 Nested case-control study design

For the nested case-control study, cases of pregnancies of women with migraine ending in miscarriage were matched to 2 pregnancies of women with migraine that did not end in miscarriage. For the cases, the index date for the study was the date of miscarriage. For the controls, a pseudo-index date was assigned, which corresponded to the gestational age at which the matched case's miscarriage occurred (figure 2.2). Cases and controls were followed up from the start of pregnancy to the index date or pseudo-index date, ensuring that the time-window for exposure was equal between the two. This method has been used in previous studies of drug exposures and miscarriage(99, 100).

There were limitations to using retrospective data from electronic health records for the pharmacoepidemiology study. In particular, prescription records were used to determine exposure to medications, which do not give an indication of whether or when medication was taken. This is especially relevant for medications taken episodically to control symptoms, such as triptans and NSAIDs. This potential impact of this is discussed further in chapter 5.

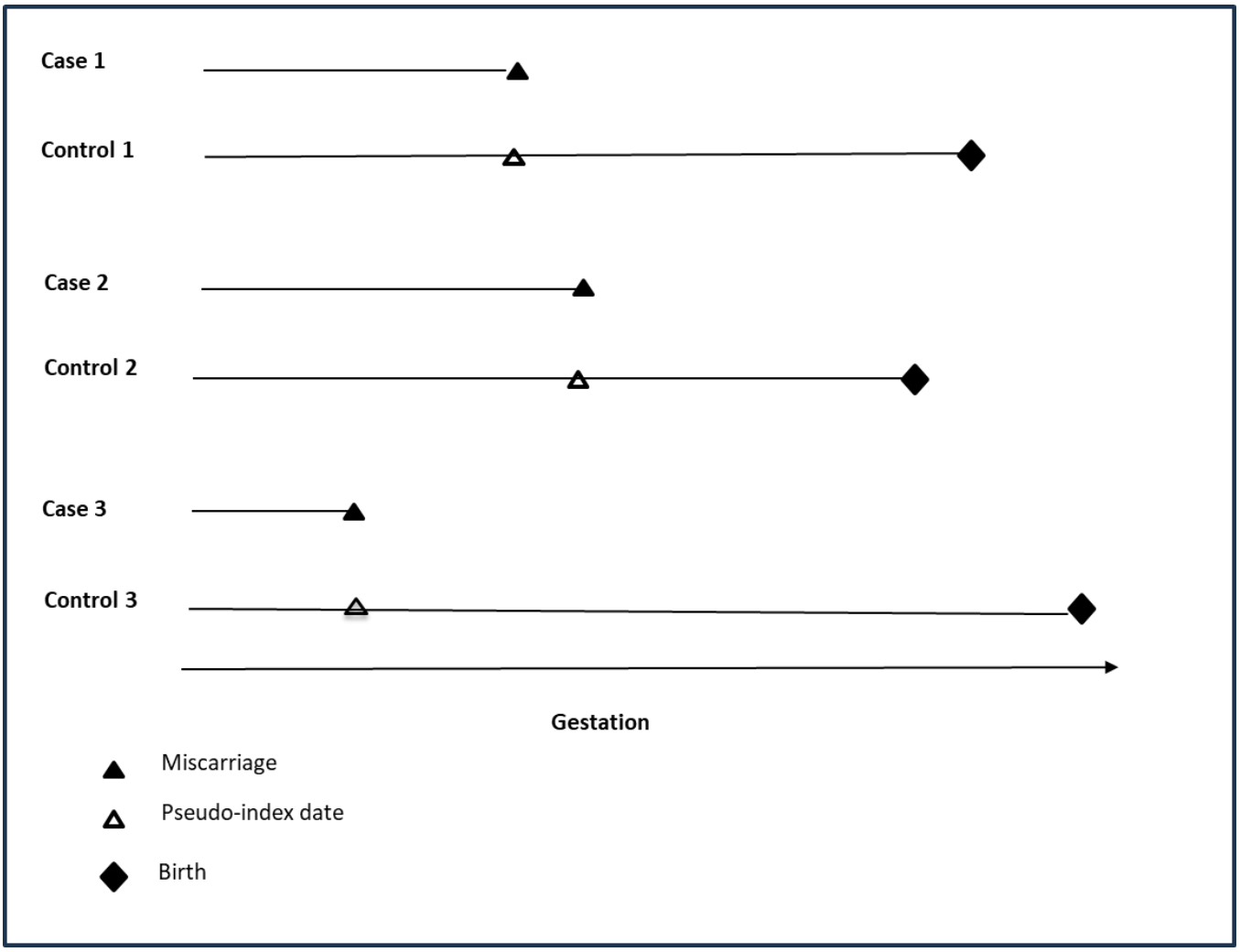


Figure 2.2: Nested case-control

Cases were pregnancies ending in miscarriage and controls were pregnancies not ending in miscarriage. The black triangle represents the date of miscarriage, and the white triangle represents the assigned pseudo-index date for the control pregnancy. This ensures equal follow up time for cases and controls.

2.5 General Statistical Methods

Details of the statistical methods used in the individual studies reported in this thesis are described in the results chapters (Chapters 3, 5 & 6). A study protocol was developed a priori for the analyses conducted in this thesis and was approved by the Independent

Scientific Advisory Committee for CPRD (reference: 22_001790). General statistical methods are described below.

CPRD pregnancy register was the source for timings and outcomes of pregnancy recorded in primary care for chapter 3 and 5, HES maternity tail and HES APC diagnoses and procedures were the source of timings and outcomes of pregnancy in chapter 6. Pregnancies contributed to the studies if their start date was between 1st January 2000 and 31st December 2019. Follow up data were available for the year following the study end date (2020) to allow for all pregnancies to reach completion and have an outcome recorded.

Demographic, lifestyle, diagnostic and prescription variables were obtained from CPRD GOLD and extraction was facilitated using data extraction for epidemiological research (DExtER). This is a novel software programme developed by the Health Informatics team at the University of Birmingham which aids with the extraction and processing of primary care electronic health record databases for research (101). Files containing patient demographic data, practice administrative data, consultation and clinical history, test results, referrals, immunisations and prescription data are supplied to the University of Birmingham by CPRD (83). DExtER employs a process known as Extract, Transform, Load (ETL) to extract the subset of data required for the research question, transform the data into a clean, standardised format and then load the data into a research-ready file format. This allows users without expertise in software programming to efficiently obtain data for research (101).

For chapters 5 and 6, matched cohorts of women with and without migraine were created using exact matching for maternal age (± 1 year) and year of pregnancy. Regression models (logistic and log binomial) were used to determine the association

between exposures and outcomes. In all models, pregnancies were the unit of analysis. As the same woman could have multiple pregnancies, statistical inference from the regression models was based on cluster-robust standard errors to account for similarities of outcomes within a woman.

All analyses were performed in Stata IC version 15 (StataCorp).

Chapter 3 : Trends in the prevalence and pharmacological management of migraine during pregnancy in the UK 2000-2018

The published manuscript of the study described in this chapter was adapted for this thesis and is presented as follows.

Published manuscript:

Phillips K, Nirantharakumar K, Wakerley BR, Crowe FL. Trends in the prevalence and pharmacological management of migraine during pregnancy in the UK, 2000–2018. Journal of Neurology, Neurosurgery & Psychiatry 2024;:jnnp-2024-33353.

Personal contribution:

- Compiled lists of Read codes and drug codes for Clinical Practice Research Datalink (CPRD)
- Developed disease phenomes with co-authors
- Applied for data access from CPRD
- Conducted analysis
- Wrote initial draft of manuscript, submitted for publication and addressed reviewers' comments

Title: Trends in the prevalence and pharmacological management of migraine during pregnancy in the UK 2000-2018

Katherine Phillips MPH1, Krishnarajah Nirantharakumar MD1,2, Benjamin R Wakerley PhD3,4*, Francesca L Crowe PhD1*

* Joint senior authors

1 Institute of Applied Health Research, University of Birmingham, Birmingham

2 Midlands Health Data Research UK, University of Birmingham, Birmingham

3 Institute of Metabolism and Systems Research, University of Birmingham, Birmingham

4 University Hospital Birmingham, Birmingham, UK

Corresponding author:

Francesca L Crowe

Lecturer Epidemiology and Health Informatics

Institute of Applied Health Research

University of Birmingham, Birmingham

Email: F.Crowe@bham.ac.uk

3.1 Abstract

3.1.1 Background

Migraine is common in women of reproductive age. This study aimed to i) describe the prevalence of migraine in pregnant women in the UK ii) identify drugs commonly prescribed for migraine during pregnancy and iii) identify characteristics associated with being prescribed medication for migraine during pregnancy.

3.1.2 Methods

The CPRD pregnancy register, a database of pregnancy episodes identified in anonymised primary care health records, was used.

Crude and age-standardised prevalence of migraine during pregnancy and the proportion of women with migraine prescribed drugs used for migraine management was calculated for each year between 2000 and 2018.

Logistic regression was used to describe the relationship between patient characteristics and being prescribed migraine medication during pregnancy.

3.1.3 Results

1,377,053 pregnancies were included, of which 187,328 were in women with a history of migraine. The age-adjusted prevalence increased from 11.4% in 2000 to 17.2% in 2018. There was an increase in the rates of prescription for numerous medications for the management of migraine.

Older women (aOR 1.41(1.20-1.66)), women of Black (aOR 1.40(1.32-1.48) and South Asian Ethnicity (aOR 1.4 (1.38-1.59)), those living in the most deprived areas (aOR 1.60 (1.54-1.66)), women who were obese (aOR 1.39(1.35-1.43)), smokers (aOR

1.15(1.12-1.18)) and those with comorbid conditions were more likely to receive a prescription during pregnancy.

3.1.4 Conclusions

Rates of recorded migraine have increased over the past two decades as well as rates of prescribing in women with migraine. Higher prescribing rates are seen in certain groups, which has the potential to exacerbate health inequalities.

3.2 Background

Global rates of migraine are thought to have remained stable over time (102), particularly in high income countries (103), with prevalence peaking in those aged 35-39 years (7). As the average maternal age is increasing in high income countries (104), it is likely that the burden of migraine during pregnancy is also increasing. As discussed in the introductory chapter (section 1.8), there is evidence that migraine increases the risk of pregnancy complications (105, 106) so it is important to understand the burden of migraine during pregnancy.

Although, as previously outlined in section 1.11, migraine often requires pharmacological therapy to both manage and prevent episodes (5) and medication use has been found to be common during pregnancy in women with migraine , there is a paucity of evidence around the safety of some migraine drugs in pregnancy (65). Understanding which medications are most commonly prescribed for migraine during pregnancy will help direct priorities for future drug safety studies.

The aims of this study were i) to estimate the annual prevalence of migraine diagnosed preconception in pregnant women between 2000 and 2018 in the UK; ii) to identify commonly prescribed drugs among pregnant women with migraine during the first trimester and throughout the whole pregnancy; and iii) to describe the characteristics associated with being prescribed medication in the treatment of migraine during pregnancy. This chapter addresses Research Objective 1:. To carry out epidemiological studies using the Clinical Practice Research Datalink (CPRD) Gold pregnancy register to describe the annual prevalence of migraine in pregnancy and the medications commonly prescribed amongst pregnant women with migraine between 2000 and 2018.

3.3 Methods

3.3.1 Study Design

A pregnancy cohort study of women with migraine was conducted to estimate annual point prevalence estimates of migraine and to identify common prescription drugs for migraine during pregnancy.

3.3.2 Data source

The Clinical Practice Research Datalink (CPRD) GOLD is a UK primary care database containing the anonymised medical records of over 20 million patients. It covers approximately 7% of the UK population and is comparable in terms of age and sex to the general population. Symptoms, diagnoses and referrals are documented in CPRD GOLD using Read codes, a hierarchical clinical coding system, used to document symptoms, diagnoses and referrals. Prescriptions issued in primary care are recorded using drug codes An algorithm has been developed and validated within CPRD GOLD to create a pregnancy register using pregnancy related Read codes. CPRD GOLD was the data source for patient demographics, diagnoses and prescriptions. The CPRD GOLD pregnancy register was the data source for pregnancy start and end dates and timings of trimesters.

3.3.3 Definition of Study Population

All women aged between 15 and 50 years in the CPRD GOLD pregnancy register with pregnancies that occurred between 2000 and 2018 formed the source population. Eligibility to enter the study began when participants fulfilled the following criteria: i) acceptable patient flag, ii) minimum 1 year of registration with a practice or 1 year after up-to-standard date of the registered practice whichever was the latest date. All eligible

women in the CPRD pregnancy register were included in the denominator for the estimation of prevalence trends for migraine.

For the study of prescribing trends and outcomes recorded in primary care, the study population was all eligible women from the pregnancy cohort who also had a coded diagnosis of migraine or a prescription for medications used exclusively in the treatment of migraine prior to their pregnancy start date.

3.3.4 Definition of variables

The exposure was the presence of a coded diagnosis of migraine or a prescription for medications used exclusively in the treatment of migraine (triptans, calcitonin gene-related peptide inhibitors and Migraine combination drugs (acetylsalicylic acid or paracetamol, combined with codeine, caffeine and/or an antiemetic)) prior to their pregnancy start date.

To describe trends in prescribing patterns, the presence of a code for the prescription of the following drugs used in the treatment of migraine were used:

- Amitriptyline
- Acetylsalicylic acid
- Antiemetics (Prochlorperazine, Metoclopramide, Domperidone, Cyclizine)
- Beta blockers
- Calcitonin gene-related peptide inhibitors
- Candesartan
- Duloxetine
- Flunarizine

- Migraine combination drugs
- Mirtazapine
- Non-steroidal anti-inflammatory drugs (NSAIDs) (Diclofenac, Ibuprofen, Naproxen, Tolfenamic acid, Mefenamic acid)
- Paracetamol
- Pizotifen
- Sodium valproate
- Topiramate
- Triptans
- Venlafaxine

Codelists used to define diagnoses and prescriptions are included in supplementary table 3.1.

3.3.5 Statistical Analysis

Estimation of prevalence and incidence trends:

Annual prevalence of migraine before pregnancy was calculated for each year between 2000 and 2018 by dividing the number of women meeting the migraine exposure definition whose pregnancy started within the given year by the total number of pregnancies that started within the year.

Age standardised prevalence was calculated using the direct method. Prevalence rates for each year were applied to the European Standard Population 2013 (ESP2013)(107).

Analysis of Prescription Trends

For each annual cohort, the number of women with a recorded prescription for a drug used in the treatment of migraine during pregnancy was divided by the total number of pregnancies of women with migraine that started within that year. This was stratified by acute drugs (pain relief, antiemetics, combinations, triptans) and prophylactic drugs (beta blockers, topiramate, amitriptyline, candesartan, sodium valproate, flunarizine, pizotifen, calcitonin gene-related peptide inhibitors). This analysis was performed for prescriptions given over the whole pregnancy and restricting to those given in the first trimester.

Analysis of characteristics associated with receiving a prescription

Logistic regression was used to estimate odds ratios, adjusted odds ratios and 95% confidence intervals to describe the relationship between patient characteristics (age, ethnicity, deprivation, BMI, smoking status and comorbidities (asthma, chronic kidney disease (CKD) depression, endometriosis, hypertension, hyperthyroidism, hypothyroidism, inflammatory bowel disease (IBD), polycystic ovarian syndrome (PCOS), systemic lupus erythematous (SLE), Type 1 diabetes, Type 2 diabetes and epilepsy)) and being prescribed any medication used in the management of migraine during pregnancy.

All analysis was performed in Stata IC version 17 (StataCorp).

3.4 Results

3.4.1 Prevalence of migraine before pregnancy

There were 1,377,053 pregnancies including 769,024 women in the CPRD pregnancy register that met the data quality criteria. 187,328 pregnancies and 98,932 women had

either a coded diagnosis of migraine or had been issued a prescription for drugs used exclusively in the management of migraine prior to pregnancy.

The median age at the start of pregnancy for women both with and without migraine was 28.9 years. A slightly higher proportion of pregnancies in women with migraine were in women who were white (48.1% v 45.0%) and a slightly higher proportion of pregnancies in women without migraine were in women who had no ethnicity recorded (47.0% v 44.3%). A higher proportion of pregnancies in women with migraine were in women who were overweight or obese (21.9% v 19.5%, 18.0% v 13.4% respectively) (Table 3.1).

The overall crude prevalence of migraine in the cohort was 13.7% (95% CI 13.6-13.8). The prevalence increased from 11.5% (95% CI 11.2%-11.8%) in 2000 to 17.1% (95% CI 16.7%-17.5%) in 2018 (Figure 3.1 and Supplementary Table 3.2)**.** The age-adjusted prevalence increased from 11.4% (95% CI 10.3%-12.4%) in 2000 to 17.2% (95% CI 16.2%-18.2%) in 2018 (Figure 3.2 and Supplementary Table 3.3).

3.4.2 Acute medications

Between 2000 and 2018, the proportion of pregnant women prescribed triptans increased from 2.27% (n=108) to 3.74% (n=256) throughout pregnancy and from 2.04% (n=97) to 3.39% (n=232) in the first trimester. Over the same time, the proportion prescribed paracetamol decreased from 6.58% (n=313) to 2.60% (n=178) throughout pregnancy and from 3.19% (n=152) and 1.58% (n=108) in the first trimester. Prescriptions of opiates (co-codamol, codeine and tramadol) increased before plateauing around 2014 (figure 3.3 and supplementary figure 3.1).

3.4.3 Anti-emetics

Between 2000 and 2019, the proportion of pregnant women prescribed cyclizine increased from 0.57% (n=27) to 10.95% (n=750) throughout pregnancy and from 0.48% (n=23) to 8.99% (n=616) in the first trimester. The proportion prescribed prochlorperazine increased from 1.91% (n=91) to 4.45% (n=305) throughout pregnancy and from 1.39% (n=66) to 3.43% (n=235) in the first trimester. Prescription of metoclopramide, migraine combination drugs and domperidone remained stable over the time period (figure 3.4 and supplementary figure 3.2).

3.4.4 Prophylactic medications

Throughout pregnancy, rates of prescriptions for amitriptyline, mirtazapine, venlafaxine and duloxetine increased from 0.90% (n=43) to 1.97% (n=135), 0.06% (n=3) to 1.43% (n=98), 0.40% (n=19) to 0.92% (n=63) and 0% to 0.63% (n=43), respectively. In the first trimester, rates of prescriptions for amitriptyline, mirtazapine, venlafaxine and duloxetine increased from 0.74% (n=35) to 1.81% (n=124), 0.06% (n=3) to 1.33% (n=91), 0.40% (n=19) to 0.88% (n=60) and 0% (n=0) to 0.55% (n=38), respectively. The prescription rates of beta blockers increased from 0.57% (n=27) to 1.18% (n=81) throughout pregnancy and 0.53% (n=25) to 1.14% (n=78) (figure 3.5 and supplementary figure 3.3).

3.4.5 Characteristics associated with receiving a prescription

Women aged 45-49 years were at significantly higher odds of being prescribed drugs used in migraine (aOR 1.41(95% CI 1.20-1.66)) compared to those aged 25-29, whereas those aged 15-19 were at significantly lower odds (aOR 0.86 (95% CI 0.82-0.90)).

Compared to women of white ethnicity, women of Black ethnicity and South Asian ethnicity were at significantly higher odds of being prescribed drugs used in migraine (aOR 1.40 (95% CI 1.32-1.48) and 1.48 (95% CI 1.38-1.59), respectively).

Compared to women living in the least deprived areas, women in the most deprived areas were at significantly higher odds of receiving a prescription (aOR 1.60 (95% CI 1.54-1.66)). Compared to women with a record of normal pre-gravid BMI, women who were overweight of obese were at significantly higher odds of receiving a prescription (aOR 1.12 (95% CI 1.09-1.16) and 1.39 (95% CI 1.35-1.43)). Compared to non-smokers, women who smoked were at higher odds of being prescribed medications used in migraine (aOR 1.15 (95% CI 1.12-1.18)).

Women with asthma, depression, endometriosis, hypertension, hyperthyroidism, hypothyroidism, inflammatory bowel disease, PCOS, SLE, Type 1 diabetes and epilepsy were also at significantly increased odds of receiving a prescription (figure 3.6).

3.5 Discussion

3.5.1 Key results

The recorded prevalence of preconception migraine increased between 2000 and 2018. There was an increase in the rates of prescription for numerous medications for the management of migraine, notably, triptans, antidepressants (including amitriptyline) and beta blockers. Older women, women of Black and South Asian Ethnicity, those living in the most deprived areas, women who were overweight or obese, smokers and those with comorbid conditions were more likely to receive a prescription during pregnancy.

3.5.2 Strengths and limitations

There are several strengths to this study, including that the cohort came from a large dataset that is generalisable to the UK population. To our knowledge, this is the first

such study to describe trends in the prevalence of migraine and migraine medications during pregnancy. The high prevalence of migraine during pregnancy highlights the importance of understanding how migraine and its associated treatments impact pregnancy outcomes.

The limitations of this study include the likelihood that migraine is unrecorded in primary care as not all cases of migraine will require medical input. As discussed below, the prevalence of migraine found was lower than would be expected in women of reproductive age(23). We attempted to improve the accuracy of our prevalence estimate by including medications used exclusively to manage migraine in our phenome definition. Despite this, the prevalence is likely affected by under-reporting. As trends in migraine are thought to have remained stable over time, it is possible that this particularly effected the earlier years and that recording of migraine has improved over time.

A limitation of using prescription data is that it is unknown whether medications were taken. Medications that can be purchased over the counter would also not have been captured, which would have led to the undercounting of medications such as paracetamol. We cannot be certain of the indication for the medications studied. Many of the medications considered are also used to manage conditions other than migraine. For instance, duloxetine, mirtazapine, and venlafaxine may be used for depression; topiramate and valproate may be used for epilepsy; and beta-blockers and candesartan may be used for hypertension. This may account for the significant increase in the odds of being prescribed medications associated with these conditions.

3.5.3 Findings in the context of other literature

The preconception prevalence of migraine in 2018 is similar to the prevalence found in a Global Burden of Disease (GBD) study in 2019 (18.6% in females aged 20-64) (23), although the overall prevalence for the time period included in this study is lower. The prevalence estimates from studies included in the GBD meta-analysis came from questionnaires or interviews. As many patients with migraine will self-manage and not need to consult with their GP, this may explain the apparent undercount in this study.

The overall prescription rate for triptans during the whole of pregnancy within women with a preconception diagnosis of migraine was 2.7%. This was lower than the prevalence of 25% found in a Norwegian study, although that study cohort composed of those already taking triptans prior to pregnancy (108). When considering women who had been prescribed triptan in the year before pregnancy, however, 16% of women with a preconception diagnosis of migraine in our cohort received a prescription for triptans during pregnancy.

The prevalence for prescriptions of triptans in this study was 2.5% for the first trimester. This was lower than the rate found in US cohort (15.1%) (109). However, that study employed a much stricter criteria for defining migraine, meaning that the prevalence in that study was only about 1%. This is likely to represent the most severe cases.

The increase in the prevalence of antidepressant prescription is in line previous reports (110). To our knowledge, this has not been described in the migraine population specifically.

A Canadian study found an increase in the prescription of labetalol (likely to reflect prescribing for pregnancy-induced hypertension) but a decline in the prescription of other beta blockers(111).

This study is in keeping with the findings of a study of rates of polypharmacy during pregnancy in the same population. That study found being older, overweight and obese, of Black and South Asian ethnicity and smoking were all risk factors for polypharmacy (112). Our study found that having comorbidities was associated with increased rates of prescribing. This is in agreement with the findings of a US study of a health insurance database looking at medication use throughout pregnancy in around 8,000 women with migraine, which found complex comorbidity was also associated with a higher prescription rate (109).

3.5.4 Interpretation

The trends reported are unlikely to be due to changes in diagnostic criteria or changes in medication use over the time period. Whilst International Classification of Headache Disorders underwent an update in 2004, this made no difference to the diagnostic criteria for the two main migraine subtypes (migraine with and without aura) (113). Likewise, throughout the time period studied there was little change in the drugs available for the treatment of migraine, with newer drugs that target CGRP having been introduced over the past few years and only for use in secondary care(114).The increase in the prevalence of migraine seen in this study might reflect a true increase in prevalence or an increase in the number of women accessing general practice for management of migraine. The increase in prescription rates may therefore partly reflect an increase in the need for migraine treatment and guidance becoming less precautionary around prescribing certain medications during pregnancy. NICE guidance has advised that triptans can be considered in the management of migraine during pregnancy since 2012 (115). Amitriptyline and beta blockers are thought to be safe at low doses and have been recommended in pregnancy. On the other hand, guidance for the use of NSAIDs during pregnancy has become more precautionary over this time

period. In 2002, the British Society of Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) advised that NSAIDs were considered safe in the first trimester, but in 2016 advised that they be used with caution. Due to concerns that NSAIDs were associated with premature closure of the ductus arteriosus, it has recently been advised that they should not be taken after 20 weeks of pregnancy (having previously been thought to be safe until 32 weeks) (70) (71) (72). Despite this, an increase in the prevalence of prescribing was seen over the study time period.

If, over time, women have been encouraged to book early with their GP or maternity services to ensure antenatal care is commenced in a timely way (116) (117), this would increase the number of women seeking care earlier in pregnancy when pregnancy symptoms, such as nausea and vomiting, or migraine episodes are more likely (26). This may have contributed to the increasing trends in prescriptions for anti-emetics and pain relief.

Prescriptions were found to be more likely in women who are already at higher risk of adverse outcomes. Women aged 45-49 were at a 40% increased risk of being prescribed medications. Advanced maternal age is associated with an increased risk of fetal growth restriction, preeclampsia, placental abruption, preterm birth and still birth(118). In England, being of Black or South Asian ethnicity or living in a socio-economically deprived area has been found to be associated with increased risk of stillbirth, preterm births and births with fetal growth restriction(119). Women with obesity and comorbidities in addition to migraine had higher rates of prescription. Maternal obesity is associated with gestational diabetes, preeclampsia, preterm birth and large for gestational age babies (weight >90th centile for gestational age)(120) and pre-pregnancy multimorbidity is also associated with increased rates of maternal morbidity and

mortality(121). Any harms associated with these medications will therefore contribute to the risk of adverse outcomes in these groups.

3.5.5 Implications for research and practice

Migraine is commonly classified as being with and without aura (2). As those with aura have been found to have a higher risk of stroke (17), it may be important to understand the burden of migraine with aura during pregnancy. This was explored in this dataset, but only a small proportion of the population (~3.5%) had aura status recorded.

Apart from for triptans, there is a paucity of evidence around the safety of migraine drugs during pregnancy (65) (64). Due to the exclusion of pregnant women from most clinical trials, much of the existing evidence for the effect of medication use during pregnancy comes from observational studies. The inherent limitations and biases of these studies can mean it is difficult for clinicians and women to make decisions around medication use in pregnancy. This study highlights the increasing burden of pharmacological therapies in women with migraine during pregnancy and therefore the urgent need for further research into drug safety in pregnancy. As the most commonly prescribed medications included triptans, antidepressants (including amitriptyline) and beta blockers, the association between exposure to these medications and risk of miscarriage was taken forward for investigation in chapter 5. Pregnant women have been historically excluded from clinical trials. More recently there have been calls for their inclusion (122). This study provides further justification of the need for this.

The increasing trend in medication use during pregnancy in women with migraine also raises concerns about medication overuse headache. The prevalence of this condition during pregnancy and impact on pregnancy outcomes are not well understood and warrant further study (123).

3.6 Conclusion

The recorded prevalence of migraine prior to pregnancy has increased over the last two decades, as has the rate of prescribing in pregnant women with migraine. Certain groups are at higher risk of being prescribed medication, meaning any adverse effects could exacerbate health inequalities.

Ethics statements

Ethical Approval

CPRD has ethics approval from the Health Research Authority to support research using anonymised patient data. The study has been approved by the Independent Scientific Advisory Committee for CPRD (reference: 22_001790)

Data availability statement

The data that support the findings of this study are available from CPRD but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Funding

This study was not specifically funded but was supported by the MuMPreDiCT consortium which is funded by the Strategic Priority Fund “Tackling multimorbidity at scale” programme (grant number MR/W014432/1) delivered by the Medical Research Council and the National Institute for Health Research in partnership with the Economic and Social Research Council and in collaboration with the Engineering and Physical Sciences Research Council.

This work was also supported by Health Data Research UK (HDRUK2023.0030), which is funded by UK Research and Innovation, the Medical Research Council, the

British Heart Foundation, Cancer Research UK, the National Institute for Health and Care Research, the Economic and Social Research Council, the Engineering and Physical Sciences Research Council, Health and Care Research Wales, Health and Social Care Research and Development Division (Public Health Agency, Northern Ireland), Chief Scientist Office of the Scottish Government Health and Social Care Directorates.

Dissemination to participants and related patient and public communities: We plan to disseminate these research findings to relevant stakeholders by presenting our findings at relevant conferences, through our PPI channels and by engaging with the media through press releases.

Contributors: KP, KN, FC and BW conceived the study, designed the initial analysis and defined definitions for exposures, covariates and outcomes. KP undertook the analysis and all authors contributed to interpretation of an improvements to the analysis. KP drafted the manuscript and led the revision process. All authors critically reviewed the manuscript, approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Competing Interests:

All authors have completed the Unified Competing Interest form (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

The Corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study

have been omitted; and that any discrepancies from the study as originally planned have been explained.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ editions and any other BMJPGL products and sublicences such use and exploit all subsidiary rights, as set out in our licence."

Table 3.1: Baseline characteristics

	Pregnancies of women with migraine	**Pregnancies of women without migraine**
Number of pregnancies, n	187,328	1,189,725
Number of women, n	98,932	670,092
Age at start of pregnancy, median (IQR)	28.9 (24.2-33.2)	28.9 (23.8-33.2)
Age categories, number of pregnancies (percentage of pregnancies)		
15-19 years	15,005 (8.0)	138,245 (11.6)
20-24 years	38,306 (20.5)	231,699 (19.5)
25-29 years	53,059 (28.3)	304,102 (25.6)

30-34 years	48,681 (26.0)	308,110 (25.9)
35-39 years	25,362 (13.5)	165,741 (13.9)
40-44 years	6,211 (3.3)	38,284 (3.2)
45-49 years	704 (0.4)	3,544 (0.3)
Ethnicity, number of pregnancies (percentage of pregnancies)		
White	90,109 (48.1)	532,664 (45.0)
South Asian	4,328 (2.3)	34,511 (2.9)
Black	5,786 (3.1)	33,288 (2.8)
Mixed Ethnicity	856 (0.5)	7,504 (0.6)
Others	2,885 (1.5)	19,547 (1.6)
Missing	83,364 (44.3)	559,211 (47.0)
IMD, number of pregnancies (percentage of pregnancies)		
1 (Most deprived)	41,284 (22.0)	239,881 (20.2)
2	32,538 (17.4)	202,749 (17.0)
3	30,887 (16.5)	198,538 (16.7)
4	27,012 (14.4)	173,129 (14.6)
5 (Least deprived)	28,895 (15.4)	192,330 (16.2)

Missing	26,712 (14.3)	183,098 (15.4)
BMI (kg/m^2), number of pregnancies (percentage of pregnancies)		
Underweight (<18.5)	6,489 (3.5)	42,858 (3.6)
Normal weight (18.5-<25)	78,858 (42.1)	518,522 (43.6)
Overweight (25-<30)	41,109 (21.9)	232,171 (19.5)
Obese (≥30)	33,714 (18.0)	159,342 (13.4)
Missing	27,158 (14.5)	236,802 (19.9)
Smoking status, number of pregnancies (percentage of pregnancies)		
Non-smoker	97,305 (51.9)	626,159 (52.6)
Ex-smoker	29,013 (15.5)	161,622 (13.6)
Smoker	54,374 (29.0)	323,356 (27.2)
Missing	6,636 (3.5)	78,587 (6.6)

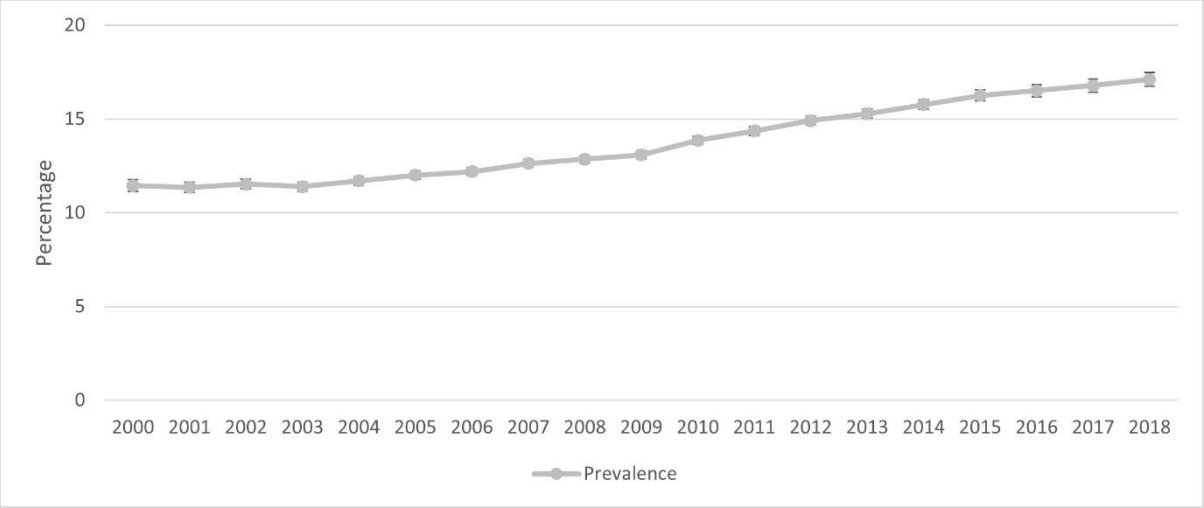


Figure 3.1: Prevalence of migraine prior to pregnancy in the Clinical Practice Research Database (CPRD) Gold pregnancy register 2000-2018

Annual prevalence was calculated as the percentage of all pregnancies with a start date within the year in women who had a diagnostic code for migraine within their record or a prescription for a medication used exclusively to manage migraine prior to the pregnancy start date

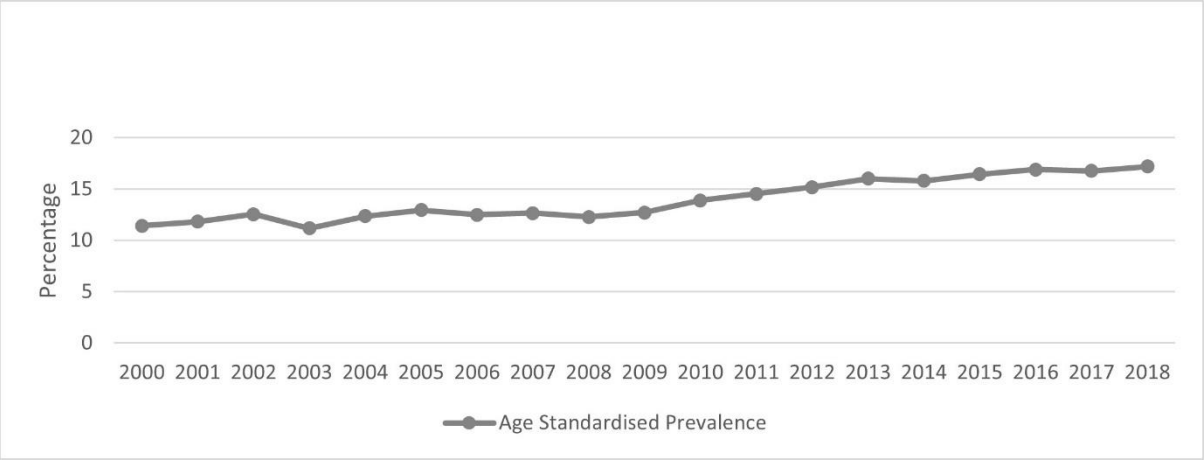


Figure 3.2: Age standardised prevalence of migraine prior to pregnancy in the Clinical Practice Research Database (CPRD) Gold pregnancy register 2000-2018

Age- standardised prevalence calculated using the direct method. Prevalence rates for each year were applied to the European Standard Population 2013 (ESP2013)

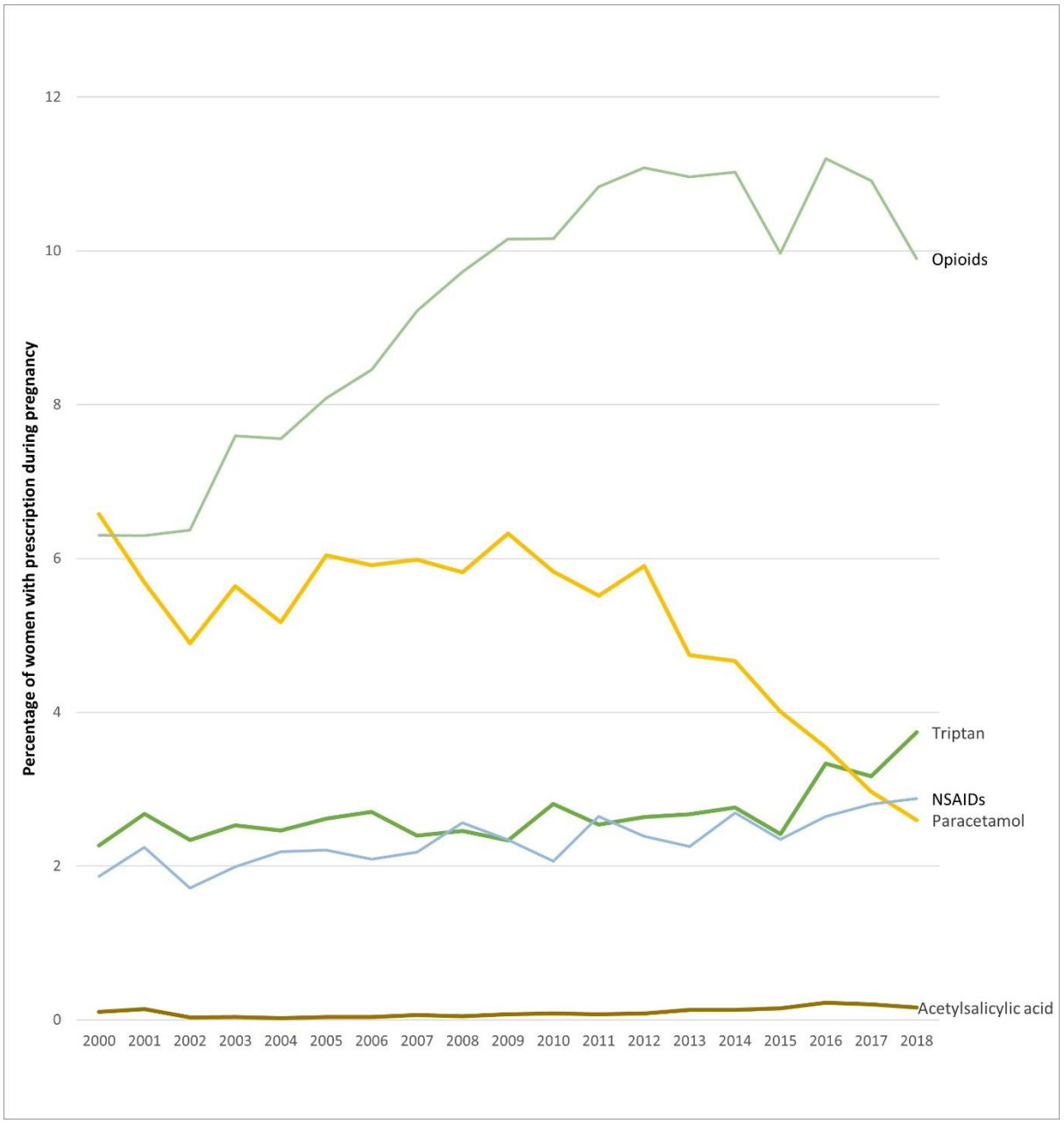


Figure 3.3: Prevalence of prescriptions for the acute management of migraine in women with pre-pregnancy migraine in the Clinical Practice Research Database (CPRD) GOLD pregnancy register 2000-2018

Annual prevalence calculated as the proportion of pregnancies with a start date within the year in women with a recorded diagnosis of migraine or a prescription for a

medication used exclusively to manage migraine prior to the pregnancy start date who were prescribed the medication of interest during the pregnancy

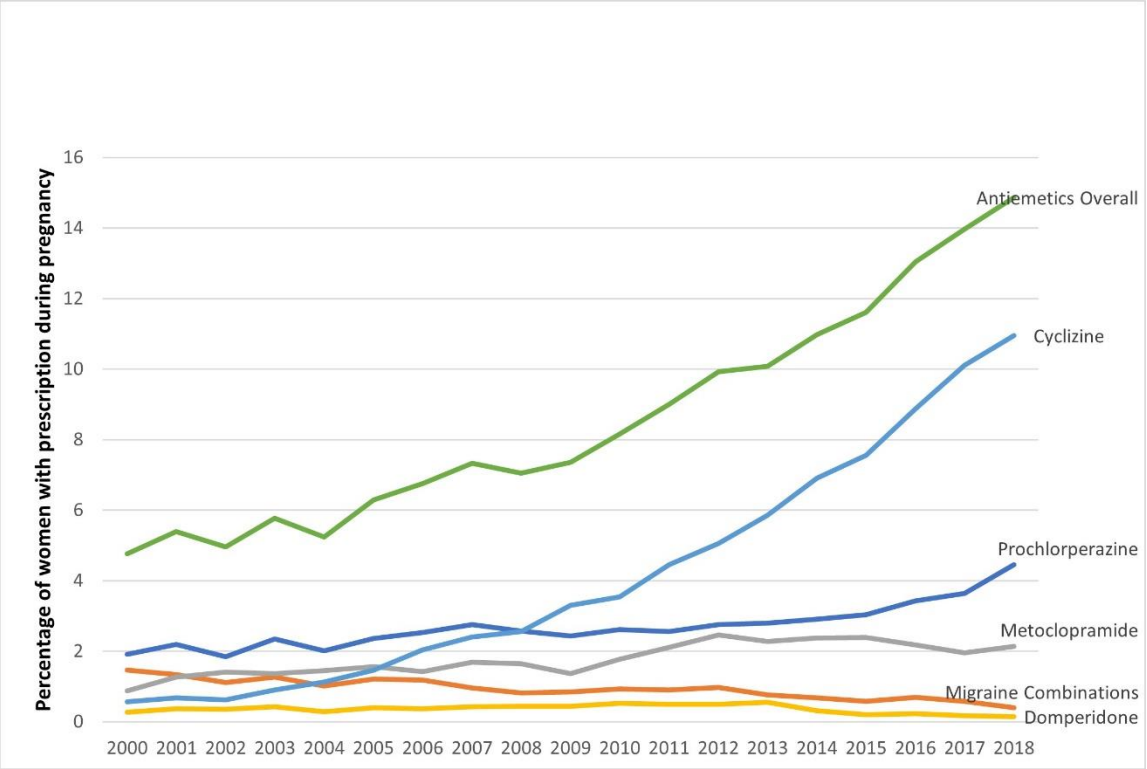


Figure 3.4: Prevalence of prescriptions for anti-emetics in patients with migraine in women with pre-pregnancy migraine in the Clinical Practice Research Database (CPRD) GOLD pregnancy register 2000-2018

Annual prevalence calculated as the proportion of pregnancies with a start date within the year in women with a recorded diagnosis of migraine or a prescription for a medication used exclusively to manage migraine prior to the pregnancy start date who were prescribed the medication of interest during the pregnancy

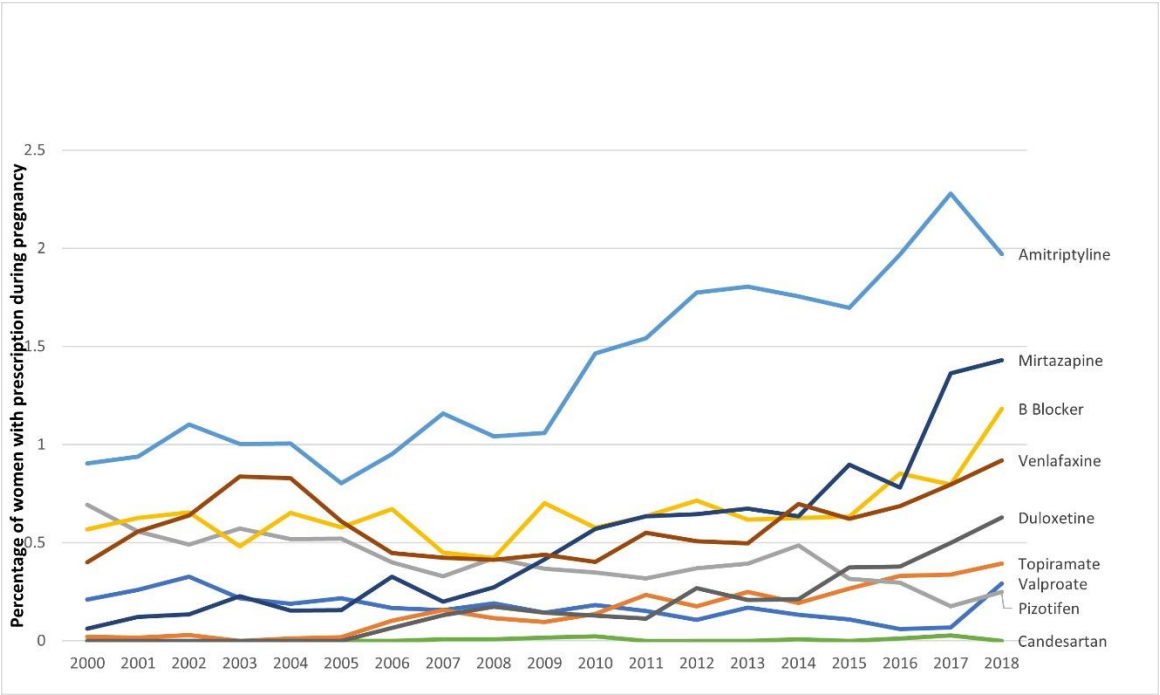


Figure 3.5: Prevalence of prescriptions for the prophylactic management of migraine in women with pre-pregnancy migraine in the Clinical Practice Research Database (CPRD) GOLD pregnancy register 2000-2018

Annual prevalence calculated as the proportion of pregnancies with a start date within the year in women with a recorded diagnosis of migraine or a prescription for a medication used exclusively to manage migraine prior to the pregnancy start date who were prescribed the medication of interest during the pregnancy

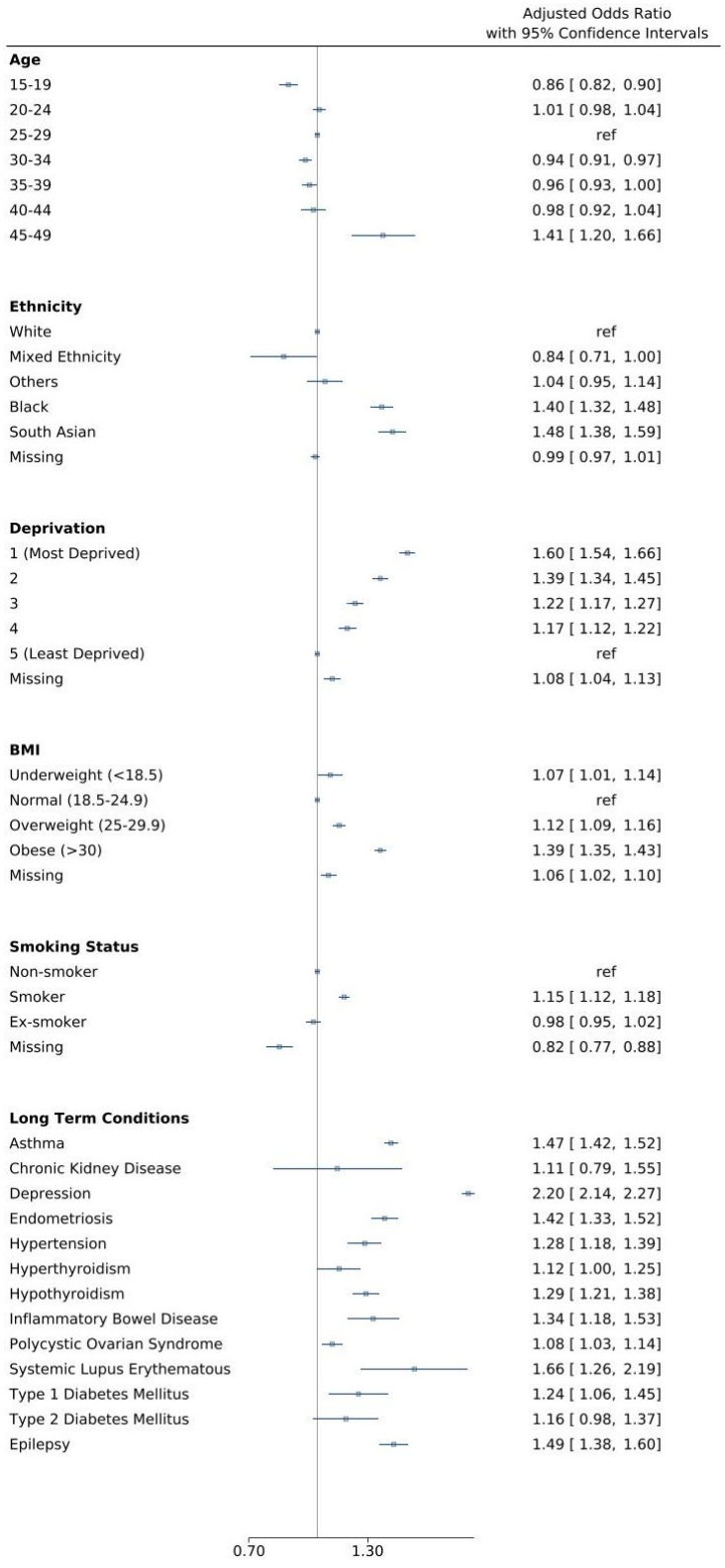


Figure 3.6: Factors associated with receiving a prescription for medications used in migraine during the whole pregnancy of women with pre-pregnancy migraine in Clinical Practice Research Database (CPRD) Gold Pregnancy Register 2000-2018

A logistic regression analysis of the association between patient demographics, lifestyle factors and comorbidities and receiving a prescription for any medication used in the management of migraine in women with a pre-pregnancy diagnosis of migraine in the CPRD pregnancy register 2000-2018

Chapter 4 : How migraine and its associated treatment impact on pregnancy outcomes: Umbrella Review with Updated Systematic Review and Meta-Analysis

The published manuscript of the study described in this chapter was adapted for this thesis and is presented as follows.

Published manuscript:

Phillips K, Clerkin-Oliver C, Nirantharakumar K, Crowe FL, Wakerley BR. How migraine and its associated treatment impact on pregnancy outcomes: Umbrella review with updated systematic review and meta-analysis. Cephalalgia. 2024;44(2)

Personal contribution:

- Developed the review question and study design guided by co-authors
- Identified, searched, appraised and extracted data as first reviewer for umbrella review and systematic review
- Synthesised data and wrote first draft of the manuscript
- Submitted for publication and addressed reviewers' comments

Title: How migraine and its associated treatment impact on pregnancy outcomes: Umbrella Review with Updated Systematic Review and Meta-Analysis

Katherine Phillips MPH[1], Conor Clerkin-Oliver MSc[2], Krishnarajah Nirantharakumar MD[1,3], Francesca L Crowe PhD[1]*, Benjamin R Wakerley PhD[4,5]*

* Joint senior authors

1 Institute of Applied Health Research, University of Birmingham, Birmingham

2 Re:Cognition Health, 100 Hagley Road, Birmingham, B16 8LT

3 Midlands Health Data Research UK, University of Birmingham, Birmingham

4 Institute of Metabolism and Systems Research, University of Birmingham, Birmingham

5 University Hospital Birmingham, Birmingham, UK

Corresponding author:

Francesca L Crowe

Lecturer Epidemiology and Health Informatics

Institute of Applied Health Research

University of Birmingham, Birmingham

Email: F.Crowe@bham.ac.uk

4.1 Abstract

4.1.1 Background

Migraine is common in reproductive aged women. Understanding the impact of migraine and associated treatments on pregnancy outcomes remains very important. An umbrella review of systematic reviews, with or without meta-analyses, examined the link between migraine and pregnancy outcomes.

4.1.2 Methods

We systematically searched Medline, Embase and Cochrane to 15th November 2023. Quality appraisal was carried out using the AMSTAR2 tool.

An established framework was used to determine whether included reviews were eligible for update.

4.1.3 Results

Four studies met review criteria. Migraine was reported to be associated with increased odds ratio (OR) of pre-eclampsia, low birth weight and peripartum mental illness (pooled OR = 1.75 (1.20–2.54)). Triptan-exposed women had increased odds of miscarriage compared to women without migraine (pooled OR 3.54 (2.24-5.59)).

In updated meta-analyses, migraine was associated with an increased odds of pre-eclampsia and preterm birth (pooled OR 2.05 (1.47-2.84) and 1.26 (1.21-1.32) respectively).

4.1.4 Conclusion

Migraine is associated with increased odds of pre-eclampsia, peripartum mental illness and preterm birth. Further investigation of the relationship between migraine and

placental abruption, low birth weight and small for gestational age is warranted, as well as the relationship between migraine, triptans and miscarriage risk.

Systematic Review Registration: Prospero CRD42022357630

4.2 Introduction

As outlined in sections 1.7 and 1.8 of the Introduction, there is a well-established association between migraine and cardiovascular disease risk (16, 19) and a significantly increased risk of pre-eclampsia and low birth weight have been described in the literature(124). A subsequent large cohort study of a Danish population registry also found an increased risk of pregnancy-associated hypertension disorders, miscarriage, preterm birth and caesarean section(125). Findings of this study and other newer studies may alter the effect estimates reported in existing reviews.

As described in the Introductory chapter (section 1.11), recommended treatment options for migraine during pregnancy include paracetamol, NSAIDs (prior to the third trimester) or triptans for symptom relief and aspirin, beta blockers and amitriptyline for migraine prophylaxis(126), although a paucity of evidence as to their safety in pregnancy means it is advised that they are used with caution(127) (128). Despite this, medication use and polypharmacy are prevalent in pregnant women with migraine. A US study of an insurance claims found that around 15% received a triptan in the first trimester and preventative medication use ranged from 10-16% (109). A systematic review studying the treatments provided in migraine and associated adverse pregnancy outcomes found no increased risk when comparing with migraine who took triptans during pregnancy to women with migraine who did not take triptans, but insufficient evidence to evaluate the safety of other drugs, such as beta-blockers and amitriptyline, used in the management of migraines(129).

As described in section 1.7 of the introduction, migraine with aura has been associated with greater increased risk of ischaemic heart disease and stroke than migraine alone (16, 19) (130), however, it is not clear what impact the presence of aura has on pregnancy outcomes.

The aim of this study was to review and synthesise existing evidence on outcomes of pregnancies of women with migraine, including in those treated and untreated and those with and without aura. The objectives were: to identify and appraise higher level evidence (systematic reviews with or without meta-analyses) reporting on the association between migraine and pregnancy outcomes, to consolidate evidence from systematic reviews and meta-analyses using narrative synthesis and, where appropriate, quantitative synthesis and to update existing systematic reviews and meta-analyses. This study was conducted to address research objective 2: to conduct an umbrella review of the literature comparing outcomes of pregnancy in i) women with and without migraine ii) women with migraine who are treated and untreated during pregnancy.

4.3 Methods

An umbrella review of systematic reviews with or without meta-analyses of the association between migraine and pregnancy outcomes was performed.

4.3.1 Population, outcomes and comparator

The population included all women, irrespective of age and setting, who were included in observational studies reporting on migraine and pregnancy outcomes. Exposures considered were a) Migraine, b) Pharmacological therapy for the management of migraine (including medications used exclusively in the management of migraine and those with other indications, provided they were studied in the migraine population) c) Migraine with aura and comparators were a) Women without migraine b) Women with migraine not managed with pharmacological therapy c) Migraine without aura.

4.3.2 Outcome

The outcomes of interest were derived from our literature review from an ongoing study for developing core outcome set for pregnancies with multiple long term conditions (131) (Supplementary table 4.1):

4.3.3 Search Methods

Searches were conducted in Medline, Embase and the Cochrane database of systematic reviews from inception to 15th November 2023. No restrictions were applied to language or setting when selecting the studies. The search strategy combined subject headings and free text keywords for migraine, pregnancy and pregnancy outcomes (supplementary section 4.1). The search was limited to systematic reviews and meta-analyses.

4.3.4 Eligibility Criteria

Systematic reviews and meta-analyses were included. A study was considered to be a systematic review if it met the following criteria: it described the methodology used in adequate detail; a systematic approach was used to identify all relevant primary studies; and it performed quality appraisal of included studies (132). The following types of publications were not included: protocols, review articles, conference abstracts, guidelines, consensus, documents or expert position papers, summaries, comments, letters, and brief reports.

4.3.5 Study Selection and Data Extraction

After removing duplicate studies, two reviewers independently conducted the title and abstract screening, and ineligible studies were excluded. Full text screening of eligible studies was conducted by two reviewers (KP and CCO) independently and a third senior

reviewer (FLC) was consulted to resolve any discrepancy. De-duplication, abstract and full-text screening were carried out using Rayyan (133).

The list of excluded studies was maintained with the reasons for exclusion documented.

The details of the steps involved in study selection was reported using PRISMA flowchart.

A standardised data extraction form was used by KP, and data extracted from the studies were checked by second researcher (CCO). In the case of a conflict, a third reviewer was consulted (FLC). Data extracted included: author, year of publication, review aim, databases searched, time period, population, exposures, comparators, outcomes, covariates, study designs, exposure/ outcome definition, data synthesis method, quality assessment tool, number of qualitative/ quantitative analyses, results of meta-analysis and authors conclusion.

4.3.6 Quality Assessment

The AMSTAR 2 tool was used to assess the methodological quality (134). This was chosen as it has been demonstrated to be effective for assessing methodological quality (135) and has been used in previous similar reviews (95). The online AMSTAR 2 (A Measurement Tool to Assess systematic Reviews) was completed by two reviewers independently. Out of the 16 points the AMSTAR 2 tool, one point was awarded for each of the criteria met. As per the AMSTAR guidance, the following domains were considered critical weaknesses; protocol registered before review, adequacy of literature search, justification for excluding individual studies, risk of bias from individual studies included in the review, appropriateness of meta-analytical methods, consideration of risk of bias when interpreting results, assessment of presence and likely impact of publication bias. The reviews were rated as high quality (none or one non-critical

weakness), moderate quality (more than one non-critical weakness), low quality (one critical flaw with or without non-critical weakness) or critically low quality (more than one critical flaw, with or without non-critical weaknesses). To resolve any disagreements a third reviewer was consulted.

4.3.7 Overlapping reviews

Reviews were considered to overlap if they evaluated the same outcomes and possibly included the same primary studies. In the case of overlapping, the degree of overlap was presented graphically using a citation matrix which mapped systematic reviews against primary studies. Overlap was quantified using corrected covered area (CCA). Overlap was rated as slight (0-5), moderate (6-10), high (11-15) and very high (>15) (136). In the case of high or very high overlap, one review was selected for inclusion. This was based on the following criteria: AMSTAR rating, year of publication, whether meta-analyses are reported and the number of participants.

4.3.8 Update of existing reviews

An established framework was used to determine whether included reviews were eligible for update. The following criteria was applied:

- The key search terms from the review's search strategy identified new studies which met the review inclusion criteria.
- The findings of the new studies would have potentially changed the conclusion of the review.

Only high and moderate quality systematic reviews were eligible for update.

4.3.9 Data analysis

Results from reviews were synthesised in narrative synthesis. Study characteristics were presented in a table. Where adjusted and unadjusted risk estimates were available, both were extracted. The findings were presented in forest plots which were created in Stata Statistical Software: Release 17 (StataCorp LLC, College Station, TX).

4.4 Results

The database search yielded 291 articles. Following duplicate removal and title and abstract screening, 17 full text articles were assessed for eligibility. Following full text screening, four reviews were found to be eligible, two of which compared pregnancy outcomes between women with and without migraine(124, 137) and two of which compared pregnancy outcomes between treated and untreated women with migraine(129) (64) (Supplementary Figure 4.1). The reasons for exclusion of full text articles are given in Supplementary Table 4.2. No reviews reported on the association of aura with pregnancy outcomes. The characteristics of included studies are summarised in table 4.1 and Supplementary Table 4.3.

4.4.1 Methodological quality

One study (Aukes et al(124)) was rated as moderate and three were rated as low quality. Brown et al(137), Dudman et al(129) and Marchenko et al(64) were all rated as low quality because they were found to have critical weaknesses that included absence of an explicit statement that the review methods were established prior to the conduct of the review. Dudman et al(129) did not assess publication bias and Marchenko et al(64) did not account for risk of bias when interpreting results (Table 4.2).

4.4.2 Overlapping reviews

When considering overlap of reviews, both Dudman et al(129) and Marchenko et al(64) reviewed the effects of triptans on preterm birth and included overlapping studies (CCA 50%). According to the criteria, Dudman(129) would have been included as it is the most recent. However, Dudman(129) et al only performed meta-analysis on studies comparing patients exposed to triptan with the general population. As Marchenko(64) compared triptan exposed patients with migraine control patients, both studies were included.

4.4.3 Eligibility for updates

As only moderate or high-quality reviews could be considered eligible for update, Aukes et al(124) was the only review that met this criterion. We were aware of large primary studies that had been published since Aukes et al(124) conducted their search, which reported results that may change the outcome of the meta-analyses. Therefore, a scoping search was performed to identify relevant studies that had been published since the systematic review. We found several studies that met the eligibility criteria, three of which also reported a significantly higher odds of preterm birth. Aukes et al(124), therefore, met the criteria for an update.

4.4.4 Update to Aukes et al

A detailed description of the results of the search, screening, quality assessment, data extraction and more detailed results are available in supplementary section 4.2.

4.4.5 Findings of included and updated studies

The findings from included and updated studies are summarised in figure 4.1 and Supplementary Figure 4.2.

4.4.6 Pre-eclampsia

Aukes et al found women with migraine were at increased odds of pre-eclampsia (pooled odds ratio (OR) 2.07 (95% CI 1.37-2.76)) compared to women without migraine(124).

The updated search found an additional six peer-reviewed studies and one abstract. In total, fourteen studies investigating a total of 1,415,249 women, reported on the association between migraine and preeclampsia. The updated meta-analysis found women with migraine had more than twice the odds of pre-eclampsia (pooled unadjusted OR was 2.05 (1.47-2.84)). The pooled OR was also statistically significantly higher for migraine for studies that included adjustment for confounding (pooled adjusted Odds Ratio (aOR) 2.22 (1.34-3.68)) (Figure 4.2a).

Assuming a baseline risk of 46 cases per 1000 pregnancies (138), migraine is associated with an additional 44 cases of pre-eclampsia per 1000 (95% CI 20-77 cases per 1000).

The odds ratios remained significant in sensitivity analyses which restricted the meta-analysis to prospective cohorts and case-control studies and when abstracts were included in the meta-analysis. A meta-analysis of studies reporting adjusted risk ratios also found a significantly increased risk of pre-eclampsia. Only one study at low risk of bias reported adjusted odds ratios and this found a non-significantly increase in the odds of pre-eclampsia, although the pooled adjusted odds ratios for studies at low risk of bias remained significant (Supplementary Figure 4.3).

There were sufficient studies to construct a funnel plot. Visual inspection of the plot indicated potential publication bias (Supplementary Figure 4.4).

4.4.7 Preterm birth

Aukes et al found no significant association between migraine and preterm birth when the OR from 5 studies, including a total of 72,394 women, were pooled (1.23 (95% CI 0.97-1.55). However, when the results of two studies that reported aOR were pooled, migraine was associated with 25% increased odds of preterm birth (95% CI 1.13-1.38) (124).

From the updated search, six further studies were found of which four were peer reviewed and two were abstracts. In the updated meta-analysis, the pooled results of the nine studies, including a total of 364,079 women, found that; compared to women without migraine, women with migraine had a 26% higher odds of pre-term birth with a pooled OR of 1.26 (1.21-1.32). Three studies also reported adjusted OR (pooled aOR 1.32 (1.15-1.51)) (Figure 4.2b).

Assuming a baseline risk of 99 per 1000 pregnancies (139), migraine is associated with an additional 23 cases of preterm birth per 1000 (95% CI 19-28 cases per 1000).

The odds ratios remained significant in sensitivity analyses which restricted inclusion to the studies with low risk of bias and prospective cohort studies and in a meta-analysis which included abstracts (Supplementary Figure 4.5). There were sufficient studies to construct a funnel plot. Visual inspection of the plot again indicated potential publication bias (Figure 4.6).

4.4.8 Placental abruption

Aukes et al retrieved only one study reporting on placental abruption, which found a more than twofold increase in the risk (aOR 2.14 (95% CI 1.22-3.75)) (124).

In the updated search, two further studies were found of which one was an article published in a peer reviewed journal and one was an abstract. The 2 studies that were

included in the meta-analysis included a total of 251,908 women. The odds of placental abruption were more than 50% higher in women with migraine, but this was not statistically significant (OR 1.51 (0.81-2.84)) (Figure 4.2c). When the abstract was included, the odds of placental abruption was more than one third higher in women with migraine, which was statistically significant (OR 1.35(1.05-1.75) (Supplementary Figure 4.7).

4.4.9 Low birth weight

Aukes et al found that maternal migraine was associated with an increased odds of low birth weight (significant in unadjusted analysis only: pooled OR 1.18 (95% CI 1.03-1.34), 3 studies, n=38,300; pooled aOR 1.27 (95% CI 0.89-1.82), 2 studies, n=30,151).

Two further studies were found in the updated review. A total of five studies, investigating a total of 350,020 women reported on the association between migraine and low birth weight. In the updated meta-analysis, the odds of low birth weight was 18% higher for women with migraine; pooled unadjusted OR was 1.18 (1.11-1.24). The odds of low birth weight were higher in two studies that reported an adjusted OR, but this was not statistically significant (pooled aOR of 1.27 (0.89-1.82)) (Figure 4.2d).

Assuming a baseline risk of 146 per 1000 pregnancies (47), migraine is associated with an additional 22 cases of low birth weight per 1000 (95% CI 13-29 cases per 1000).

4.4.10 Small for gestational age

Aukes et al found, when pooling the results of two studies, that maternal migraine was not significantly associated with an increased odds of small for gestational age babies. Pooled OR 1.06 (0.98-1.15) and aOR 1.06 (0.99-1.14).

A further three studies were found in the updated review. A total of five studies investigating a total of 291,279 women, reported on the association between migraine

and small for gestational age. In the updated meta-analysis, there was a slightly higher risk of small for gestational age in the unadjusted analysis, but this was not statistically significant; pooled unadjusted OR of 1.08 (0.95-1.23). For the studies that provided aOR, the pooled aOR was 8% higher, a result that was statistically significant; 1.08 (1.01-1.15) (Figure 4.2e). The pooled unadjusted OR was not significant in sensitivity analyses of the two articles published in peer reviewed journals only or at low risk of bias only (four studies) (Supplementary Figure 4.8).

4.4.11 Peripartum mental illness

Brown et al found, when pooling the results of two studies, that maternal migraine was associated with increased odds of peripartum mental illness (OR 1.75 (1.20-2.54)).

4.4.12 Migraine medications and pregnancy outcomes

With regards to pregnancy outcomes in women treated with migraine medication, triptans were the only medication that were assessed in a meta-analysis. Marchenko et al found triptans were associated with more than three times the odds of miscarriage for women treated with triptans compared to healthy controls (pooled OR 3.54 (2.24-5.59), 2 studies, n=51,043). However, when comparing women with migraine who were exposed to triptans during pregnancy to women with migraine who were not exposed to triptans during pregnancy, a non-significant association was found (pooled OR 1.27 (0.58-2.79), 2 studies, n=260) (64).

Dudman et al only compared women treated with triptans to the general population in their meta-analysis. They did, however, report pooled prevalences of pregnancy outcomes in women with migraine comparing those who did and did not receive treatment in pregnancy. In agreement with Marchenko et al, this review did not find a significant difference in the prevalence of miscarriage associated with triptan use (8.2%

(95% CI 6.1%-10.6% in those receiving no medication versus 10.2% (95% CI 5.3%-16.1%) receiving triptans). There was, however, a higher prevalence of miscarriage in patients receiving NSAIDs (22.6% (95% CI 20.7%-24.9%).

Marchenko et al found triptans were not significantly associated with risk of preterm birth in comparison to both untreated migraine controls (pooled OR 0.9 (0.35-2.30) and healthy controls (pooled OR 1.16 (0.67-1.99)). Dudman et al, on the other hand, reported a significantly lower prevalence of preterm birth in women receiving triptans compared to those not receiving medications (6.6% (5.6%-7.7%) versus 10.4% (8.9%-12%).

4.5 Discussion

4.5.1 Summary of findings.

In this umbrella review of systematic reviews, women with migraine had a higher odds of pre-eclampsia, low birth weight and peripartum mental illness. Women exposed to triptans had a higher odds of miscarriage compared to healthy controls, but not in comparison with women with migraine who were not exposed to triptans in pregnancy (it is worth noting there were low numbers of subjects in the included studies, which likely led to wide confidence intervals for the pooled odds ratio).

This updated systematic review showed that women with migraine had a higher odds of preterm birth. However, it should be noted that no distinction was made between spontaneous and medically indicated preterm birth, meaning the interpretation of this finding with regards to potential underlying mechanisms is difficult. When results of non-peer reviewed abstracts were included, an association between migraine and placental abruption was also found. It confirmed the finding that there is an association between migraine and pre-eclampsia. In keeping with Aukes et al, a small significant

association between migraine and low birth weight was found when unadjusted odds ratios were pooled. In contrast with Aukes et al, the updated meta-analysis found an association between migraine and small for gestational age when adjusted odds ratios were pooled.

4.5.2 Strengths and limitations

This review has several strengths. A predefined protocol was used, and a comprehensive search of multiple databases was conducted. Studies were screened, selected and quality assessed by two independent reviews. Data extraction was checked by an independent reviewer. The update to one review meant we were able to gain more clarity around association with some pregnancy related outcomes.

However, there are also some limitations to the study. Firstly, most of the reviews were of low to moderate quality. As the primary studies that were included were observational, we are limited in our ability to make conclusions about causality. In the meta-analyses, there was high heterogeneity between studies for some of the outcomes including preterm birth and pre-eclampsia. Additionally, asymmetry was observed in the funnel plots of the results of studies for pre-eclampsia and preterm birth, suggesting potential publication bias. The quality of included studies could have been improved by taking these biases into account in sensitivity analyses or in their interpretation of results. The studies included in included reviews and the updated systematic review were largely from Europe and North America, which will likely impact on the generalisability of findings. Some important outcomes, such as miscarriage, have not been included in systematic reviews, so were not considered in this study.

In the updated review, migraine prevalence varied depending on method by which authors identified diagnosis of migraine. Studies that used self-report found a

prevalence of 17-19%, which is similar to the prevalence found in the Global Burden of Diseases study. Studies that relied on coding of diagnosis of migraine in electronic health records tended to report a lower prevalence of migraine (7.8-11%). Overall, it is possible that migraine diagnoses were under ascertained, but it is not clear what the impact this may have had on the effect estimates. Including women with migraine in the unexposed groups may have led to an underestimate of the impact of migraine on pregnancy complications. On the other hand, as these studies mostly relied on coding within secondary care (with one also using prescriptions for migraine medication) it may be that only the most severe migraine cases were captured, as less severe cases can be self-managed or managed in primary care. It is unclear from the studies found in this review what, if any, impact severity of migraine has on the risk of complications. However, if more severe migraine is associated with an increased risk, this may have led to an overestimate of the effect. Many of the included studies did not consider whether migraine was active at the time of pregnancy, or whether symptoms resolved during pregnancy(140). One study included by Aukes et al found a 13-fold increase in the risk of pregnancy-induced hypertension in those whose headache worsened compared to those who resolved(141). However, this study was based on small numbers of cases and relied on a retrospective recall of headache during pregnancy. As headache is also a symptom of pregnancy-induced hypertension, reverse causality cannot be ruled out.

It should be noted that many of the medications used in the management of migraine (including amitriptyline and beta blockers) have other indications. There may be reviews and studies of the pregnancy outcomes associated with these medications that were conducted outside of the migraine population. These were beyond the scope of this review but may provide insight into their safety in pregnancy.

Some studies used prescription of medications as part of their definition of migraine, and, as found by Dudman et al, there is a lack of evidence around the safety outcomes for most migraine medications. It is therefore unclear whether migraine treatment, and not the underlying disease, could be contributing to some of the outcomes found.

4.5.3 Biological plausibility

Migraine is a complex polygenic neurovascular disorder. There are well established associations between migraine and increased risk of cardiovascular disease and stroke. Women of childbearing age with migraine and aura are at increased risk of stroke and advised to avoid oestrogen-containing contraception, which further increases the risk (142). Potential biological mechanisms underlying this association include; increased burden of cardiovascular risk factors (such as hypertension) in women with migraine, endothelial dysfunction and hypercoagulability (19) (16). Migraine has also been found to be associated with a pro-inflammatory state, with raised CRP found in some patients with the condition. It is hypothesised that sterile inflammation of the cerebral vessels may contribute to cerebral atherosclerosis and stroke (143). There is hypothesised to be shared pathologies linking migraine and adverse pregnancy outcomes. A pro-inflammatory state has been found in pregnancies affected by pre-eclampsia (31) and preterm birth (35). Endothelial dysfunction and hypercoagulability have also been found in pregnancies effected by pre-eclampsia (32) (33) (34).

Marchenko et al concluded that the association between triptans and miscarriage is biologically plausible due to the serotonergic, vasoconstrictive properties of triptans (64). Miscarriage due to utero-placental hypoperfusion has been suggested with frequent triptan use (144). However, as the association was only significant when comparing triptan-exposed women to healthy controls ,the association of triptans and miscarriage could be due to an association between migraine and miscarriage, which

has been previously reported (125). Endothelial dysfunction in the placenta has been implicated in miscarriage and may, again, account for this association (36).

The higher prevalence of miscarriage in patients taking NSAIDs found by Dudman et al is in keeping with a previous meta-analysis (not restricted to the migraine population) which reported a more than twofold higher risk of miscarriage when NSAIDs were taken around the time of conception(68). A suggested mechanism for this is the inhibition of prostaglandin synthesis by NSAIDs may cause utero-placental hypoperfusion and miscarriage secondary to mal-implantation in early pregnancy (145) (146) (147).

4.5.4 Implications for future research and practice

Evidence for associations between migraine, low birth weight and small for gestational age remains unclear and therefore, more studies examining the relationship between migraine and, preterm birth, small for gestational age and low birth weight are required. The stronger association between migraine and preterm delivery may be the main reason for babies being low birth weight; however, as migraine was associated with small for gestational age (albeit non-significantly), we cannot rule out the possibility of an association between migraine and fetal growth restriction. In addition, as mentioned above, most studies of migraine and preterm birth do not distinguish between spontaneous and medically indicated preterm birth. In order to understand the potential biological mechanisms underlying this association, future studies should examine spontaneous and medically indicated preterm birth separately. The uncertainties around how migraine affects the risk of preterm birth, low birth weight and small for gestational age informed the study reported in chapter 6.

It may be that more severe cases of migraine, or migraine that does not improve or worsens in pregnancy may have a stronger association with miscarriage. These women will be more likely to take triptans during pregnancy, leading to an apparent association between triptans and miscarriage. Further investigation of this potential confounding by indication is necessary, as is further investigation of the safety of other drugs used in the treatment of migraine, particularly NSAIDs. These were further investigated in chapter 5.

The lower prevalence of preterm birth in women who took triptans during pregnancy compared to those who did not also warrants further investigation. Studies examining this association have found conflicting results (148) (149).

No systematic reviews were found which examined the impact of migraine with aura on pregnancy outcomes. As aura is associated with an increased risk of stroke (16), it is possible that aura will also increase the risk of pregnancy complications. Features such as aura or migraine related to the menstrual cycle have been found to affect whether migraine resolves during pregnancy(150). This is therefore an important area to focus on in future.

4.6 Conclusion

There is strong evidence to suggest that women with migraine have a higher risk of pre-eclampsia, preterm birth and peripartum mental illness. Further investigation of the relationship between migraine and placental abruption, preterm birth, low birth weight and small for gestational age is warranted, as well as the relationship between migraine, triptans and risk of miscarriage. There is a lack of information about the safety of other medications used for the treatment of migraine in pregnancy.

Table 4.1: Characteristics of systematic reviews included in this umbrella review of migraine and pregnancy complications

Characteristic	Aukes et al	Brown et al	Dudman et al	Marchenko et al
Title	Associations Between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis	Chronic Medical Conditions and Peripartum Mental Illness: A Systematic Review and Meta-Analysis	A systematic review and meta-analyses on the prevalence of pregnancy outcomes in migraine treated patients: a contribution from the IMI2 ConcePTION project	Pregnancy Outcome Following Prenatal Exposure to Triptan Medications: A Meta-Analysis
Publication year	2019	2018	2021	2015
Author	Annet M. Aukes, , Feyza N. Yurtsever, Amélie Boutin, , Marieke C. Visser, and	Hilary K. Brown, Amna Qazilbash, Nedda Rahim, Cindy-Lee Dennis, and	Daniel C. Dudman, Fatima Tauqeer, Moninder Kaur, Mary E. Ritchey, Hu Li, Sandra Lopez-Leon	Alexander Marchenko, MD; Fatma Etwel, MSc; Olukayode Olutunfese, MD; Cheri Nickel, BSW; Gideon

	Christianne J. M. de Groot	Simone N. Vigod		Koren, MD; Irena Nulman, MD
Geographical Area	The Netherlands	Canada	USA, Norway, UK	Canada
Aim of review	To determine the association of adverse pregnancy outcomes including pre-eclampsia, preterm birth, low birth weight, small for gestational age, and placental abruption with a history of migraine through a systematic review and meta-analysis.	To examine the association between maternal chronic conditions and peripartum mental illness.	To summarise the safety profile of the medications used to treat migraine during pregnancy by performing a systematic review and meta-analysis	To determine the reproductive safety of triptan medications by performing a literature review and a meta-analysis

Databases searched	Medline (Pubmed), Embase, Cochrane Library	MEDLINE, Embase, CINAHL, Psych-INFO	Embase, PubMed, PsychInfo, Scopus, Web of Science	Medical Literature Analysis and Retrieval System Online (via Object, View and Interaction Design [OVID]), Excerpta Medica Database, SCOPUS, Toxicology Information Online Special (via Toxicology Data Network), DART: Developmental and Reproductive Toxicology, ReproTox, Teratogen Information System, OVID International Pharmaceutical Abstracts, Cumulative Index

				to Nursing and Allied Health Literature, Shepard's Citations, Google Scholar, Cochrane Library, World Cat, Digital Dissertations, Global Health, Institute for Scientific Information Proceedings, and Biosciences Information Service Previews.
Search period	Inception to 11th November 2018	Inception to September 2017	Inception to 31st Dec 2020	1991 (when triptans first introduced) to Dec 2013
Population	Pregnant women	Pregnant women	Pregnant women	Pregnant women

Exposures	History of migraine	Chronic medical conditions of which one was migraine	Exposure to antimigraine medications anytime during pregnancy	Triptan medications during at least the first trimester of pregnancy
Comparator	No history of migraine	No chronic medical condition	Untreated migraine patients or general population	Women with migraine who were not treated with triptans or healthy controls
Outcomes	Pre-eclampsia, low birth weight, small for gestational age, premature birth, placental abruption	Peri-partum mental illness	All pregnancy outcomes	Major congenital malformations, prematurity, spontaneous abortion
Covariates	All studies adjusted for maternal age. Other confounders adjusted for were parity, adiposity or	One study adjusted for age and ethnicity	Alcohol, BMI, concomitant medications, delivery method, age, education, comorbidities, parity, previous children with birth	None

	body mass index, ethnicity, education, marital status, income, chronic hypertension, diabetes mellitus, hyperlipidemia, coronary heart disease, a family history of hypertension in pregnancy, smoking, physical exercise during pregnancy, and sex of the neonate.		defects, miscarriages, smoking were considered, but most only adjusted for maternal age, parity and smoking	
Study designs	Case-controls, cohorts	Cross-sectional,	Retrospective and prospective cohorts	RCT, case-control, observational cohort

		prospective cohort		
Definition of Exposure	Varied: questionnaires or structured interviews (ranging from asking if diagnosed to meeting diagnostic criteria from International Society of Headache (ISH); recorded in medical notes	Unclear	Any medication for the management of migraine as ascertained by prescription records or interview	Prescription or dispensing of triptans
Definition of Outcome	Pre-eclampsia: any definition but considered blood pressure of ≥140/90 mm Hg combined with	Depression via Patient Health Questionnaire	Unclear. Sources of outcomes included birth registry data, obstetrician or physician reports or medical records	Unclear.

	proteinuria >300 mg/24 hours or >30 mg/dL after 20 weeks of gestation as most valid definition, premature birth (<37 weeks or 259 days' gestational age), Low birth weight (≤2500 g), Small for gestational age (birth weight below the 10th percentile for gestational age),			

Table 4.2: Quality of the systematic reviews included in this umbrella as assessed using the AMSTAR 2 tool

Study	Aukes et al	Brown et al	Dudman et al	Marchenko et al
Did the research questions and inclusion criteria for the review include the components of PICO?				
Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?				
Did the review authors explain their selection of the study designs for inclusion in the review?				
Did the review authors use a comprehensive literature search strategy?				
Did the review authors perform study selection in duplicate?				
Did the review authors perform data extraction in duplicate?				
Did the review authors provide a list of excluded studies and justify the exclusions?				
Did the review authors describe the included studies in adequate detail?				
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?				
Did the review authors report on the sources of funding for the studies included in the review?				
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?				
If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?				
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?				
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?				
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?				
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?				
Overall rating	**Moderate**	**Low**	**Low**	**Low**
Key		Yes		
		Partial yes		
		No		

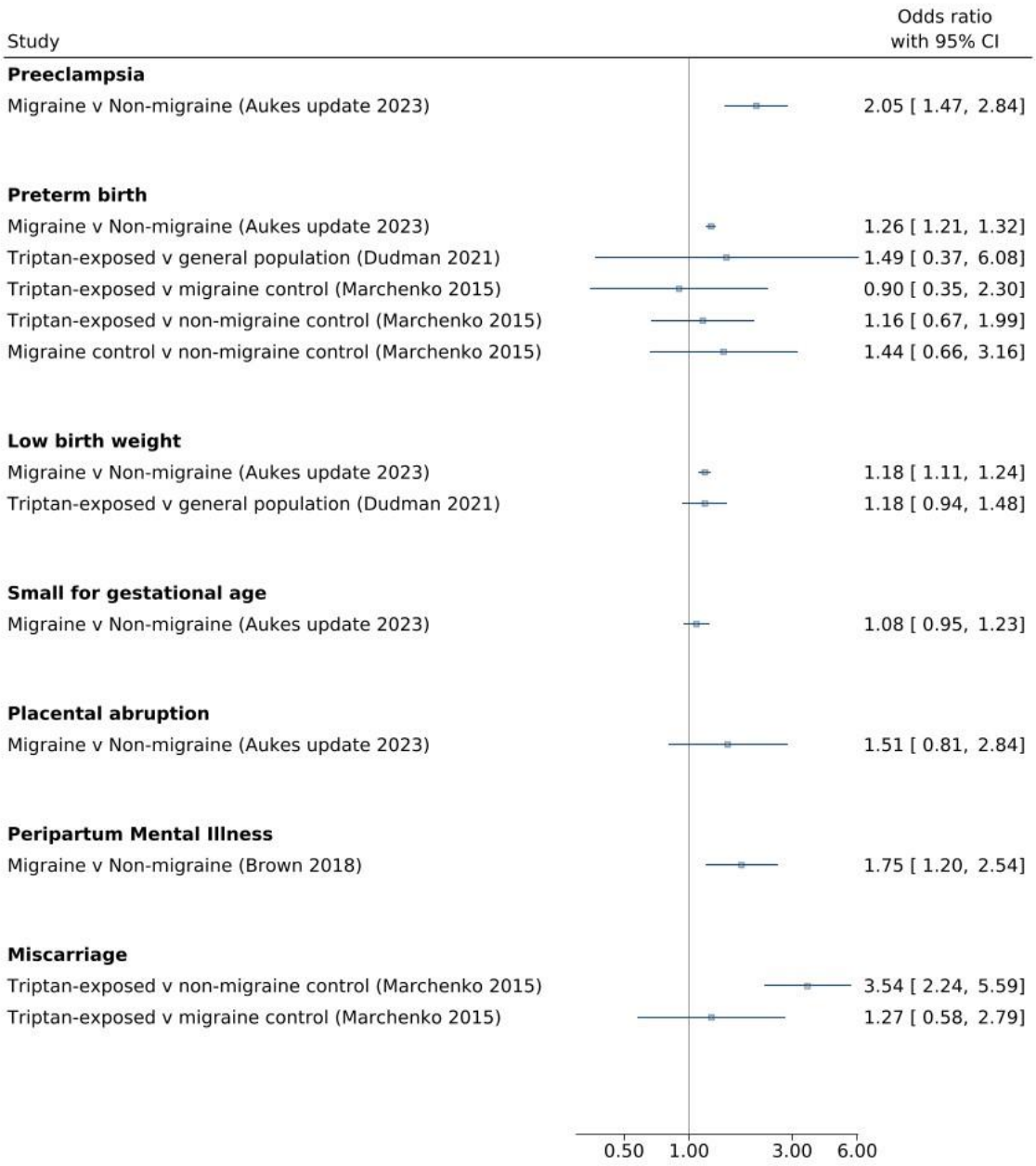
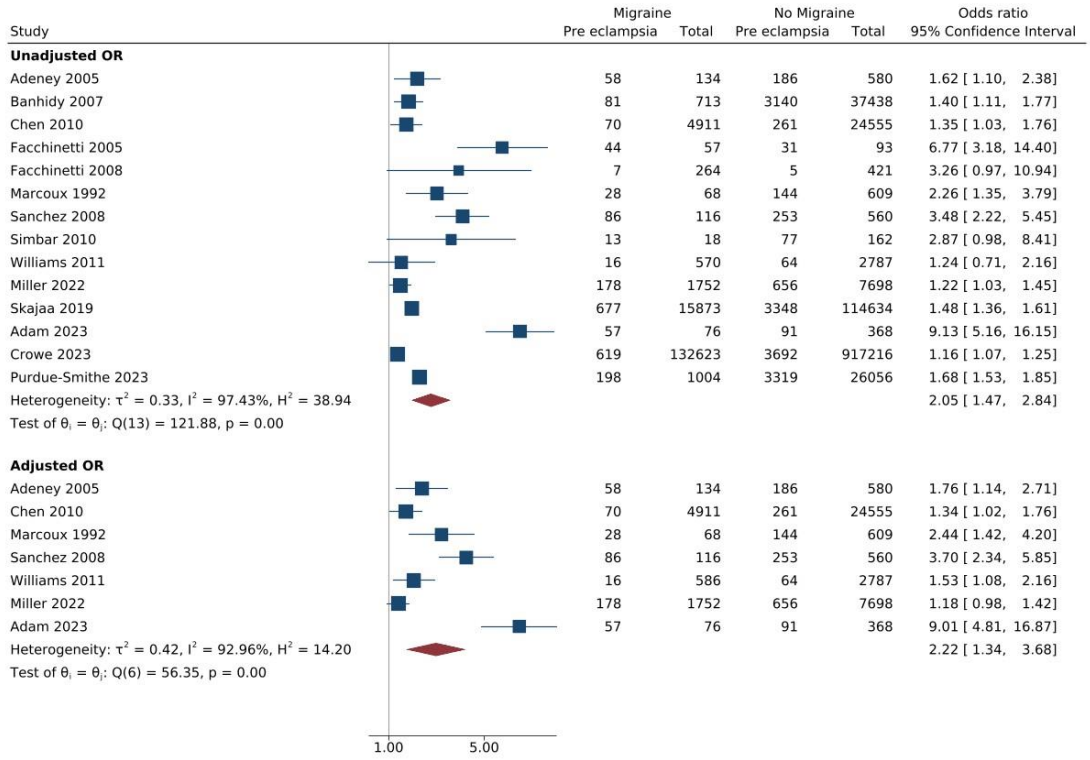


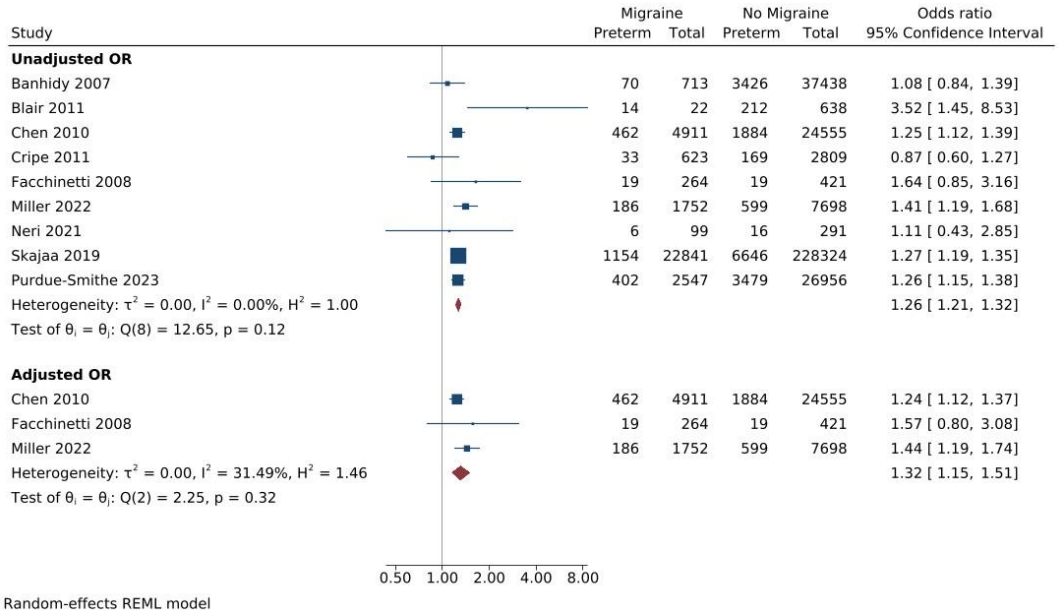
Figure 4.1: Forest plot summarising the odds ratios (95% confidence intervals) for associations between migraine, migraine treatments and pregnancy outcomes

Pooled odds ratios from systematic reviews identified in umbrella review (Brown, Dudman and Marchenko) and from meta-analysis performed as part of the update of Aukes et al

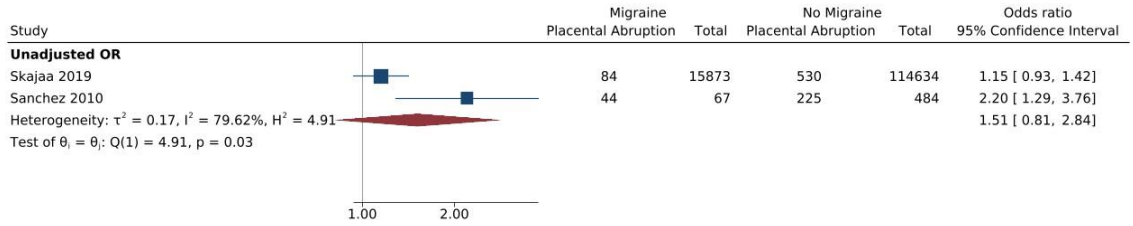
a)


Migraine
No Migraine
Odds ratio
Study
Pre eclampsia Total Pre eclampsia Total 95% Confidence Interval
Unadjusted OR
Adeney 2005 58 134 186 580 1.62 [1.10, 2.38]
Banhidy 2007 81 713 3140 37438 1.40 [1.11, 1.77]
Chen 2010 70 4911 261 24555 1.35 [1.03, 1.76]
Facchinetti 2005 44 57 31 93 6.77 [3.18, 14.40]
Facchinetti 2008 7 264 5 421 3.26 [0.97, 10.94]
Marcoux 1992 28 68 144 609 2.26 [1.35, 3.79]
Sanchez 2008 86 116 253 560 3.48 [2.22, 5.45]
Simbar 2010 13 18 77 162 2.87 [0.98, 8.41]
Williams 2011 16 570 64 2787 1.24 [0.71, 2.16]
Miller 2022 178 1752 656 7698 1.22 [1.03, 1.45]
Skajaa 2019 677 15873 3348 114634 1.48 [1.36, 1.61]
Adam 2023 57 76 91 368 9.13 [5.16, 16.15]
Crowe 2023 619 132623 3692 917216 1.16 [1.07, 1.25]
Purdue-Smithe 2023 198 1004 3319 26056 1.68 [1.53, 1.85]
Heterogeneity: τ^2 = 0.33, I^2 = 97.43%, H^2 = 38.94 2.05 [1.47, 2.84]
Test of $\theta_i = \theta_j$: Q(13) = 121.88, p = 0.00
Adjusted OR
Adeney 2005 58 134 186 580 1.76 [1.14, 2.71]
Chen 2010 70 4911 261 24555 1.34 [1.02, 1.76]
Marcoux 1992 28 68 144 609 2.44 [1.42, 4.20]
Sanchez 2008 86 116 253 560 3.70 [2.34, 5.85]
Williams 2011 16 586 64 2787 1.53 [1.08, 2.16]
Miller 2022 178 1752 656 7698 1.18 [0.98, 1.42]
Adam 2023 57 76 91 368 9.01 [4.81, 16.87]
Heterogeneity: τ^2 = 0.42, I^2 = 92.96%, H^2 = 14.20 2.22 [1.34, 3.68]
Test of $\theta_i = \theta_j$: Q(6) = 56.35, p = 0.00
1.00
5.00
Random-effects REML model

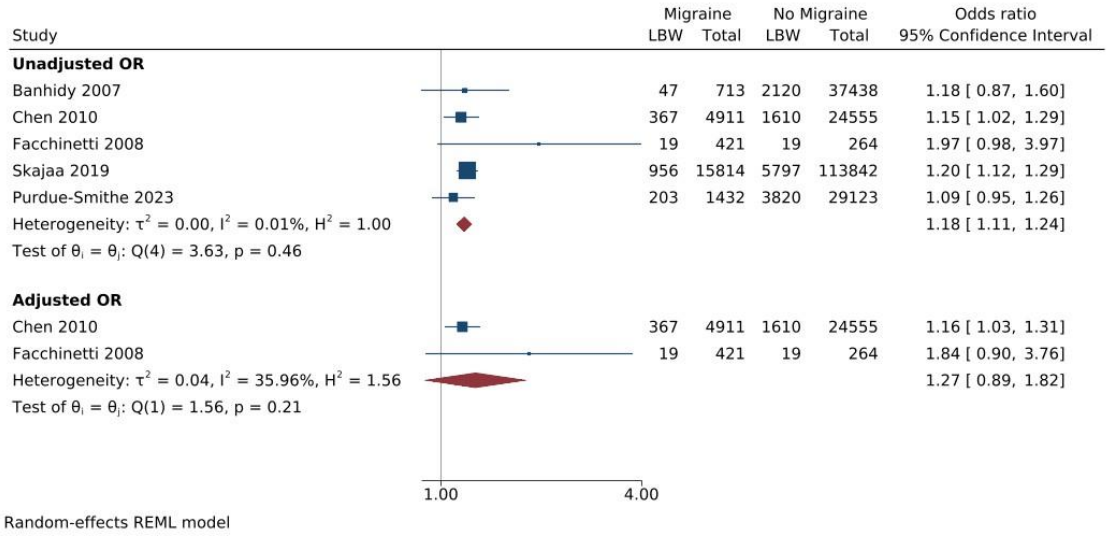
b)


Migraine
No Migraine
Odds ratio
Study
Preterm Total Preterm Total 95% Confidence Interval
Unadjusted OR
Banhidy 2007 70 713 3426 37438 1.08 [0.84, 1.39]
Blair 2011 14 22 212 638 3.52 [1.45, 8.53]
Chen 2010 462 4911 1884 24555 1.25 [1.12, 1.39]
Cripe 2011 33 623 169 2809 0.87 [0.60, 1.27]
Facchinetti 2008 19 264 19 421 1.64 [0.85, 3.16]
Miller 2022 186 1752 599 7698 1.41 [1.19, 1.68]
Neri 2021 6 99 16 291 1.11 [0.43, 2.85]
Skajaa 2019 1154 22841 6646 228324 1.27 [1.19, 1.35]
Purdue-Smithe 2023 402 2547 3479 26956 1.26 [1.15, 1.38]
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00 1.26 [1.21, 1.32]
Test of $\theta_i = \theta_j$: Q(8) = 12.65, p = 0.12
Adjusted OR
Chen 2010 462 4911 1884 24555 1.24 [1.12, 1.37]
Facchinetti 2008 19 264 19 421 1.57 [0.80, 3.08]
Miller 2022 186 1752 599 7698 1.44 [1.19, 1.74]
Heterogeneity: τ^2 = 0.00, I^2 = 31.49%, H^2 = 1.46 1.32 [1.15, 1.51]
Test of $\theta_i = \theta_j$: Q(2) = 2.25, p = 0.32
0.50
1.00
2.00
4.00
8.00
Random-effects REML model

c)


Study
Migraine
Placental Abruption
Total
No Migraine
Placental Abruption
Total
Odds ratio
95% Confidence Interval
Unadjusted OR
Skajaa 2019 84 15873 530 114634 1.15 [0.93, 1.42]
Sanchez 2010 44 67 225 484 2.20 [1.29, 3.76]
Heterogeneity: τ² = 0.17, I² = 79.62%, H² = 4.91 1.51 [0.81, 2.84]
Test of θi = θj: Q(1) = 4.91, p = 0.03
1.00
2.00
Random-effects REML model

d)


Study
Migraine
LBW
Total
No Migraine
LBW
Total
Odds ratio
95% Confidence Interval
Unadjusted OR
Banhidy 2007 47 713 2120 37438 1.18 [0.87, 1.60]
Chen 2010 367 4911 1610 24555 1.15 [1.02, 1.29]
Facchinetti 2008 19 421 19 264 1.97 [0.98, 3.97]
Skajaa 2019 956 15814 5797 113842 1.20 [1.12, 1.29]
Purdue-Smithe 2023 203 1432 3820 29123 1.09 [0.95, 1.26]
Heterogeneity: τ² = 0.00, I² = 0.01%, H² = 1.00 1.18 [1.11, 1.24]
Test of θi = θj: Q(4) = 3.63, p = 0.46
Adjusted OR
Chen 2010 367 4911 1610 24555 1.16 [1.03, 1.31]
Facchinetti 2008 19 421 19 264 1.84 [0.90, 3.76]
Heterogeneity: τ² = 0.04, I² = 35.96%, H² = 1.56 1.27 [0.89, 1.82]
Test of θi = θj: Q(1) = 1.56, p = 0.21
1.00
4.00
Random-effects REML model

e)

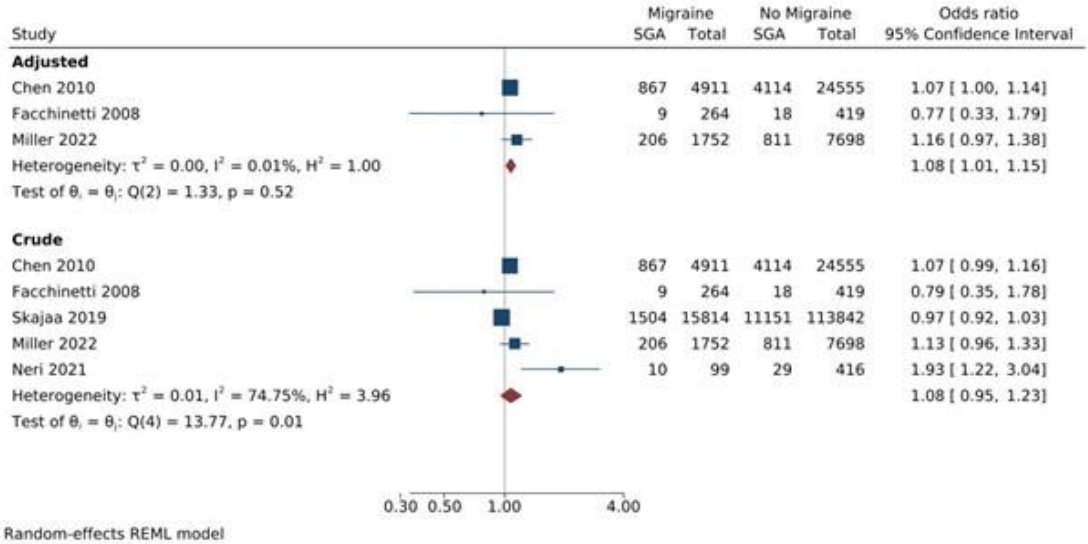

Study
Migraine
SGA
Total
No Migraine
SGA
Total
Odds ratio
95% Confidence Interval
Adjusted
Chen 2010 867 4911 4114 24555 1.07 [1.00, 1.14]
Facchinetti 2008 9 264 18 419 0.77 [0.33, 1.79]
Miller 2022 206 1752 811 7698 1.16 [0.97, 1.38]
Heterogeneity: τ² = 0.00, I² = 0.01%, H² = 1.00 1.08 [1.01, 1.15]
Test of θi = θj: Q(2) = 1.33, p = 0.52
Crude
Chen 2010 867 4911 4114 24555 1.07 [0.99, 1.16]
Facchinetti 2008 9 264 18 419 0.79 [0.35, 1.78]
Skajaa 2019 1504 15814 11151 113842 0.97 [0.92, 1.03]
Miller 2022 206 1752 811 7698 1.13 [0.96, 1.33]
Neri 2021 10 99 29 416 1.93 [1.22, 3.04]
Heterogeneity: τ² = 0.01, I² = 74.75%, H² = 3.96 1.08 [0.95, 1.23]
Test of θi = θj: Q(4) = 13.77, p = 0.01
0.30
0.50
1.00
4.00
Random-effects REML model

Figure 4.2: Forest plots of random effects meta-analysis of unadjusted and adjusted odds ratios for a) preeclampsia, b) preterm birth, c) placental abruption, d) low birth weight and e) small for gestational age in women with and without migraine

Pooled adjusted and unadjusted odds ratios from meta-analysis performed as part of update of Aukes et al

Acknowledgements

Competing Interest

Benjamin Wakerley is founder of Ceftronics Limited.

Funding

This project was not specifically funded.

Author Contribution and Guarantor

All authors were involved in the conception and design of this work. KP conducted the searches. KP and CCO selected studies, extracted relevant information and performed quality appraisal. FLC was consulted as a third reviewer when discrepancies arose. KP synthesised the data. All authors were involved in the drafting of the manuscript. KP is the guarantor of this review.

Chapter 5 : Migraine, associated treatments and risk of miscarriage: a matched cohort study and nested case-control study using the CPRD pregnancy register

The manuscript for this study has been prepared for submission and an adapted version is presented in this thesis.

Manuscript under submission

Phillips K, Gokhale K, Damase-Michel C et al. Migraine, associated treatments and risk of miscarriage: a matched cohort study and nested case-control study using the CPRD pregnancy register. Journal of Neurology, Neurosurgery & Psychiatry: under review

Personal contribution:

- Designed study and analysis under guidance from co-authors
- Created codelists for exposures, covariates and outcomes
- Led the analysis
- Drafted manuscript and led the revision process

Title: Migraine, associated treatments and risk of miscarriage: a matched cohort study and nested case-control study using the CPRD pregnancy register

Katherine Phillips[1], Clinical Research Fellow and Registrar in Public Health, Krishna Gokhale[1], Research Fellow, Christine Damase-Michel[2,3], Associate Professor, Helen Dolk[4], Professor of Epidemiology and Health Services Research, Catherine Nelson-Piercy[5], Professor of Obstetric Medicine and Consultant Obstetric Physician, Benjamin R Wakerley[6], Honorary Senior Clinical Lecturer and Consultant Neurologist, Francesca Crowe*[1], Lecturer, Krishnarajah Nirantharakumar*[1], Professor of Health Data Science and Public Health and Honorary Consultant in Public Health

* FC and KN are joint senior authors

Affiliations

1 Institute of Applied Health Research, University of Birmingham, Birmingham, UK.

2 Medical and Clinical Pharmacology, School of Medicine, Université Toulouse III, Toulouse, France.

3 Center for Epidemiology and Research in Population Health (CERPOP), INSERM, Toulouse, France.

4 The Institute of Nursing and Health Research, University of Ulster, Belfast, UK.

5 Guy's & St Thomas' Foundation Trust, London, UK

6 Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK.

Correspondence to:

Prof Krishnarajah Nirantharakumar k.nirantharan@bham.ac.uk

5.1 Abstract

5.1.1 Objective

To estimate the risk of miscarriage amongst pregnant women with migraine compared to pregnant women without migraine. To compare the odds of miscarriage in women taking medication for migraine to women with migraine who did not take medication and to explore this association with different types of medications.

5.1.2 Design

Matched cohort study and nested case-control

5.1.3 Setting

Clinical Practice Research Datalink pregnancy register. All pregnancies meeting data quality requirements between 2000 and 2019 were eligible for inclusion.

5.1.4 Participants

Cohort study: 193,208 pregnancies of women with migraine were matched one-to-one to women without migraine. Nested case-control: 20,778 pregnancies of women with migraine that ended in miscarriage were matched to 41,122 pregnancies of women with migraine that did not end in miscarriage.

5.1.5 Main outcome measures

Cohort study: miscarriage recorded in primary care. Nested case-control: odds of miscarriage amongst migraineurs using migraine medication.

5.1.6 Results

Miscarriage occurred in 10% (n=19,233) of women without migraine compared to 10.8% (n=20,778) of women with migraine. Having migraine was associated with an 8% higher risk of miscarriage (risk ratio (RR) 1.08, 95% confidence interval (CI) 1.06-

1.10) and remained significant after adjustment for demographic factors, BMI, smoking and comorbidities (aRR 1.06 95% CI (1.04-1.08)).

Of the pregnancies ending in miscarriage, 722 (3.47%), 380 (1.83%), 173 (0.83%) and 733 (3,52%) were exposed to triptans, amitriptyline, beta blockers and NSAIDs respectively. Of the matched pregnancies that did not end in miscarriage 1,100 (2.74%), 542 (1.35%), 294 (0.73%) and 780 (1.94%) were exposed to these medications respectively.

Exposure to triptans, amitriptyline and NSAIDs were associated with a significantly higher odds of miscarriage (aORs 1.24 (1.11-1.38), 1.25 (1.08-1.45) and 1.74 (1.57-1.93) respectively). Beta blockers were not associated with a higher risk of miscarriage.

5.1.7 Conclusions

Migraine and triptan, amitriptyline and NSAID exposure were all associated with higher risk of miscarriage. Further work is needed to understand the potential causative mechanisms.

5.2 Introduction

As the meta-analysis conducted in chapter 4 demonstrates, migraine is associated with a significantly increased risk of pre-eclampsia, which supports the view that migraine is a complex vascular disorder that can also affect systems outside the brain.

The association between migraine and miscarriage, remains less clear. Recently, two large electronic health record database studies assessed the association between migraine and miscarriage. Results from a Danish pregnancy cohort study of 228,324 women showed an elevated risk of miscarriage in pregnant women with migraine (adjusted prevalence ratio 1.10 (95% confidence intervals (95% CI): 1.05-1.15)) (106); however, a much smaller, non-significant, association was found between migraine and miscarriage in a Norwegian study of 593,009 pregnant women (adjusted odds ratio 1.02 (95% CI: 0.98-1.05)) (151). These studies are limited by potential under-ascertainment of migraine diagnosis: both reported a prevalence of only 3-3.5% in their cohorts. This has the potential to bias the risk towards the null. A prospective cohort study following up women with migraine who were planning pregnancies showed similar findings to the Norwegian study (hazards ratio 1.03 (95% CI 0.91-1.06)), although this had a relatively low number of participants (n=7890) (78).

As described in section 1.12 of the Introduction, common treatments used for migraine in pregnancy include headache-specific therapies such as triptans and other therapies such as NSAIDs, amitriptyline and propranolol (127) (152). The umbrella review reported in chapter 4 found that women exposed to triptans during pregnancy were at increased risk of miscarriage compared to a healthy control population. In a study published since the meta-analysis included in the umbrella review, Berard et al. found an increase in the odds of miscarriage, by almost two thirds, in women taking triptans during pregnancy. However this study did not exclusively include women with

migraine, thus overlooking potential confounding by indication (153). Other medications commonly used for migraine, such as non-steroidal anti-inflammatory drugs (NSAIDs), amitriptyline, and beta-blockers, have not been studied specifically in pregnant women with migraine. There are inconsistent findings around the association between NSAIDs and miscarriage; a systematic review and meta-analysis (of 207,341 studies) found a non-significant increased risk (OR=1.37 95%CI 0.99-1.99)(154). Out of three studies investigating the effect of tricyclic antidepressants on pregnancy outcomes, two found an increased risk of miscarriage in studies of drugs used in the management of depression (155) (156) (99). No evidence of an association between beta blockers and miscarriage has been found.

The aims of this study were to estimate the risk of miscarriage amongst pregnant women with a preconception diagnosis of migraine compared to those without and, in those women with migraine whose pregnancies ended in miscarriage, compare the risk of being prescribed common medications for the treatment of migraine to those whose pregnancies did not end in miscarriage. The study reported in this chapter was conducted to address, in part, the final objective: to describe the risk of adverse pregnancy outcomes, comparing i) women with and without migraine ii) women with migraine who are treated and untreated during pregnancy using the CPRD Gold pregnancy register and Hospital Episode Statistics (HES) maternity tail.

5.3 Methods

5.3.1 Study population

This analysis includes two study designs; 1) A retrospective cohort study of pregnant women with migraine matched to pregnant women without migraine to assess the association of pre-pregnancy migraine with miscarriage; 2) a nested case-control study

of pregnant women with migraine to compare the medication intake of those who had a miscarriage to those who did not have a miscarriage.

The Clinical Practice research datalink (CPRD) GOLD is an anonymised database of routinely collected primary care health records, which covers 7% of the UK population including almost 1000 GP practices. The database includes patient-level data on demographics (age, ethnicity, and social deprivation), symptoms, diagnoses, prescriptions and laboratory investigation results. Within this, an algorithm has been developed to identify pregnancy episodes, from which a validated pregnancy register has been created (86). This formed the source population for the study.

All women aged between 15 and 50 years with pregnancies that occurred between January 1, 2000 and December 31, 2019 were eligible for inclusion. Eligibility criteria also included 1) having an acceptable patient flag within CPRD GOLD (which indicates sufficient data quality) 2) a minimum of 1 year of registration with a practice or 1 year of registration after the up-to-standard date of the registered practice, whichever was later.

A known issue with the CPRD pregnancy register is the presence of "uncertain" pregnancy episodes where one episode can overlap with another in the same woman, pregnancies with outcomes that are inconsistent with the length of gestation, or where no pregnancy outcome is documented (88). Where pregnancy episodes overlapped, pregnancies with more complete data were selected, whereas pregnancies with an implausible length of gestation were removed so that no overlapping pregnancies remained for the final analysis. The handling of pregnancy episodes with no recorded outcome is described in the statistical methods section.

5.3.2 Exposure and outcome definition for matched cohort study

For the matched cohort, the exposure was defined by the presence of a Read code (a hierarchical clinical coding system to document patients' symptoms, diagnoses and referrals(85)) for diagnosis of migraine or a single prescription of medications used exclusively in the management of migraine in UK practice (triptans, migraine combination treatments (Migraleve, Migravess, Femigraine), or calcitonin gene-related peptide (CGRP) inhibitors) at any time prior to the pregnancy start date. For each pregnancy in women with migraine, one pregnancy in a woman without migraine was matched using exact matching for maternal age (±1 year) and year of pregnancy. As it was anticipated there would be a number of women without a history of migraine, recorded, women with a history of headaches were excluded from the unexposed population. Each pregnancy episode within the pregnancy register was assigned an outcome by the algorithm. Miscarriage (the outcome of interest) was identified by the presence of a Read code in the primary care record. The methodology and codelists are described elsewhere (86).

5.3.3 Case definition and exposures for the nested case control study

For the nested case-control study, the pregnant women with migraine formed the source population. Cases were defined as pregnancies where the outcome was recorded as miscarriage in the CPRD pregnancy register. Each pregnancy ending in miscarriage was matched to two pregnancies that did not end in miscarriage. Exact matching was used, matching on maternal age (±1 year) and year of pregnancy. For the cases, the index date was assigned as the date of miscarriage. For controls, the index date was assigned to the date that corresponded to gestational age at the end of the matched case pregnancy. This was to ensure that the same window of exposure was considered for both cases and controls, hence avoiding time-window bias (97).

The exposure variables for the nested case-control study were defined as the presence of a prescription code for triptans, amitriptyline, beta blockers, or NSAIDs during the exposure window (the period between the pregnancy start date and index date) recorded in the CPRD GOLD GP data. The codelists for variables used in both studies are available in supplementary table 5.1.

5.3.4 Statistical methods

Data related to pregnancy timings and outcomes were obtained from the CPRD pregnancy register (86). Extraction of other demographic, lifestyle, diagnostic and prescription variables was facilitated using the data extraction for epidemiological research (DExtER) tool (88). This tool is described in the General Statistical Methods (section 2.5) in chapter 2.

Covariates in the analysis included demographic and lifestyle factors derived from patient records. These were selected based on what previous similar studies had adjusted for (78) (106) and from a literature search for conditions associated with both migraine and miscarriage. Missing values for smoking status, ethnic group and Townsend deprivation quintile were treated as a separate missing category for each variable. The absence of a record of any diagnosis in primary care data was taken to indicate the absence of these conditions. These included age (15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-50), latest body mass index (BMI) prior to conception (Underweight (<18.5), Normal weight (18.5-<25), Overweight (25-<30), Obese (≥30) and Missing), preconception smoking status (Non-smoker, Ex-smoker, Smoker and Missing), patient level Index of Multiple Deprivation quintiles (IMD;) and ethnicity (white, South Asian, Black, Other and Missing) and comorbidities defined by the presence of Read codes (depression, asthma, type 1 and Type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease (IBD), endometriosis,

systemic lupus erythematosus (SLE), chronic kidney disease (CKD) and polycystic ovary syndrome (PCOS); yes or no). These were derived from reviewing the literature for conditions associated with migraine, miscarriage, or both.

Baseline characteristics were described using appropriate summary statistics, mean and standard deviations for continuous variables, and frequencies and percentages for categorical and binary variables.

For the matched cohort study, log binomial regression was used to generate risk ratios and adjusted risk ratios to describe the relationship between migraine and risk of miscarriage. The model was adjusted for demographics, lifestyle factors and comorbidities. Pregnancies were used as the unit of analysis but as a woman could have multiple pregnancies, statistical inference from the log binomial regression model was based on cluster-robust standard errors to account for similarity of outcomes within a woman. Risk of early miscarriage (at 12 weeks or earlier) was also investigated as a secondary outcome.

For the nested case-control study, logistic regression was used to estimate odds ratios and 95% CI for the association between drugs used in the management of migraine and miscarriage. Drugs for migraine prescribed during the exposure window were examined alone and in combination. The regression model was adjusted for all the covariates and statistical inference from the logistic regression model was based on cluster-robust standard errors to account for similarity of outcomes within a woman. Prescription of drugs for migraine in the year before pregnancy were also included as covariate, as a proxy for disease severity, to mitigate any potential effect that the severity of migraine may have on the risk of miscarriage. The main analysis was repeated excluding pregnancies where the outcome was unknown. In another sensitivity analysis, to

investigate the effect of selection bias in the controls, the main analysis was repeated using controls sampled as risk sets, allowing women to serve as controls for multiple cases and allowing women whose pregnancies resulted in miscarriage to serve as controls in the period before their miscarriage.

All analysis was performed in Stata IC version 15 (StataCorp). Two-sided *p* values were considered to be statistically significant.

5.3.5 Patient and public involvement (PPI)

The PPI advisory group for the MuM-PreDiCT consortium, a group working across all four nations of the UK studying multiple long-term conditions in pregnancy, were involved in this work. This is a diverse group of women who have lived experience of having multiple long term conditions during pregnancy. Members of the group provided advice on the interpretation of the results of the study and made suggestions about how findings could be presented to clinicians and lay audiences. It is intended that patient and public representatives will continue to be involved in further work around communication of medication use in pregnancy that will arise from this thesis.

5.4 Results

1,526,061 pregnancies in the CPRD pregnancy register that occurred between 2000 to 2019 met data eligibility requirements. Once “uncertain” pregnancy episodes were removed from the dataset, 1,410, 329 pregnancies remained, representing 783,811 women. Of these, 193,208 pregnancies were pregnancies of women with migraine, representing 108,897 women (figure 1).

5.4.1 Baseline Characteristics

The distribution of demographic characteristics such as age and IMD were similar between the pregnancies of women with migraine and women without migraine.

However, the prevalence of obesity, depression, asthma, hypertension, hypothyroidism, endometriosis and PCOS was higher in the pregnancies of women with migraine (Table 5.1).

Similarly, the prevalence of obesity, depression, asthma, type 1 and 2 diabetes, hypertension, hypothyroidism, endometriosis and PCOS were higher in women with pregnancies that ended in miscarriage (Table 5.2).

5.4.2 Results of matched cohort

Eleven percent (10.8%, n=20,778) of pregnancies of women with migraine, regardless of treatment, ended in miscarriage compared to 10% in those without migraine (n=19,233). Having migraine was associated with an 8% higher risk of miscarriage (risk ratio (RR) 1.08, 95% confidence interval (CI) 1.06-1.10) and remained significant after adjustment for demographic factors, BMI, smoking and comorbidities (aRR 1.06 95% CI (1.04-1.08)). The risk ratios remained unchanged when restricting to early miscarriage (Table 5.3).

5.4.3 Results of Nested Case-Control

Of the 20,778 pregnancies ending in miscarriage, 722 (3.47%), 380 (1.83%), 173 (0.83%) and 733 (3,52%) were exposed to triptans, amitriptyline, beta blockers and NSAIDs respectively. Of the 40,122 matched pregnancies that did not end in miscarriage 1,100 (2.74%), 542 (1.35%), 294 (0.73%) and 780 (1.94%) were exposed to triptans, amitriptyline, beta blockers and NSAIDs respectively.

Exposure to triptans, amitriptyline and NSAIDs were associated with a significantly higher odds of miscarriage (aORs 1.24 (1.11-1.38), 1.25 (1.08-1.45) and 1.74 (1.57-1.93) respectively). Beta blockers were not associated with a higher risk of miscarriage (aOR 1.02 (0.82-1.27)) (Table 5.4).

Similar results were seen for the sensitivity analyses for early miscarriage, risk set sample and when removing those with unknown pregnancy outcome (Supplementary Tables 5.2-4).

A higher percentage of pregnancies that ended in miscarriage had individual and combinations of prescriptions during pregnancy compared to pregnancies not ending in miscarriage; triptans (2.9% v 2.5%), amitriptyline (1.4% v 1.1%) and NSAIDs (3% v 1.7%) individually, triptans and amitriptyline (0.24 v 0.17%), triptans and NSAIDs (0.3 v 0.1%), amitriptyline and NSAIDs (0.2 v 0.1%) and all three in combination (numbers too small to report). Odds ratios for being prescribed combinations in women with miscarriage versus women without miscarriage were higher for combinations of medications than for medications prescribed individually (figure 5.2).

Similar results were seen for the sensitivity analyses for early miscarriage, risk set sample and outcome unknown (supplementary tables 5.5-7).

5.5 Discussion

Results from the matched cohort study showed a small, but significant higher risk of miscarriage for pregnancies in women with migraine compared to those without. Findings from the nested case control analysis showed that women with migraine whose pregnancies ended in miscarriage had a higher odds of having been prescribed triptans, amitriptyline and NSAIDs than women with migraine whose pregnancies did not end in miscarriage. Women whose pregnancies ended in miscarriage also had significantly higher odds of being prescribed triptans and NSAIDs in combination and amitriptyline and NSAIDs in combination.

5.5.1 Strengths and limitations

This study has several strengths. The inclusion of 193,208 pregnancies of women with migraine means this is one of the largest cohort studies to assess the association of pre-pregnancy migraine with risk of miscarriage. We used a validated pregnancy register from a large database that is representative of the UK(86). We captured migraine diagnosis using Read codes and prescriptions of drugs used exclusively in the management of migraine. A considerable number of conditions that were known to be more prevalent in patients with migraine or associated with miscarriage were adjusted for in the analysis.

The prevalence of migraine in this study was 13.7%, the same as found in the study reported in chapter 3, which is lower than the expected prevalence (~20%), meaning that a small proportion of the comparator group in the cohort study likely also had migraine. While we excluded women with other headache disorders from the comparator group, some women with unrecorded migraine may have remained, potentially leading to an underestimation of the effect size. On the other hand, it is possible that we have selected women with more severe cases of migraine and, if severity of migraine is associated with an increased risk, the effect size for migraine and miscarriage may have been overestimated. The prevalence of miscarriage in the women eligible for inclusion in this study was 10%, again lower than the expected prevalence(87). This is likely to reflect early miscarriage that occurred before pregnancy was reported to the GP. This potentially means that the results cannot be applied to the risk of early miscarriage. However, it is unlikely there would be a difference in reporting of miscarriage between those with and without migraine or those who were or were not prescribed medications. Although there were a number of pregnancies without

a recorded outcome, we took this into consideration by undertaking a sensitivity analysis excluding these pregnancies.

Conducting the case-control analyses in women with migraine will have mitigated any potential confounding by indication. However, it may be that the severity of migraine impacts on the risk of miscarriage and also increased the chance of medication, (and particularly combinations of medications), being prescribed. We attempted to account for this by adjusting for use of these medications in the year prior to pregnancy. However, there may still have been residual confounding. Data were not available for prior history of miscarriages, paternal age and alcohol intake which are known to be related to miscarriage. As alcohol is a common migraine trigger, it may be that the migraine population have a lower consumption. Not being able to adjust for alcohol in the analysis may have lead to an underestimation of the risk ratio. It may also have been useful to consider the impact of the presence of aura on miscarriage, particularly as migraine with aura is associated with a higher vascular risk than migraine without aura (18), but only a small proportion of women with migraine had aura coded in the structured data. Reverse causality, whereby triptans or NSAIDs are taken in response to a miscarriage-associated migraine or miscarriage associated pain, must also be considered as a possible explanation. In addition, the decline in oestrogen associated with miscarriage (157) could be a potential trigger for a migraine episode (158).

As only prescription data were considered in this analysis, this only indicates that a prescription was issued and not dispensed (or taken) resulting in an over- or underestimation of these associations with miscarriage. We were also unable to determine the frequency of use of medications. In addition to this, over the counter medication was not captured in this analysis. As some NSAIDs and triptans are available over the counter in the UK, this may have had a particular effect on these

analyses, although it is likely that a pharmacist would recommend a pregnant woman with headaches consult her GP. Newer medications, such as CGRP inhibitors, were not prescribed in sufficient numbers during pregnancy to analyse their effects.

5.5.2 Findings in the context of other literature

Our findings of an association between migraine and miscarriage are in agreement with those of a Danish pregnancy cohort study which found an adjusted prevalence ratio of 1.10 (1.05-1.15) (106). While a Norwegian registry linkage study by Magnus et al showed a small non-significant association (aOR 1.02(0.98-1.05)) (151), this might be because of the low prevalence of migraine (3.14%), which is likely to be an under-ascertainment, meaning that their comparator population also included women with migraine. In a prospective cohort study of pregnancy planners, Crowe et al found a non-significant association of a similar magnitude between migraine and miscarriage (HR 1.03 (0.91-1.06)) (78). This study included 1,683 pregnant women with migraine, a much smaller cohort than our study and the other registry- based studies. This study relied on self-reported migraine diagnosis, which has the advantage of capturing cases that have not presented to health services. On the other hand, they did not use a validated criteria to confirm the diagnosis, so it is possible that other headache disorders were misclassified as migraine, potentially diluting the results. It is worth noting that, as around a third to a half of pregnancies are unplanned (79) (80), this cohort may not be representative of pregnant women in general. Taken together with the results from our studies, the totality of evidence would suggest a slightly higher risk of miscarriage in women with migraine.

This study helped to address a gap in the identified in chapter 4. The effect size of the association between triptans and miscarriage is comparable to those of a meta-analysis by Marchenko et al (159) identified in the umbrella review reported in Chapter 4, with

results showing a pooled OR of 1.27 (95% CI 0.58-2.79) when comparing triptan exposed women with migraine controls. This was based on the results of two small studies which included 360 women, which may account for the wide confidence intervals. Results from a nested case-control in a Canadian pregnancy register published since this meta-analysis, showed that, in comparison to healthy controls, women exposed to triptans during pregnancy had a higher odds of miscarriage (aOR: 1.63 (95% CI 1.34–1.98)). To account for indication bias, the authors of this study adjusted for migraine diagnosis during pregnancy or in the year prior to pregnancy in their analysis, meaning their migraine prevalence was around 2%. In addition, dispensed triptans were considered as the exposure, which perhaps will better reflect medication that was taken than prescribed medication (153).

No previous studies have considered amitriptyline treatment and its impact on miscarriage. Two studies have found a significant higher risk of miscarriage in patients with depression. One found an increase risk in disease-matched controls (RRR 1.3 (1.1-1.5)) (155) and the other found an increased risk in comparison to patients without depression (RR 1.47 (1.28-1.70)) (156), but this did not remain significant when the analysis was restricted to women with depression. Another study did not find any significant association (99). It is worth noting that the tricyclic dosage for the management of depression is higher than the dosage used in the management of pain such as that used for migraine prophylaxis.

A meta-analysis of the impact of NSAID exposure on the risk of miscarriage pooled the results of ten studies and shower a higher risk that was not statistically significant (OR 1.37 (0.99-1.88)). However, there was a significantly higher risk of miscarriage for NSAIDs when the analysis was restricted to studies where NSAIDs were taken around the time of conception (2.32 (1.16-4.66)) (154).

5.5.3 Biological plausibility

The potential vascular effects of migraine and drugs used to treat migraine should be considered, especially in relation to utero-placental perfusion.

Migraine is characterised by endothelial dysfunction, which may explain the increased risk of cardiovascular disease and stroke in patients with migraine (19) (16) Endothelial dysfunction has been suggested as one of the underlying causes of both miscarriage and pre-eclampsia(160). The well-established link between migraine and pre-eclampsia would appear to support this hypothesis (105).

Triptans are contraindicated in patients with cardiovascular disease and ischaemic stroke due to their serotoninergic vasoconstrictive properties (22). Miscarriage secondary to utero-placental hypoperfusion has been postulated with frequent triptan use (144). The serotoninergic effect of triptans, through their binding to 5HT receptors, has been suggested as a potential causal mechanism (159). A serotonergic mechanism has also been hypothesised to be involved in miscarriage (161). Some tricyclic antidepressants, in particular amitriptyline, have a serotonin inhibition effect, which may also explain the link between amitriptyline and miscarriage found in this study (153).

Although it is widely accepted that NSAIDs are contraindicated in late pregnancy (> 30 weeks) (162), due to premature closure of the ductus arteriosus, they are widely prescribed in early pregnancy (127) (163). Inhibition of prostaglandin synthesis by NSAIDs may also cause utero-placental hypoperfusion and miscarriage secondary to mal-implantation in early pregnancy (99) (164) (146) (165).

5.5.4 Implications for research and practice

Reverse causality and confounding by indication may have impacted the results of this study. Further research to address these limitations is proposed in the General Discussion.

Previous studies have found associations between migraine and other pregnancy complications, such as preterm birth(106) and low birth weight (105). It is less clear what, if any, impact medications have on these outcomes. There has been some suggestion of an association between triptans and low birth weight (148), whereas conflicting results have been found in studies of the impact of triptans on preterm birth, with both an association(148) and protective effect(148) being reported. Further research on the impacts of migraine medications on other pregnancy outcomes is warranted. This information is vital for women and clinicians to make informed decisions about care during pregnancy.

Much evidence around medications in pregnancy comes from observational studies which have associated limitations and biases. This lack of robust evidence, alongside the legacy of incidents such as thalidomide (52), has led to a precautionary, “better safe than sorry”, approach to prescribing during pregnancy (166). Recently, there have been calls for more nuanced discussions of risk during pregnancy (166) (167). An approach that supports shared decision making with women is warranted, for example through the use of decision aids (168).

5.6 Conclusion

In this large cohort study and nested case-control analysis, migraine and its treatment with triptans, NSAIDs and amitriptyline were found to be associated with a higher risk of miscarriage. Although measures were taken to account for the potential impact of

severity of migraine on the risk miscarriage, the effects of confounding by indication and potential for reverse causality must be considered when interpreting the results of this study. Further work is needed to understand the potential causative mechanisms.

Ethics statements

Ethical Approval

CPRD has ethics approval from the Health Research Authority to support research using anonymised patient data. The study has been approved by the Independent Scientific Advisory Committee for CPRD (reference: 22_001790)

Data availability statement

The data that support the findings of this study are available from CPRD but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Funding

This study was not specifically funded but was supported by the MuMPreDiCT consortium which is funded by the Strategic Priority Fund “Tackling multimorbidity at scale” programme (grant number MR/W014432/1) delivered by the Medical Research Council and the National Institute for Health Research in partnership with the Economic and Social Research Council and in collaboration with the Engineering and Physical Sciences Research Council.

This work was also supported by Health Data Research UK (HDRUK2023.0030), which is funded by UK Research and Innovation, the Medical Research Council, the British Heart Foundation, Cancer Research UK, the National Institute for Health and Care Research, the Economic and Social Research Council, the Engineering and

Physical Sciences Research Council, Health and Care Research Wales, Health and Social Care Research and Development Division (Public Health Agency, Northern Ireland), Chief Scientist Office of the Scottish Government Health and Social Care Directorates.

Dissemination to participants and related patient and public communities: We plan to disseminate these research findings to relevant stakeholders by presenting our findings at relevant conferences, through our PPI channels and by engaging with the media through press releases.

Contributors: KP, KN, FC and BW conceived the study, designed the initial analysis and defined definitions for exposures, covariates and outcomes. KP and KG undertook the analysis and all authors contributed to interpretation of an improvements to the analysis. KP drafted the manuscript and led the revision process. All authors critically reviewed the manuscript, approved the final version of the manuscript and agree to be accountable for all aspects of the work. KN is the guarantor for this work.

Competing Interests:

All authors have completed the Unified Competing Interest form (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

KN, the Corresponding author, affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ editions and any other BMJPGL products and sublicences such use and exploit all subsidiary rights, as set out in our licence."

Acknowledgements: We would like to thank the patient and public involvement representatives for the MuMPreDiCT group for their input to this study.

Table 5.1- Baseline characteristics for matched cohort of pregnancies according to exposed and unexposed to migraine

	Pregnancies of women with migraine	**Pregnancies of women without migraine**
Number of pregnancies	N=193,208	N= 193,208
Number of women	107,625	137,549
Age, median (IQR)	28.9 (24.2-33.2)	28.9 (24-2-33.2)
Age categories, n (%)		
15-19 years	15,267 (7.90)	15,529 (8.04)
20-24 years	39,302 (20.34)	39,153 (20.26)
25-29 years	54,708 (28.32)	54, 921 (28.43)
30-34 years	50,635 (26.07)	50,337 (26.05)
35-39 years	26,336 (13.63)	26,501 (13.72)
40-44 years	6,482 (3.35)	6,084 (3.15)
45-50 years	748 (0.39)	683 (0.35)
Ethnicity, n (%)		
White	93,339 (48.31)	88,480 (45.80)
South Asian	4,496 (2.33)	5,001 (2.59)
Black	5,964 (3.09)	4,928 (2.55)
Mixed Ethnicity	896 (0.46)	1,062 (0.55)
Others	2,934 (1.52)	2,622 (1.36)
Missing	85,579 (44.29)	91,115 (47.16)

IMD, n (%)		
1 (Most deprived)	42,631 (22.06)	41,229 (21.34)
2	33,708 (17.45)	35,214 (18.23)
3	31,973 (16.55)	33,523 (17.35)
4	27,933 (14.46)	28,022 (14.50)
5 (Least deprived)	29,803 (15.43)	28,726 (14.87)
Missing	27,160 (14.06)	26,494 (13.71)
BMI (kg/m^2), n (%)		
Underweight (<18.5)	6,659 (3.45)	6,997 (3.62)
Normal weight (18.5-<25)	80,932 (41.89)	83,543 (43.24)
Overweight (25-<30)	42,441 (21.97)	38,873 (20.12)
Obese (≥30)	35,205 (18.22)	28,042 (14.51)
Missing	27,971 (14.48)	35,753 (18.50)
Smoking status, n (%)		
Non-smoker	101,487 (52.53)	100,742 (52.14)
Ex-smoker	27,021 (13.99)	30,043 (15.55)
Smoker	53,854 (27.87)	55,682 (28.82)
Missing	10,846 (5.61)	6,741 (3.49)
Comorbidities, n (%)		
Asthma	18,696 (9.68)	12,510 (6.47)
CKD	177 (0.09)	131 (0.07)
Depression	25,034 (12.96)	15,073 (7.80)
Endometriosis	4845 (2.46)	2,715 (1.41)

Hypertension	2,780 (1.44)	1,751 (0.91)
Hypothyroidism	4,911 (2.54)	3,772 (1.95)
Hyperthyroidism	1,691 (0.88)	1,168 (0.60)
Inflammatory bowel disease	1,261 (0.65)	919 (0.48)
PCOS	8,549 (4.42)	6,293 (3.26)
SLE	243 (0.13)	154 (0.08)
Type 1 DM	868 (0.45)	860 (0.45)
Type 2 DM	712 (0.37)	569 (0.29)

Abbreviations: BMI: Body Mass Index, CKD: Chronic Kidney Disease, DM: Diabetes Mellitus, IBD: Inflammatory Bowel Disease, IQR: Interquartile Range, IMD: Index of Multiple Deprivation, PCOS: Polycystic Ovarian Syndrome, SLE: Systemic Lupus Erythematous

Table 5.2 Baseline characteristics of miscarriage cases and matched controls

	Women with pregnancies ending in miscarriage	**Women with pregnancies not ending in miscarriage**
Number of pregnancies	20,778	40,122
Number of women		
Age (years), median (IQR	30.8 (25.8-35.8)	30.2 (25.2-35.2))
Age categories, n (%)		
15-19 years	1,439 (6.93)	2,413 (6.01)
20-24 years	3,507 (16.88)	6,610 (16.47)
25-29 years	5,046 (24.29)	9,839 (24.52)

30-34 years	5,292 (25.47)	10,606 (26.43)
35-39 years	3,962 (19.07)	8,039 (20.04)
40-44 years	1,434 (6.90)	2,458 (6.13)
45-50 years	98 (0.39)	98 (0.47)
Ethnicity, n (%)		
White	10,224 (49.21)	19,597 (48.84)
South Asian	500 (2.41)	883 (2.20)
Black	695 (3.34)	1,226 (3.06)
Mixed Ethnicity	73 (0.35)	161 (0.40)
Others	398 (1.98)	703 (1.75)
Missing	8,888 (42.78)	17,552 (53.75)
IMD, n (%)		
1 (Most deprived)	4,348 (20.93)	8,478 (21.13)
2	3,671 (17.67)	6,912 (17.23)
3	3,540 (17.04)	6,637 (16.54)
4	3,126 (15.04)	5,946 (14.82)
5 (Least deprived)	3,315 (15.95)	6,552 (16.33)
Missing	2,778 (13.37)	5,597 (13.95)
BMI, n (%)		
Underweight (<18.5)	708 (3.41)	1,228 (3.06)
Normal weight (18.5-<25)	8,642 (41.59)	17,269 (43.04)
Overweight (25-<30)	4,591 (22.10)	8,986 (22.40)
Obese (≥30)	4,082 (19.65)	7,205 (17.96)
Missing	2,755 (13.26)	5,434 (13.54)

Smoking status		
Non-smoker	10,994 (52.91)	21,436 (53.43)
Ex-smoker	3,358 (16.16)	6,317 (15.74)
Smoker	5,787 (27.85)	11,014 (27.45)
Missing	639 (3.08)	1,355 (3.38)
Comorbidities, n (%)		
Asthma	2,150 (10.35)	3,852 (9.60)
CKD	26 (0.13)	45 (0.11)
Depression	2,959 (14.24)	5,096 (12.70)
Endometriosis	641 (3.08)	984 (2.45)
Hypertension	429 (2.06)	641 (1.60)
Hypothyroidism	644 (3.10)	1,106 (2.76)
Hyperthyroidism	220 (1.06)	365 (0.91)
Inflammatory bowel disease	163 (0.78)	282 (0.70)
PCOS	1,071 (5.15)	1,773 (4.42)
SLE	30 (0.14)	54 (0.13)
Type 1 DM	124 (0.60)	158 (0.39)
Type 2 DM	122 (0.59)	156 (0.39)

Abbreviations: BMI: Body Mass Index, CKD: Chronic Kidney Disease, DM: Diabetes Mellitus, IBD: Inflammatory Bowel Disease, IQR: Interquartile Range, IMD: Index of Multiple Deprivation, PCOS: Polycystic Ovarian Syndrome, SLE: Systemic Lupus Erythematous

Table 5.3: Risk ratio (RR) and 95% CI of miscarriage for pregnancies of women with or without migraine.

	Pregnancies of women with migraine (n=193,208)	Pregnancies of women without migraine (n=193,208)
All miscarriage		
Number of miscarriages, n (%)	20,778 (10.8)	19,233 (10.0)
Unadjusted RR (95% CI)	1.08 (1.06-1.10)	
Adjusted* RR (95% CI)	1.06 (1.04-1.08)	
Early Miscarriage		
Number of early miscarriages, n (%)	18,943 (9.8)	17,568 (9.1)
Unadjusted RR (95% CI)	1.08 (1.06-1.10)	
Adjusted* RR (95% CI)	1.06 (1.04-1.08)	

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of pregnancy, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD and PCOS.

Table 5.4: Odds ratios and 95% CI for miscarriage by type of medication used for migraine

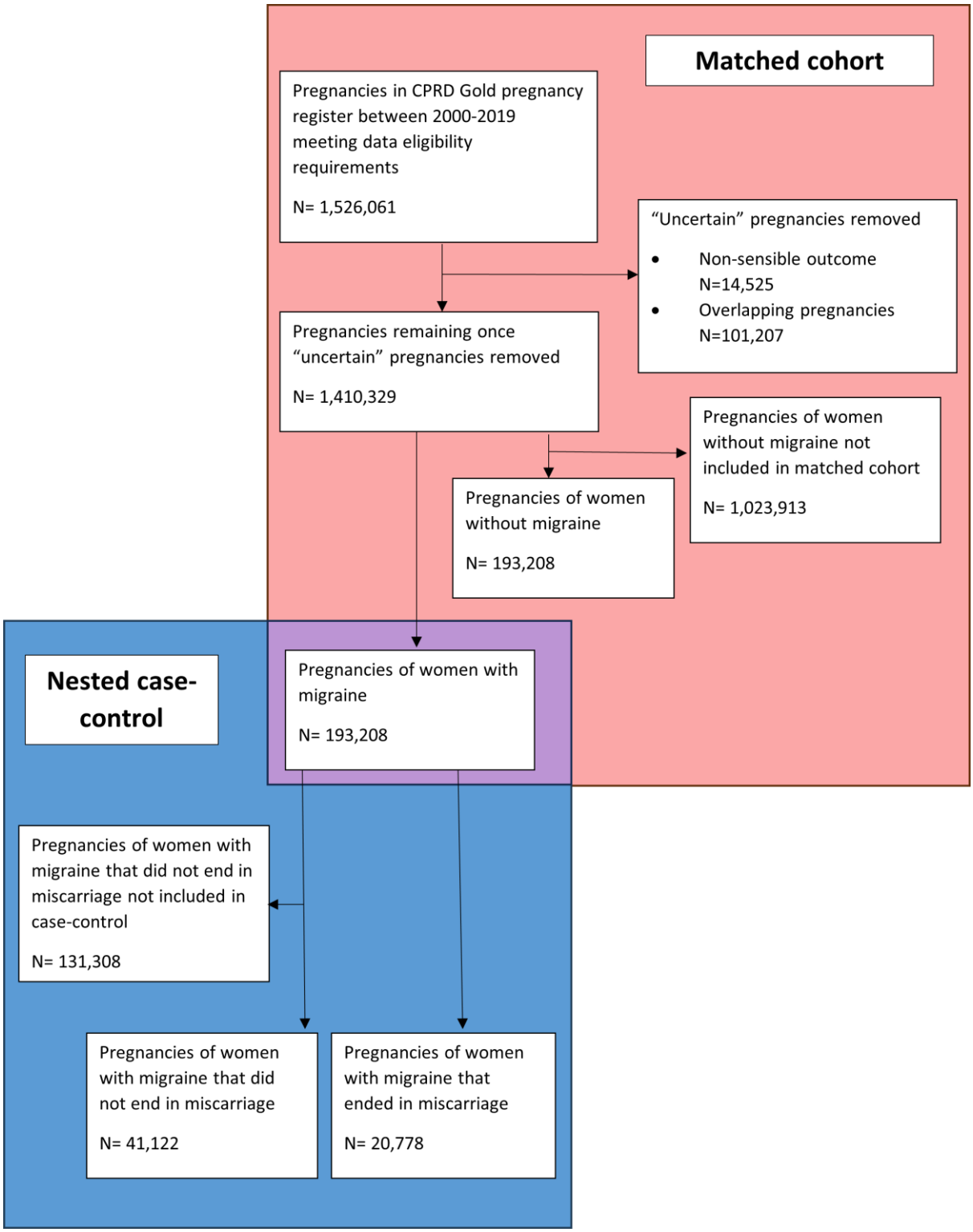
	Migraine patients whose pregnancies ended in miscarriage n= 20,778	**Migraine patients whose pregnancies did not end in miscarriage n= 40,122**
Exposure to triptans		
Pregnancies exposed to triptan n (%)	722 (3.47)	1,100 (2.74)
Unadjusted OR (95% CI)	1.28 (1.16-1.41)	
Adjusted* OR (95% CI)	1.24 (1.11-1.38)	
Exposure to Amitriptyline		
Pregnancies exposed to amitriptyline n (%)	380 (1.83)	542 (1.35)
Unadjusted OR (95% CI)	1.36 (1.19-1.56)	
Adjusted* OR (95% CI)	1.25 (1.08-1.45)	
Exposure to Beta Blockers		
Pregnancies exposed to beta blockers n (%)	173 (0.83)	294 (0.73)
Unadjusted OR (95% CI)	1.14 (0.94-1.38)	
Adjusted* OR (95% CI)	1.02 (0.82-1.27)	
Exposure to NSAIDs		
Pregnancies exposed to NSAIDs n (%)	733 (3.52)	780 (1.94)
Unadjusted OR (95% CI)	1.84 (1.66-2.04)	

Adjusted* OR (95% CI)	1.74 (1.57-1.93)

Abbreviations: NSAIDs: Non-steroidal anti-inflammatories, CI: confidence intervals, OR: odds ratios

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, asthma, depression, year of pregnancy, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

Figure 5.1: Study flow diagram



Flow chart to illustrate how study population for the matched cohort were derived from pregnancies occurring in the CPRD GOLD pregnancy register between 2000 and 2019

and how population for the matched cohort were derived from the cohort of women with a pre-pregnancy diagnosis of migraine

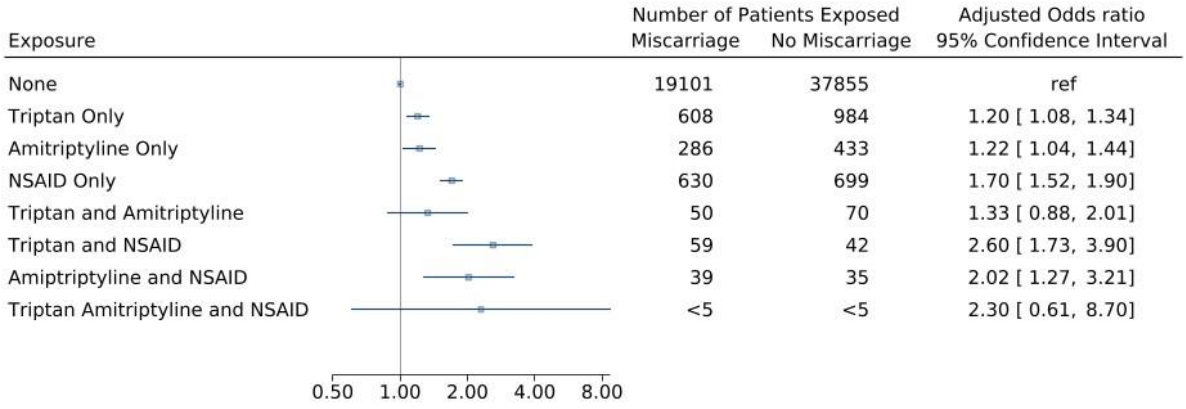


Figure 5.2: Results of logistic regression of association between combinations of medications and miscarriage

Logistic regression performed to examine association between medications (prescribed alone and in combination) and miscarriage in women with pre-pregnancy migraine in the CPRD pregnancy register 2000-2019. The regression model was adjusted for age, latest body mass index (BMI) prior to conception, preconception smoking status, patient level Index of Multiple Deprivation quintiles and ethnicity, comorbidities (depression, asthma, type 1 and Type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease (IBD), endometriosis, systemic lupus erythematosus (SLE), chronic kidney disease (CKD) and polycystic ovary syndrome (PCOS) and prescription of drugs for migraine in the year before pregnancy and statistical inference from the logistic regression model was based on cluster-robust standard errors

Chapter 6 : Migraine and risk of adverse obstetric outcomes: a matched cohort study of UK linked electronic health records

6.1 Introduction

This study further investigates the inconsistent findings from the umbrella review reported in chapter 4 around how migraine affects the risk of low birth weight and small for gestational age and how this relates to preterm birth. The updated recent systematic review reported in chapter 4 found an association between migraine and preterm birth (pooled adjusted odds ratio (aOR) 1.32 (95% confidence interval (CI) 1.15-1.51)), although there was some indication of potential publication bias. This pooled result was driven by three large cohort studies from Denmark, Taiwan and the United States, which found a 17-24% increased risk of preterm birth associated with migraine (106) (169) (170). The Danish and Taiwanese studies drew their migraine cases from those diagnosed in secondary care and reported a prevalence of <4%, suggesting they captured only the most severe cases (106) (169). The US study was an analysis of the Nurse's Health Study II cohort, which relied on self-reported migraine diagnosis (prevalence 11%) and pregnancy outcomes (170). None of these studies differentiated between spontaneous and medically indicated preterm birth. Other, smaller studies that have reported on this have found inconsistent results (171) (172).

The updated systematic review found an association between migraine and low birth weight, when the results of studies reported unadjusted odds ratios were pooled OR 1.18(1.11-1.24) but no significant association was found when adjusted odds ratios were pooled (aOR 1.27 (0.89-1.82)). An association between migraine and small for gestational age was found when adjusted odds ratios were pooled (aOR 1.08 (1.01-1.15)), but not when unadjusted odds ratios were pooled (OR 1.08 (0.95-1.23)) (173). Further investigation of these inconsistent findings, and how they relate to preterm birth, is warranted.

Previous studies have reported 16-20% increase in the risk of caesarean delivery associated with migraine. No study distinguished between emergency and elective caesarean(106) (174), despite these having different indications(175) and associated risks(176) No significant association between migraine and stillbirth has been described (106, 177, 178).

The aim of this study is to investigate the relationship between migraine and preterm birth (including spontaneous versus medically indicated), low birth weight, small for gestational age, mode of delivery (including emergency versus elective) and stillbirth. The study reported in this chapter was conducted to address, in part, the final objective: To describe the risk of adverse pregnancy outcomes, comparing i) women with and without migraine using the Hospital Episode Statistics (HES) maternity tail.

6.2 Methods

6.2.1 Study design and data source

A retrospective cohort study of pregnant women with migraine matched to pregnant women without migraine was conducted to assess the association of pre-pregnancy migraine with delivery outcomes.

Data from this study came from Clinical Practice Research Datalink (CPRD) GOLD linked to Hospital Episode Statistics (HES) maternity tail.

CPRD GOLD is a dataset of electronic health records (EHRs) from General Practices (GPs) using Vision software. It contains data on patient demographics, diagnoses, symptoms and prescriptions and covers 7% of the UK population across almost 1000 practices(83).

The HES Admitted Patient Care dataset comprises data on all admissions to National Health Service (NHS) hospitals. When a birth admission occurs in an NHS hospital, delivery episodes are generated in the mother's records. This includes a maternity tail which has information about birth outcomes including method of onset of labour, live and still birth, length of gestation and birth weight (90).

6.2.2 Study population

The study population was selected from patients within the CPRD primary care dataset who met the following data quality requirements: 1) having an acceptable patient flag within CPRD GOLD (which indicates sufficient data quality) 2) prior to pregnancy, a minimum of 1 year of registration with a practice or 1 year of registration after the up-to-standard date of the registered practice, whichever was later. Women aged 15-50 with a singleton delivery recorded in HES maternity tail between January 1, 2000 and December 31, 2019 were eligible for inclusion. As it was anticipated that some women with migraine would not have this coded in their records, we excluded women with a history of headaches from the potential control population.

6.2.3 Exposure and outcome definitions

Migraine, the exposure, was defined by the presence of a Read code indicating a diagnosis or a single prescription of medications used exclusively in the management of migraine in UK practice (triptans, migraine combination treatments (acetylsalicylic acid or paracetamol, combined with codeine, caffeine and/or an antiemetic) or calcitonin gene-related peptide (CGRP) inhibitors) at any time prior to the pregnancy start date. Exact matching on maternal age (±1 year) at the start of pregnancy and year of pregnancy was used to match pregnancies of women with migraine to pregnancies of women without migraine. Women with a history of any headache were excluded from

the unexposed population as it was anticipated there would be a number of women with a history of migraine who did not have it recorded.

Preterm birth was defined by having a gestational age less than 37 weeks as recorded in the maternity tail or ICD 10 codes for preterm birth in the secondary care records. Where gestational age was recorded, preterm birth was further sub-divided into very preterm (<32 weeks) and extremely preterm (<28 weeks). Where onset of delivery was recorded in the maternity tail, preterm birth was also sub-divided into spontaneous or medically indicated (where onset was by caesarean or medical or surgical induction).

Low birth weight was defined as having a birthweight of less than 2500g recorded in the HES maternity tail. This was further sub-divided into very low birth weight (<1500g) and extremely low birth weight (<1000g). Birthweight was recorded in the maternity tail, but no ICD 10 codes were available for low birth weight in the secondary care records.

Small for gestational age was defined as birthweight below the 10th centile for gestational age and sex as compared to international standards. Birthweight, gestational age and sex were into software tools from the INTER-GROWTH 21st project to calculate the weight for gestational age centile.

Mode of delivery was classified using the delivery method recorded in the maternity tail, ICD10 and OPCS codes into the following categories: vaginal delivery, emergency caesarean, elective caesarean and unknown.

Stillbirth was defined by the birth status variable in the maternity tail.

6.2.4 Statistical methods

Data related to delivery outcomes and secondary care diagnoses and procedures were obtained from HES Admitted Patient Care provided by CPRD. Extraction of primary care recorded demographic, lifestyle, diagnostic and prescription variables was facilitated using the data extraction for epidemiological research (DExtER) tool(101).

Deliveries were the unit of analysis for this study. Summary statistics for baseline characteristics stratified by exposure to migraine prior to pregnancy. Frequencies and percentages were reported for binary variables. Median and interquartile range were reported for non-normally distributed continuous variables.

Logistic regression was performed for binary outcomes (preterm, low birth weight, SGA, stillbirth) and multinomial logistic regression was performed for categorical outcomes (mode of delivery and type of preterm) to provide unadjusted and adjusted relative risk ratios. Covariates were selected based on what previous similar studies (106) (169) (170) (171) have adjusted for and from a literature search for conditions associated with both migraine and adverse obstetric outcomes.

Models were adjusted for age (15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-50 years), year of pregnancy, ethnicity (white, South Asian, black, other and missing), Index of Multiple Deprivation (IMD) in quintiles (1 – most deprived, 2, 3, 4, 5 – least deprived and missing), latest BMI prior to conception (underweight (<18.5), normal weight (18.5-<25), overweight (25-<30), obese (≥30) kg/m^2 and missing), pre-conception smoking status (non-smoker, ex-smoker, smoker and missing), pre-existing diabetes asthma, systemic lupus erythematous, thyroid disorders, hypertension, chronic kidney disease, gestational diabetes and pre-eclampsia. As a woman could have multiple

pregnancies, statistical inference from the log binomial regression model was based on cluster-robust standard errors to account for similarity of outcomes within a woman.

To account for missing variables, complete case analysis (CCA) and analysis assuming missing to mean absence of outcome was performed.

All analysis was performed in Stata version 17. Two-sided p values were considered statistically significant.

6.3 Results

There were 428,217 pregnancies of 317,016 women meeting data quality criteria with a linked delivery in the HES maternity tail. Of these, 46,560 (10.9%) had a history of migraine prior to pregnancy (figure 6.1).

6.3.1 Baseline Characteristics

The distribution of age and IMD were similar in the deliveries of women with and without migraine. However, a higher proportion of the women with migraine were white and fewer were from Black, South Asian, and other ethnic groups. The prevalence of obesity, smoking, pre-existing diabetes, gestational diabetes and pre-eclampsia were also higher in pregnancies of women with migraine (table 6.1).

6.3.2 Delivery outcomes: Preterm birth

3,519 (7.56%) deliveries of women with migraine were preterm compared to 3,331 (7.15%) of those without. In those deliveries with gestational age recorded, 890 (1.91%) and 409 (0.88%) of deliveries of women with migraine were very preterm and extremely preterm respectively, compared to 954 (2.05%) and 363 (0.78%) of those without migraine respectively (table 6.2).

There was no significant association between migraine and preterm birth in the complete case analysis (adjusted risk ratio (aRR) 1.03 (95% confidence intervals (CI) 0.97-1.09)). A small significant increase in the odds of preterm birth was found in the analysis treating missingness of gestational age as absence of preterm birth (RR 1.06 (95% CI 1.01-1.12)) but this did not remain significant in the adjusted analysis. No significant association was found between migraine and very preterm birth in either analysis (CCA: aRR 0.96 (95% CI 0.86-1.06) and when assuming missing gestational age as absence of very preterm birth: aRR 0.99 (95% CI 0.85-1.14)). However, there was a significant association between migraine and extremely preterm birth in the adjusted analysis (CCA: aRR 1.18 (95% CI 1.01-1.37) and when assuming missing gestational age as absence of extremely preterm birth: aRR 1.17 (95% CI 1.002-1.36)) (table 6.3 & 6.4).

Of the deliveries of women with migraine that were preterm, 1,397 (39.7%) were medically indicated and 1,616 (45.9%) were spontaneous, compared to 1,202 (36.1%) and 1,664 (50.0%) of those without migraine. Compared to term birth, migraine was associated with an increased risk of medically indicated preterm birth (aRR 1.11 (95% CI 1.02-1.20)), but not spontaneous preterm birth (aRR 0.98 (0.98 (95%CI 0.91-1.06)). (table 6.3).

6.3.3 Low birth weight

2,287 (4.91%) babies of women with migraine were low birth weight compared to 2,201 (4.73%) babies of those without migraine. 410 (0.88%) and 215 (0.46%) babies of women with migraine were very low birth weight and extremely low birth weight, respectively, compared to 394 (0.85%) and 203 (0.44%) babies of women without migraine, respectively (table 2). No significant association was found between migraine and low birth weight (CCA: aRR 1.02 (95% CI 0.95-1.08), treating absence of

birthweight as normal birthweight: 1.01 (95% CI 0.95-1.08)), very low birth weight (CCA: aRR 0.99 (95% CI 0.86-1.14), treating absence of birthweight as birthweight > 1500g: 0.99 (95% CI 0.85-1.14)) or extremely low birth weight (CCA: aRR 1.01 (95% CI 0.83-1.23), treating absence of birthweight as birthweight > 1000g: 1.00 (95% CI 0.83-1.22)) (table 6.3 & 6.4).

6.3.4 Small for gestational age

1,689 (3.63%) babies of women with migraine were small for gestational age compared to 1,771 (3.80%) babies of women without migraine. No significant association was found between migraine and small for gestational age (CCA: aRR 0.96 (95% CI 0.89-1.03), treating missing as gestational age >10th centile: aRR 0.96 (95% CI 0.89-1.03)) (table 6.3 & 6.4).

6.3.5 Mode of delivery

28,935 (62.15%) of the deliveries of women with migraine were vaginal compared to 28,959 (62.2%) of those without. Of the deliveries of women with migraine, 5,097 (10.95%) and 5,699 (12.24%) were elective Caesarean and emergency Caesarean, respectively compared to 4,704 (10.10%) and 5,579 (11.98%) of deliveries of women without migraine. In the complete case analysis, migraine was associated with an increased risk of elective caesarean delivery (RR 1.08 (95% CI 1.04-1.14)), compared to vaginal delivery but this did not remain significant after adjustment (aRR 1.04 (95% CI 0.99-1.09)). There were similar findings in the analysis that treated missing mode of delivery as vaginal delivery. No significant association was found between migraine and risk of emergency section (CCA: aRR 1.01 (95% CI 0.97-1.06), treating missing as vaginal delivery: aRR 1.03 (95% CI 0.98-1.07)) (table 6.3 & 6.4).

6.3.6 Stillbirth

182 (0.39%) of babies of women with migraine were stillborn compared to 177 (0.38%) of babies of women without migraine. No significant association was found between migraine and stillbirth (aRR 1.00 (95% CI 0.81-1.24)) (table 6.3).

6.4 Discussion

In this study, migraine was associated with an increased risk of extremely preterm delivery and medically indicated preterm delivery.

6.4.1 Strengths and Limitations

This study has several strengths. It included over 40,000 pregnancies of women with migraine drawn from a database representative of the UK population, meaning it is one of the largest studies to examine delivery outcomes in the migraine population. As over 97% of births nationally occur in NHS hospitals (179), the sample will also be representative of deliveries in the UK. Using linked primary care data to capture migraine diagnosis codes and prescriptions meant that we were able to include a considerable number of migraine cases than have been reported in previous studies that relied on secondary care diagnosis (169) (106). We were able to distinguish between spontaneous and medically indicated preterm delivery, giving more indication as to the underlying mechanisms behind the association with migraine. As far as we are aware, this is the first study in the migraine population to separate elective and emergency Caesarean, which is important, again due to differing indications(175) and associated risks(176). We accounted for important factors associated with preterm birth including adjusting for maternal age, smoking status, and maternal conditions prior to and during pregnancy. We restricted the analysis to singleton delivery, as multiples are at higher risk of preterm birth and intrauterine growth restriction (180).

However, despite including primary care diagnosis, the prevalence of migraine found in this study was 10.9%, which was lower than expected (~20%) (6). This means that there were potentially women with unrecorded migraine in the control group. We attempted to mitigate this by excluding women with a diagnosis of other headache disorders, but nevertheless, there may be women remaining who had never consulted their GP for headache. Furthermore, black, South Asian and other ethnic groups appeared to be under-represented in the migraine cohort. This may reflect true differences in prevalence between ethnic groups, as reported in previous studies (181). On the other hand, there is evidence that certain ethnic groups face barriers to care for headache disorders (182), which may have impacted these results. For example, African American people with migraine have been found to experience barriers to accessing specialty headache clinics (182), despite prevalence of migraine being higher in this group (183). We were unable to examine the impact of migraine subtypes or severity on the outcomes. Migraine with aura has been found to be associated with a higher vascular risk (18). However, aura status was only present in the structured data in a small proportion of women.

Despite being able to determine whether preterm delivery was medically-indicated, no information was available as to what the indication was and whether it was for maternal or fetal reasons. Small for gestational age is often used as a proxy for fetal growth restriction, or failure of the fetus to reach its growth potential. (48) However, SGA also does not capture deceleration of fetal growth throughout pregnancy. A baby who is above the 10th centile for gestational age at birth may still have had restricted growth if there was a drop in their estimated fetal weight percentiles throughout pregnancy (184). Furthermore, a fetus' growth potential is influenced by factors such as parity, parental height and ethnicity meaning babies may be below the 10th centile because they are constitutionally small(185).

Missingness of data affected all outcomes for this study and ranged from around 14-30%. This was addressed by conducting both complete case analysis and assuming that any missing data for the outcomes to mean absence of the outcome. Both types of sensitivity analysis showed that this made little difference to the results. Unmeasured confounders may have impacted on the results. Covariates that were not adjusted for, and which have been linked to preterm birth and intrauterine growth restriction, include congenital anomalies, maternal infections, short interpregnancy intervals and anaemia (186). In particular, there is some evidence to suggest that migraine is associated with a risk of congenital anomalies (64), which may have impacted on some of the associations found. Finally, multiple outcomes were studied in the analysis, increasing the likelihood that statistically significant results were found by chance(187).

6.4.2 Findings in the context of other literature

The findings of no significant association between migraine and preterm birth overall are not consistent with those of the umbrella review and updated systematic review reported in chapter 4. These were largely driven by the results of two other large database analyses and a prospective cohort study. A Danish birth cohort study reported that migraine was associated with a higher risk of preterm (aPR 1.21(1.13-1.30)) and very preterm (aPR 1.35(1.14-1.60)) birth (106). A Taiwanese study also found a higher odds of preterm birth (aOR 1.24 (1.13-1.39) (169). It is worth noting that both studies relied on secondary care-recorded diagnosis of migraine. This is likely to reflect more severe cases of migraine. It could be that more severe migraine is associated with preterm birth and this may be the reason that we did not find a higher overall risk of preterm birth with migraine in our study.

On the other hand, a US study of a cohort of nurses, which relied on self-report of (physician-diagnosed) exposures and outcomes, also found a significantly higher risk of

preterm birth in women with migraine (aRR 1.17 (1.01-1.35) (without aura), aRR 1.17 (1.01-1.36) (with aura)) (170). This study reported a similar prevalence to ours (11.3%). A possible explanation for this could relate to differences in practices between countries and over time. This study enrolled women between 1989 to 2009 and surveyed them about previous pregnancies (which could have occurred earlier than the enrolment period). Preterm birth increased in the US during the 1990-2000s, a trend that was attributed to an increase in obstetric interventions over time. This was followed by a drive to reduce non-medically indicated or elective deliveries prior to 39 weeks gestation (188) (189). However, as none of these large studies differentiated between spontaneous or indicated preterm birth, it is not possible to judge whether this could account for differences in findings.

The small studies that differentiated between spontaneous and medically indicated preterm birth reported inconsistent findings. Findings from a US study investigating the relationship between migraine with comorbid mood disorder and pregnancy outcomes found no significant association with migraine alone and spontaneous (aOR 0.79(0.51-1.26)) or medically indicated (aOR 1.03(0.57-1.85)) preterm birth. However, this study included a relatively small number of participants with migraine (N=550) (172). On the other hand, another US study found that migraine was associated with a higher odds of both medically indicated (aOR 1.44 (1.08-1.89)) and spontaneous preterm birth (aOR 1.40 (1.11-1.77)) (171). This study reported a prevalence of migraine of 19.1%, suggesting a more complete capture than our study. It is possible that our study included a number of women with unrecorded migraine in the unexposed group, potentially diluting any association between migraine and preterm birth.

In contrast to the findings of this study, two previous studies have reported a significant increase in the risk of low birth weight. Skajaa et al reported a 14% increase in the risk

(aPR 1.14 (1.06-1.23)) (106), and Chen et al reported a 16% increase (aOR 1.16(1.03-1.31)) (169). These are the same studies which found an association between migraine and preterm birth. As neither study adjusted for gestational age, it is likely that preterm birth was driving this association.

No single study has found an association between migraine and small for gestational age. However, a meta-analysis of studies found a small significant association (pooled aOR 1.08 (1.01-1.15)) (173).

The findings in this study of no overall association between migraine and caesarean delivery contrast with the findings of the Danish and Taiwanese cohort studies which found an aPR 1.20(1.15-1.25) and aOR 1.16 (1.07-1.24) respectively (106) (169). Again, this may reflect a difference in the severity of migraine in the populations studied.

The finding of no significant association between migraine and stillbirth is in keeping with the findings from other studies (106) (171).

6.4.3 Interpretation

The findings of an association between migraine and medically indicated preterm birth, but not for spontaneous preterm birth suggest that other underlying risk factors may be at play. There is a well-established association between migraine and pre-eclampsia (173) and in severe cases of pre-eclampsia, delivery may be medically indicated prior to 37 weeks (190). the association remained when adjusting for pre-eclampsia in the models, although, confounding may exist after adjustment. Other pre-existing conditions that are commonly comorbid with migraine and are associated with preterm birth include asthma, hypertension, CKD, hyperthyroidism and SLE (44). These were also adjusted in the adjusted models. These factors may also account for the association

found between migraine and elective caesarean delivery as no significant association remained after adjustment for them. Other risk factors for medically indicated preterm birth that were not adjusted for include placental complications such as placental abruption (45). There has been some suggestion of an association between migraine and placental abruption, so further investigation of this is warranted. However, this is a rare pregnancy complication, affecting 0.4-1% of pregnancies (191), so may not account for all the remaining association. Fetal indications for preterm delivery must also be considered. Although no association was found between migraine and SGA babies, as discussed above, SGA is an imperfect proxy for fetal growth restriction. As migraine is associated with pre-eclampsia, which can lead to fetal growth restriction (192), this may be another mechanism whereby migraine could lead to indicated preterm delivery. Fetal distress, another fetal indication for preterm delivery, was not measured in this study.

The finding of an increased risk of extremely preterm delivery has not been reported previously. Of note, the association only became significant in the adjusted analysis. Further exploration was conducted to identify which covariates contributed to this. When ethnicity was adjusted for, the odds ratio for extremely preterm birth went from 1.12 (0.96-1.30) in the unadjusted model to 1.20 (1.03-1.40). This reflected a threefold increase in the odds of extremely preterm delivery in Black and mixed ethnicity women and a fourfold increase in women of South Asian ethnicity compared to women of white ethnicity. Black and South Asian women are more likely to have preterm birth in the UK (193). As discussed above, it is unclear whether the under representation of non-white ethnic groups in the migraine cohort is reflective of the true prevalence in these groups. If there is a systematic underreporting of migraine in some ethnic groups, this may have biased the association with preterm birth.

6.4.4 Implications for future research

The underlying medical indications for preterm delivery in women with migraine should be further investigated. The role of maternal factors such as pre-eclampsia and long-term conditions commonly comorbid with migraine could be explored. Although no association was found between migraine and SGA babies, as discussed above, there are issues with the definition of SGA used in this study. Fetal indications for preterm delivery in women with migraine should, therefore, still be considered. There is a well-established association between migraine and pre-eclampsia, hypothesised to be related to common pathophysiological mechanisms between the two conditions including a pro-inflammatory state, endothelial dysfunction and hypercoagulability. It is therefore suggested that women with migraine have poor vascular compensatory mechanisms to stressors such as pregnancy, meaning complications such as pre-eclampsia are more likely (30). Pre-eclampsia is associated with placental insufficiency (where the placenta is unable to transfer enough blood to the fetus) (194), which is a major cause of intrauterine growth restriction(195). Additionally, previous studies have reported a link between migraine and SGA (173). The association between migraine and intrauterine growth restriction could be investigated further using more reliable measures of intrauterine growth restriction such as customised growth charts(196) (which take into account factors such as parity, maternal and paternal height and ethnicity) or measuring deceleration of growth throughout pregnancy(184).

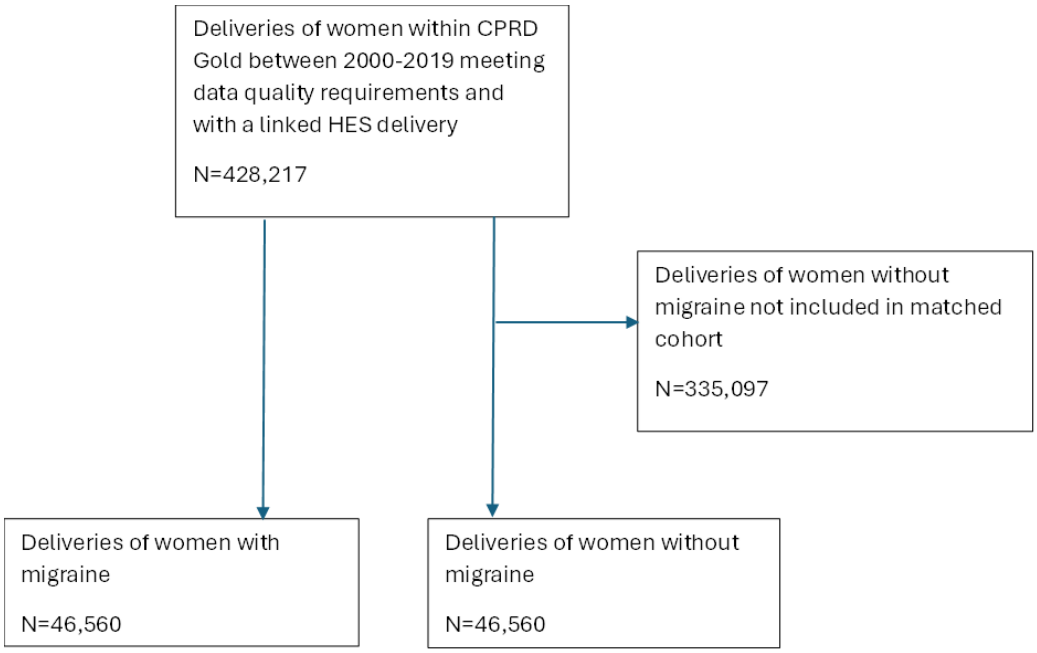
Further research into the impact of severity and type of migraine on delivery outcomes is warranted. It may be that the differences between the findings of this study and previous studies are due to the differences in severity of migraine in the populations studied. Severity of migraine likely impacts the choices for migraine treatment during pregnancy, which may, in turn, contribute to the risk of adverse obstetric outcomes. As

migraine with aura has been found to confer higher vascular risk (18), further investigation into the relationship between migraine type and delivery outcomes may also be useful. There are limitations with using retrospective, routinely collected healthcare data to answer these questions, namely, that aura status, severity and frequency of migraine attacks, resolution of symptoms with pregnancy are poorly recorded and prescription data often do not contain information about indication; timing, duration or frequency of use; or whether medication was complied with. Prospective studies, whereby women with are followed up from the pre-conception period throughout pregnancy, could be undertaken to address this. Potential future work is described further in the General Discussion.

6.5 Conclusion

In this large delivery cohort study, migraine was associated with an increased risk of extremely preterm and medically indicated preterm delivery. Further work is required to understand the potential reasons behind these associations.

Figure 6.1: Study flow diagram



Flow chart to illustrate how study population for matched cohort was derived from deliveries of women within CPRD GOLD between 2000 and 2019 with linked HES delivery

Table 6.1: Baseline characteristics of pregnancies of women with migraine and matched cohort of women without migraine

	Pregnancies of women with migraine	**Pregnancies of women without migraine**
Number of pregnancies	46,560	46,560
Number of women	34,506	42,851
Maternal Age, median (IQR)	29.9 (25.7-34.0)	30.0 (25.9-33.9)
Ethnicity, n (%)		
White	42,199 (90.6)	39,233 (84.3)
South Asian	1,553 (3.3)	2,349 (5.1)
Black	878 (1.9)	1,457 (3.1)
Mixed Ethnicity	437 (0.9)	536 (1.2)
Others	910 (2.0)	1,863 (4.0)
Missing	583 (1.3)	1,122 (2.4)
IMD, n (%)		
1 (Most deprived)	8,502 (18.3)	8,656 (18.6)
2	8,727 (18.7)	8,679 (18.6)
3	9,160 (19.7)	9,125 (19.6)
4	9,021 (19.4)	8,650 (18.6)
5 (Least deprived)	10,286 (22.1)	9,415 (20.2)
Missing	864 (1.9)	2,035 (4.4)
BMI (kg/m^2), n (%)		
Underweight (<18.5)	1,561 (3.4)	1,726 (3.7)

Normal weight (18.5-<25)	20,246 (43.5)	21,325 (45.8)
Overweight (25-<30)	10,224 (22.0)	9,716 (20.9)
Obese (≥30)	8,158 (17.5)	6,393 (13.7)
Missing	6,371 (13.7)	7,400 (15.9)
Smoking status, n (%)		
Non-smoker	24,470 (52.6)	25,968 (55.8)
Ex-smoker	7,681 (16.5)	6,863 (14.7)
Smoker	12,818 (27.5)	11,284 (24.2)
Missing	1,591 (3.4)	2,445 (5.3)
Maternal Morbidities, n (%)		
Asthma	10,944 (23.5)	7,098 (15.2)
Chronic kidney disease	20 (0.04)	22 (0.05)
Gestational diabetes	1,284 (2.8)	1,181 (2.5)
Hypertension	383 (0.82)	236 (0.51)
Thyroid disorder	646 (1.4)	551 (1.2)
Pre-existing diabetes	188 (0.4)	150 (0.32)
Pre-eclampsia	1,074 (2.3)	952 (2.0)
Systemic lupus erythematous	31 (0.07)	14 (0.03)

N=number of deliveries

BMI= Body Mass Index

IMD= Index of Multiple Deprivation

Table 6.2: Frequencies and percentages of delivery outcomes for deliveries of women with and without migraine

	Pregnancies of women with migraine	**Pregnancies of women without migraine**
Gestational age at delivery, n (%)		
Term (≥37 weeks)	30,715 (65.97)	30,569 (65.66)
Preterm Birth (<37 weeks gestational age or coded as preterm in record)	3,519 (7.56)	3,331 (7.15)
Very preterm (<32 weeks)	890 (1.91)	954 (2.05)
Extremely preterm (<28 weeks)	409 (0.88)	363 (0.78)
Coded as preterm in record, no gestational age recorded	717 (5.50)	639 (4.80)
Gestational age missing (no preterm code)	12,326 (26.47)	12,660 (27.19)
Onset of preterm birth, n (%)		
Spontaneous preterm birth	1,616 (45.9)	1,664 (50.0)
Medically indicated preterm birth	1,397 (39.7)	1,202 (36.1)
Onset of delivery not recorded	506 (14.4)	465 (14.0)
Birthweight, n (%)		
Birthweight ≥2500g	36,320 (78.01)	36,042 (77.41)
LBW (<2500g)	2,287 (4.91)	2,201 (4.73)
VLBW (<1500g)	410 (0.88)	394 (0.85)
ELBW (<1000g)	215 (0.46)	203 (0.44)
Missing	7,953 (17.08)	8,317 (17.86)

Birthweight for gestational age, n (%)		
Gestational age > 10th percentile	30,722 (65.98)	30,387 (65.26)
Small for gestational age (10th percentile or below)	1,689 (3.63)	1,771 (3.80)
Missing	14,149 (30.39)	14,402 (30.93)
Mode of Delivery, n (%)		
Vaginal Delivery	28,935 (62.15)	28,959 (62.20)
Elective caesarean section	5,097 (10.95)	4,704 (10.10)
Emergency caesarean section	5,699 (12.24)	5,579 (11.98)
Missing	6,829 (14.67)	7,318 (15.72)
Stillbirth, n (%)	182 (0.39)	177 (0.38)

N= number of deliveries

LBW= Low Birth Weight

VLBW= Very Low Birth Weight

ELBW= Extremely Low Birth Weight

Table 6.3: Risk ratios and 95% confidence intervals of delivery outcomes and risk ratios and 95% confidence intervals for mode of delivery for deliveries of women with migraine compared to those without (complete case analysis)

	RR	**aRR***
Gestational age at delivery		
Preterm Birth (<37 weeks)	1.05 (1.00-1.11)	1.03 (0.97-1.09)
Very preterm (<32 weeks)	0.92 (0.83-1.02)	0.96 (0.86-1.06)
Extremely preterm (<28 weeks)	1.12 (0.96-1.30)	1.18 (1.01-1.37)
Onset of preterm delivery		
Term	1.00 (ref)	1.00 (ref)
Spontaneous preterm birth	0.98 (0.91-1.05)	0.98 (0.91-1.06)
Indicated preterm birth	1.17 (1.08-1.27)	1.11 (1.02-1.20)
Onset of preterm delivery not recorded	1.09 (0.96-1.24)	1.08 (0.95-1.23)
Birthweight		
LBW (<2500g)	1.03 (0.97-1.10)	1.02 (0.95-1.08)
VLBW (<1500g)	1.03 (0.90-1.19)	0.99 (0.86-1.14)
ELBW (<1000g)	1.05 (0.86-1.27)	1.01 (0.83-1.23)
Birthweight for gestational age		
Small for gestational age (<10^{th} centile)	0.94 (0.88-1.01)	0.96 (0.89-1.03)
Mode of Delivery		
Vaginal Delivery	1.00 (ref)	1.00 (ref)
Elective caesarean section	1.08 (1.03-1.14)	1.04 (0.99-1.09)

Emergency caesarean section	1.02 (0.98-1.07)	1.01 (0.97-1.06)
Stillbirth	1.03 (0.84-1.27)	1.00 (0.81-1.24)

* Adjusting for age, ethnicity, body mass index, smoking status, year of pregnancy, delivery method, pre-eclampsia, gestational diabetes, history of diabetes, asthma, systemic lupus erythematous, thyroid disorders, hypertension, chronic kidney disease

RR= Risk ratio

LBW= Low Birth Weight

VLBW= Very Low Birth Weight

ELBW= Extremely Low Birth Weight

Table 6.4: Odds ratios and 95% confidence intervals of delivery outcomes and risk ratios and 95% confidence intervals for mode of delivery for deliveries of women with migraine compared to those without (treating missing as absence of outcome (or missing delivery as vaginal delivery))

	RR	**aRR***
Gestational age at delivery		
Preterm Birth (<37 weeks)	1.06 (1.01-1.12)	1.04 (0.99-1.10)
Very preterm (<32 weeks)	0.93 (0.84-1.03)	0.96 (0.86-1.06)
Extremely preterm (<28 weeks)	1.13 (0.97-1.31)	1.17 (1.002-1.36)
Birthweight		
LBW (<2500g)	1.04 (0.98-1.11)	1.01 (0.95-1.08)
VLBW (<1500g)	1.04 (0.90-1.20)	0.99 (0.85-1.14)
ELBW (<1000g)	1.06 (0.87-1.29)	1.00 (0.83-1.22)
Birthweight for gestational age		
Small for gestational age (<10^{th} centile)	0.95 (0.89-1.02)	0.95 (0.88-1.02)
Mode of Delivery		
Vaginal Delivery	1.00 (ref)	1.00 (ref)
Elective caesarean section	1.10 (1.05-1.15)	1.06 (1.00-1.10)
Emergency caesarean section	1.04 (0.99-1.08)	1.03 (0.98-1.07)

* Adjusting for age, ethnicity, BMI, smoking status, year of pregnancy, delivery method, pre-eclampsia, gestational diabetes, history of diabetes, asthma, systemic lupus erythematous, thyroid disorders, hypertension, chronic kidney disease

RR= Risk ratio

LBW= Low Birth Weight

VLBW= Very Low Birth Weight

ELBW= Extremely Low Birth Weight

Chapter 7 : General Discussion

7.1 Chapter overview

The aims of this thesis were 1) to carry out epidemiological studies using electronic primary care record databases to describe the annual prevalence of migraine in pregnancy and the medications commonly prescribed amongst pregnant women with migraine (Chapter 3) 2) to conduct an umbrella review of the literature comparing adverse pregnancy outcomes in i) women with migraine to women without migraine ii) women with migraine who are treated to women with migraine who are not treated during pregnancy (Chapter 4) and 3) to undertake analysis of electronic health record data to describe the risk of adverse pregnancy outcomes, comparing i) women with migraine to women without migraine ii) women with migraine who are treated to women with migraine who are not treated during pregnancy (Chapters 5 and 6)

This chapter will summarise findings, discuss strengths and limitations of methods used, discuss implications of findings for policy, practice and future research recommendations.

7.2 Summary of findings

7.2.1 Chapter 3: Trends in the prevalence and pharmacological management of migraine during pregnancy in the UK 2000-2018

The CPRD Gold pregnancy register was used to determine the crude and age-standardised prevalence of migraine during pregnancy between 2000 and 2018. In those with migraine, the annual proportion who were prescribed drugs that are commonly used in the management of migraine was calculated. Logistic regression was used to assess the relationship between patient characteristics and being prescribed medications commonly used in the management of migraine.

Over the past two decades, there has been an increase in the age-standardised rates of recorded migraine diagnosis prior to pregnancy from 11.4% to 17%. During the same time period, there was an increase in the rates of prescribing for women with migraine

during pregnancy. Particular increases or high rates were seen for the prescription of triptans, NSAIDs, amitriptyline and beta blockers. These drugs were therefore taken forward for further investigation in chapter 5.

Older women, women of Black or South Asian ethnicity, those living in the most deprived areas, women who were obese, smokers and those with comorbid conditions had a higher risk of receiving a prescription.

7.2.2 Chapter 4: How migraine and its associated treatment impact on pregnancy outcomes: Umbrella Review with Updated Systematic Review and Meta-Analysis

An umbrella review was conducted of systematic reviews, with or without meta-analysis, that examined the link between migraine, migraine medications and pregnancy outcomes. One existing review was eligible for an update and this was also conducted.

In the umbrella review and updated systematic review, migraine was associated with a higher odds of pre-eclampsia, peri-partum mental illness and preterm birth. The relationship between migraine, low birth weight and small for gestational age was less clear and this was taken forward for further investigation in chapter 6. Women exposed to triptans had a higher odds of miscarriage compared to women without migraine. Whether this finding was due to confounding by indication was not clear and therefore, this was taken forward for further investigation in chapter 5.

7.2.3 Chapter 5: Migraine, associated treatments and risk of miscarriage: a matched cohort study and nested case-control study using the CPRD pregnancy register

A matched cohort study of women with and without migraine was conducted using the CPRD pregnancy register to compare the risk of miscarriage. Among women with migraine, a nested case control study was conducted matching those whose pregnancies ended in miscarriage to those whose did not, to compare the risk of being exposed to medications used in the management of migraine.

193,208 pregnancies of 108,897 women with migraine were matched to 193,208 pregnancies of 137,549 women without migraine. 10.8% (n=20,778) of pregnancies of women with migraine ended in miscarriage compared to 10% (n=19,233) of women without migraine. Women with migraine were therefore at 6% higher risk of miscarriage (aRR 1.06 95% CI (1.04-1.08)).

Of the 20,778 pregnancies ending in miscarriage, 722 (3.47%), 380 (1.83%), 173 (0.83%) and 733 (3.52%) were exposed to triptans, amitriptyline, beta blockers and NSAIDs, respectively. Triptans (aORs 1.24 (1.11-1.38)), amitriptyline (1.25 (1.08-1.45)) and NSAID (1.74 (1.57-1.93)) exposure were associated with significantly increased risk of miscarriage. Despite our efforts to account for confounding by indication, with limited information on severity of migraine, residual confounding is possible and therefore further work is needed to understand the potential causative mechanisms.

7.2.4 Chapter 6: Migraine and risk of adverse obstetric outcomes: a matched cohort study of UK linked electronic health records

A cohort study of women who had a delivery episode recorded in HES between 2000 and 2019 was created in which women with migraine were matched to women without. I matched 46,560 pregnancies of 34,506 women with migraine to 46,560 pregnancies of 42,851 women without migraine.

In this dataset, migraine was not associated with preterm birth overall; 3,519 (7.56%) deliveries of women with migraine were preterm compared to 3,331 (7.15%) of those without (aOR 1.04 (95% CI 0.97-1.09)). However, migraine was found to be associated with extremely preterm (<28 weeks) (aOR 1.18 (95% CI 1.01-1.37)) and indicated preterm (aRR 1.11 (95% CI 1.02-1.20)).

No significant association was found between migraine, low birth weight and small for gestational age, suggesting that migraine does not significantly affect fetal growth restriction.

7.3 Strengths and limitations

Chapters 3 (prevalence study) and 4 (umbrella review) laid the groundwork for the subsequent chapters. Strengths of umbrella review included using a rigorous methodology and conducting an update of an out-of-date review (meaning all relevant studies were included). However, it was hampered by the quality of included studies and potential publication bias.

There were several strengths to using routinely collected healthcare data for the study of migraine in pregnancy. Firstly, large datasets that were generalisable to UK population were used. As far as I am aware, these are the first studies to use these national datasets to investigate pregnancy outcomes in women with migraine. The pregnancies and deliveries were drawn from a validated pregnancy register(86) or hospital databases (90), meaning they were representative of pregnancies and births in the UK.

Compared to similar studies in other countries, capture of migraine was relatively complete, particularly in more recent years. This was enabled by the use of primary care records to identify diagnostic codes for migraine and prescriptions of drugs for the management of migraine. Previous studies have often relied on diagnosis in secondary care. As most cases of migraine can be managed without specialist input, this has led to significantly lower-than-expected rates of migraine in these studies(106, 151, 169).

A considerable number of covariates that are associated either with migraine or pregnancy outcomes were adjusted for in the analyses, including maternal characteristics such as ethnicity, IMD, BMI and smoking status; maternal comorbidities,

including asthma, depression, type 1 diabetes type 2 diabetes, hypertension and thyroid disorders; and pregnancy complications such as pre-eclampsia and gestational diabetes.

Outcomes that are often unavailable in large cohort datasets were investigated in this thesis. Using the CPRD pregnancy register enabled miscarriage to be studied as an outcome. As birth cohorts are often restricted to live and stillbirths, miscarriage is not usually available as an outcome. In addition, data were available for onset and mode of delivery, allowing the investigation of birth outcomes that had not previously been studied in large cohorts or at all such as elective vs. emergency caesarean and onset of preterm delivery (spontaneous vs. medically indicated).

Using databases of electronic health records to conduct a pharmacoepidemiology study in chapter 5 (migraine and miscarriage) overcame the usual ethical barriers to drug safety studies in pregnancy. However, there are limitations to the use of routinely collected healthcare data. Despite best efforts, the prevalence of migraine captured in this database was lower than expected in reproductive aged women (13.7% in chapters 3 and 5 and 10.9% in chapter 6 (prevalence and delivery outcomes studies), compared to an expected prevalence of around 20%)(6). To mitigate against contamination of the unexposed group with women with migraine, women with other headache conditions were excluded from the control groups. However, it is possible that some of the unexposed cohort had unrecorded migraine in the studies reported in chapters 5 and 6. It is unclear what the impact of this may have been. If migraine had an association with the outcomes of interest, this misclassification may have shifted the effect estimate towards the null. On the other hand, the cases captured are likely to represent patients with more severe migraine who require input from their GPs to help manage symptoms. If there is a relationship between severity of migraine and likelihood of adverse pregnancy outcomes such as miscarriage, this may have exaggerated the effect size.

Missingness of data affected the data sources used in chapters 3, 5 and 6 (prevalence, miscarriage, and delivery outcomes studies). For the CPRD pregnancy register, used in chapters 3 and 5 (prevalence and miscarriage studies), this affected some of the covariates adjusted for in the analysis, particularly BMI, ethnicity and IMD. The decision was made to create "missing" categories for these covariates (197). This was thought to be the best option as conducting a complete case analysis would have resulted in a high proportion of the cohort being discarded. Imputation was not used as variables such as BMI were likely to be "missing not at random" (198) or could not be imputed using available data (199). For chapter 6 (migraine and delivery outcomes study), which used the HES maternity tail as its data source, missingness affected the outcome variables, including birthweight and gestational age at delivery. Complete case analysis was conducted initially in this analysis. As it is possible that the data were "missing not at random", for example, gestational age may have been more likely to be recorded for preterm births, an additional analysis, treating missingness of an outcome variable as absence of the outcome was also conducted. Reassuringly, these two analyses yielded similar results. Despite measures taken to mitigate the effects missing data, it is possible that they still may have biased results.

Despite adjusting for numerous confounders in the analyses, a limitation common to all observational studies is the potential effect of residual confounding. In particular, data were not available for several potentially important covariates. For example, in chapter 5 (miscarriage study)and paternal factors (200), such as age and medical history, were unavailable and these impact on risk of miscarriage.

Specific biases must be considered when conducting pharmaco-epidemiological studies (201). Of particular importance for the study reported in chapter 5 (miscarriage study) were the potential for confounding by indication and reverse causality. Confounding by

indication was addressed by conducting the study within the migraine population. However, there is a possibility that severity of migraine impacts miscarriage risk, as more severe cases are more likely to require pharmacological management, confounding by indication may still have impacted this study. Reverse causality, whereby the hormonal changes associated with having a miscarriage trigger a migraine, leading to the prescription of acute medications, may also have impacted on the results. Finally, the use of prescription data in this thesis has associated limitations. It is not possible to ascertain whether the prescription was filled, the timings of medication use or how frequently medication was used. Over the counter medications were not captured, which include NSAIDs and triptans and access to prescription data for secondary care were not available. This may have led to an underestimation of the prevalence of medication use in chapter 3 (prevalence study). It is unclear whether this could have impacted the results in chapter 5 (migraine and miscarriage study), as there is no obvious reason why there would be a differential misclassification between women with and without miscarriage.

7.4 Implications for practice, policy and future research

7.4.1 Communication of risk and uncertainty for adverse events and prescribing in pregnancy

Exclusion of pregnant women from clinical trials has meant that there is a lack of information for the safety of medications during pregnancy (50). This, in addition to the legacy of incidentss such as thalidomide (52), has led to a cautious approach to the use of medications in pregnancy. While some medications are known to be unsafe for the developing fetus, stopping medication during pregnancy can also lead to harm to the mother and in turn, the baby.

Observational studies can provide insight into associations between exposures and outcomes where randomised control trials are unfeasible or impractical. They can also

provide valuable evidence about the risks and benefits of medication use in pregnancy without having to overcome the ethical barriers that preclude interventional studies in this population. However, the limitations and biases of these studies can mean it is challenging to for clinicians to interpret results and communicate risks to patients.

Recently, there have been calls for a more nuanced discussions of risk during pregnancy (166, 167). An approach that supports shared decision making with women is warranted, for example through the use of decision aids (168). Further exploration of the best way to communicate risk and uncertainty, particularly around medication use in pregnancy is needed.

7.4.2 Further prospective studies of the role of aura, severity, migraine pattern during pregnancy

It was initially planned that this thesis would investigate the effect of aura status on the outcomes of interest. However, on investigation, fewer than 3% of women had aura status recorded in the structured data. Migraine with aura has been shown to be associated with greater vascular risk than migraine without aura(18) and one study found in the review in chapter 4 (umbrella review) reported a higher risk of pre-eclampsia associated with aura (170).

Features such as the presence of aura or having migraine attacks related to the menstrual cycle may affect whether migraine resolves during pregnancy(26). It is unclear whether those whose migraine does not improve during pregnancy have a higher risk of adverse pregnancy outcomes. The impact of severity of migraine on risk of miscarriage, as highlighted in chapter 5 (miscarriage study), would be useful to explore further.

It was not possible to study the impact of severity or aura using the electronic health record data available. It is likely that aura status is ascertained and recorded by general practitioners in reproductive aged women as oestrogen containing contraceptives are

contra-indicated in women with migraine with aura. If this is recorded in free-text notes, natural language processing methods could be used to capture the presence of aura. Severity, resolution of symptoms and timings of medication could be examined using cohort studies in which women with migraine are followed up prospectively throughout pregnancy. Data for these could be collected using maternity electronic health record systems such as Badgernet.

An important limitation of the studies in this thesis was the likely under-recording of migraine in GP records. Using a polygenic risk score as a proxy for migraine may be a useful way to overcome this in future research. One such score has been developed (202) and has been found to be statistically significantly associated with response to migraine specific treatments. (203) The use of this could be explored in future studies.

7.4.3 Further pharmacoepidemiological studies of the association between migraine drugs and other pregnancy outcomes

A previous study in CPRD GOLD found women who were treated for migraine were at higher risk of hypertensive disorders of pregnancy than those with untreated migraine(204). However, this analysis relied solely on primary care data and found a substantially lower prevalence of hypertensive disorders of pregnancy than was found in chapter 6 (delivery outcomes study) when linked secondary care data were included. Migraine medications were not examined individually and, similarly to the analysis in chapter 5 (miscarriage study), confounding by indication may have played a role. Further investigation of the impact of individual migraine medications on the risk of hypertensive disorders of pregnancy, including pre-eclampsia, is warranted.

The umbrella review reported in chapter 4 found a lower prevalence of preterm birth in women who took triptans during pregnancy compared to those who did not. Studies that

have previously examined this association have found conflicting results. A Norwegian population registry study found a higher risk of preterm birth in the disease comparator group of women with migraine not taking triptans than those who were exposed to triptans during pregnancy (OR 1.30; 95 % CI 1.06–1.60) (205), whereas a Danish cohort study found an increased risk of preterm birth associated with triptan exposure compared to women with migraine who did not take triptans (OR 6.3, 95% CI 1.2–32) (206).

Cohort and case-control studies to investigate these outcomes could be initially conducted in the same migraine cohort used in this thesis. These could be further investigated prospectively using national surveillance systems such as the UK Teratology Information Service, which collect data on pregnancy and fetal outcomes following maternal and paternal exposures to medications.

7.4.4 Further research into potential mechanisms behind associations between migraine, migraine medication and pregnancy complications

Migraine is a complex neurovascular disorder. There is evidence that it effects the vasculature outside of the brain, with higher risk of cardiovascular disease (19), chronic kidney disease(207) and retinal vasculopathy(208) in both men and women with migraine. The effects of migraine outside the brain may be due to endothelial dysfunction. Endothelial cells line blood vessel walls, forming a physical barrier and playing a role in clotting, vascular tone and inflammation. In people with migraine, endothelial dysfunction is thought to be mediated by oxidative stress. This leads to inflammation, impaired vascular reactivity and thrombosis (209). Endothelial dysfunction has been suggested as one of the underlying causes of both miscarriage and pre-eclampsia (36), suggesting this may be a potential mechanism behind the associations between migraine and these conditions. Further work to understand this

association should be carried out. This could potentially help determine which women with migraine are most at risk of pre-eclampsia, warranting closer monitoring or prophylactic treatment with low dose aspirin(190).

With regards to the association found between triptans and miscarriage, these medications are known to have serotoninergic vasoconstrictive properties through their effect on serotonin receptors (64). Higher levels of plasma serotonin have been found in patients experiencing a miscarriage, again suggesting a potential causal mechanism (161).

7.4.5 Investigating ethnic inequalities in access to migraine care

The study reported in chapter 3 (prevalence study) found that women of Black and South Asian ethnicity were at significantly higher odds of being prescribed drugs for the management of migraine (aOR 1.40 (95% CI 1.32-1.48) and 1.48 (95% CI 1.38-1.59), respectively).

On the other hand, the women in the migraine cohorts in chapters 5 and 6 (miscarriage and delivery outcomes studies) were disproportionately white.

Evidence around the prevalence of migraine in different ethnic groups is mixed. In England, lower prevalence has been reported in non-white ethnicities, but authors of this study suggested this could be due to cultural differences in the reporting of pain (24). In other countries, disparities in access to migraine care have been found. For example, in the US, African American patients have been found to experience barriers to accessing care(182), despite the prevalence of migraine being higher in this group (183).

It is possible that people from Black and South Asian ethnic groups only present with more severe migraine symptoms to their GPs, so more often require medications to manage their condition. Alternatively, it could be that these groups are not being referred for secondary care management, despite recommendations that specialist advice should be sought during pregnancy if preventative migraine therapy is required (5).

Further work is required to understand the true prevalence of migraine by ethnicity in the UK. Surveys using validated questionnaires could be carried out on representative samples of the population. Further studies to understand whether people from ethnic minority groups are being managed and referred appropriately with respect to guidelines are warranted. Qualitative work could also be carried out to understand any barriers to access for migraine care.

7.5 Conclusion

The prevalence of recorded migraine has increased in pregnant women over the past few decades. In addition to this, prescription rates for migraine medication during pregnancy have also risen, with women already at higher risk of adverse pregnancy outcomes being at higher risk of receiving a prescription. Results of an umbrella review and primary studies carried out in this thesis have shown an association between migraine and adverse pregnancy outcomes, namely pre-eclampsia, peripartum mental illness and miscarriage. An association between migraine and preterm birth has been found, potentially driven by medically indicated preterm delivery. Exposure to triptans, NSAIDs and amitriptyline in pregnant women with migraine is associated with miscarriage. Future work into how migraine type and severity impact these outcomes, the associations of migraine drugs with other pregnancy outcomes, potential underlying causative mechanisms, and ethnic inequalities in access to migraine care is needed.

Clinicians should be mindful of uncertainty and bias surrounding the results of these studies when communicating risks to pregnant women.

Supplementary Materials

Chapter 3

Supplementary Table 3.1: Codelists for migraine and comorbidities

DESCRIPTION	READ_CODE
Migraine	F26..00
Periodic migrainous neuralgia	F262500
Common migraine	F261.00
Abdominal migraine	F262200
Classical migraine	F260.00
Hemiplegic migraine	F26y000
H/O: migraine	1474
Migraine variants	F262.00
Abdominal migraine - symptom	1967
Basilar migraine	F262300
Atypical migraine	F261000
Ophthalmic migraine	F262400
Migraine - menstrual	K584.11
Ophthalmoplegic migraine	F26y100
Migraine NOS	F26z.00
[D]Abdominal migraine	R090D00
Status migrainosus	F26y200
Migraine variant NOS	F262z00
Complicated migraine	F26y300
Other forms of migraine	F26y.00
Other forms of migraine NOS	F26yz00
Common migraine NOS	F261z00
[X]Other migraine	Fyu5300
Moebius' ophthalmoplegic migraine	F26y111
H/O migraine with aura	1474000
Migraine with aura	F260.11
Migraine without aura	F261.11

Migraine induced by oestrogen contraceptive	F262800
DESCRIPTION	READ_CODE
Asthma	H33..00
Asthma monitoring	663..11
Acute exacerbation of asthma	H333.00
Asthma attack	H33z100
Severe asthma attack	H33z011
H/O: asthma	14B4.00
Childhood asthma	H330.12
Bronchial asthma	H33..11
Allergic asthma	H330.11
Mild asthma	663V100
Severe asthma	663V300
Occasional asthma	663V000
Late onset asthma	H331.11
Asthma unspecified	H33z.00
Exercise induced asthma	H33zz11
Status asthmaticus NOS	H33z000
Patient in asthma study	9Q21.00
Intrinsic asthma	H331.00
Seen in asthma clinic	9N1d.00
Hay fever with asthma	H330011
Chronic asthmatic bronchitis	H312000
Exercise induced asthma	173A.00
Extrinsic asthma with asthma attack	H330111
Emergency admission	asthma
Extrinsic (atopic) asthma	H330.00
Asthma limiting activities	663P.00
Asthma prophylactic medication used	663W.00
Asthma management plan given	663U.00
Asthma disturbing sleep	663N.00

Pollen asthma	H330.14
Asthma attack NOS	H33z111
Asthma monitored	9OJA.11
Number of asthma exacerbations in past year	663y.00
Change in asthma management plan	66Y5.00
Step up change in asthma management plan	66Y9.00
Asthma annual review	66YJ.00
Asthma medication review	8B3j.00
Suspected asthma	1J70.00
Asthma - currently active	663j.00
Asthma resolved	2126200
Asthma trigger	178..00
Asthma confirmed	1O2..00
Refuses asthma monitoring	9OJ2.00
Excepted from asthma quality indicators: Informed dissent	9hA2.00
Asthma resolved	212G.00
Late-onset asthma	H33z200
Asthma severity	663V.00
Moderate asthma	663V200
Asthma not disturbing sleep	663O.00
Asthma not limiting activities	663Q.00
Asthma disturbs sleep frequently	663N200
Asthma follow-up	66YK.00
Extrinsic asthma without status asthmaticus	H330000
Hay fever with asthma	H330.13
Asthma NOS	H33zz00
Asthma monitoring admin.	9OJ..00
Asthma control step 2	8795

Asthma control step 1	8794
Asthma monitoring due	66YE.00
Step down change in asthma management plan	66YA.00
Asthma control step 3	8796
Intrinsic asthma with asthma attack	H331111
Exception reporting: asthma quality indicators	9hA..00
Asthma monitoring by nurse	66YQ.00
Asthma treatment compliance unsatisfactory	663p.00
Asthma treatment compliance satisfactory	663n.00
Asthma monitoring check done	9OJA.00
Asthma control step 5	8798
Asthma control step 4	8797
Allergic asthma NEC	H33zz12
Occupational asthma	173c.00
Emergency asthma admission since last appointment	663d.00
Asthma causes daytime symptoms 1 to 2 times per week	663u.00
Asthma restricts exercise	663e.00
Asthma monitor 3rd letter	9OJ6.00
Asthma monitor 2nd letter	9OJ5.00
Asthma monitor 1st letter	9OJ4.00
Asthma clinical management plan	8CR0.00
Mixed asthma	H332.00
Health education - asthma	679J.00
Asthma never causes daytime symptoms	663s.00
Asthma causes daytime symptoms most days	663v.00

Asthma never restricts exercise	663f.00
Asthma severely restricts exercise	########
Asthma sometimes restricts exercise	6.63E+02
Extrinsic asthma with status asthmaticus	H330100
Intrinsic asthma without status asthmaticus	H331000
Asthma control step 0	8793
Asthma monitoring admin.NOS	9OJZ.00
Asthma monitoring by doctor	66YR.00
Asthma causing night waking	663N000
Asthma monitor phone invite	9OJ8.00
Asthma night-time symptoms	66YP.00
Asthma causes daytime symptoms 1 to 2 times per month	663t.00
Asthma monitor verbal invite	9OJ7.00
Asthma never disturbs sleep	663O000
Asthma limits walking up hills or stairs	663w.00
Asthma limits walking on the flat	663x.00
Asthma disturbs sleep weekly	663N100
Wood asthma	H35y700
Asthma causes night symptoms 1 to 2 times per month	663r.00
Brittle asthma	H334.00
Aspirin induced asthma	1780
Absent from work or school due to asthma	66YC.00
Asthma monitor offer default	9OJ3.00
Asthma daytime symptoms	663q.00
Intrinsic asthma NOS	H331z00
Extrinsic asthma NOS	H330z00
Attends asthma monitoring	9OJ1.00

Asthma accident and emergency attendance since last visit	663m.00
Detergent asthma	H47y000
Does not have asthma management plan	66YZ.00
Intrinsic asthma with status asthmaticus	H331100
Work aggravated asthma	173d.00
Sequoiosis (red-cedar asthma)	H35y600
Asthma control test	38DL.00
Patient has a written asthma personal action plan	8CMA000
Health education - asthma self management	679J000
Asthma control questionnaire	38DT.00
Under care of asthma specialist nurse	9NNX.00
Health education - structured asthma discussion	679J100
Asthma review using Roy Colleg of Physicians three questions	66Yp.00
Mini asthma quality of life questionnaire	38DV.00
Asthma trigger - seasonal	1787
Asthma trigger - pollen	1781
Asthma causes symptoms most nights	66Yr.00
Asthma causes night time symptoms 1 to 2 times per week	66Yq.00
Asthma trigger - respiratory infection	1789
Asthma limits activities 1 to 2 times per month	663P000
Asthma trigger - exercise	178B.00
Asthma limits activities 1 to 2 times per week	663P100

Asthma trigger - warm air	1783
Health education - structured patient focused asthma discuss	679J200
Asthma trigger - animals	1786
Asthma never causes night symptoms	66Ys.00
Royal College Physician asthma assessment 3 question score	388t000
Asthma trigger - cold air	1788
Asthma trigger - airborne dust	178A.00
Asthma trigger - damp	1785
Asthma trigger - emotion	1784
Asthma trigger - tobacco smoke	1782
Asthma limits activities most days	663P200
[X] Adverse reaction to antiasthmatics	U60F611
Asthma self-management plan review	661N100
Asthma self-management plan agreed	661M100
Chronic asthma with fixed airflow obstruction	H335.00
Number days absent from school due to asthma in past 6 month	66Yu.00
Asthma management plan declined	66Yz000
Childhood Asthma Control Test	38QM.00
Asthma monitorng invit SMS (short message servce) txt messge	9OJB.00
Asthma monitoring invitation email	9OJC.00
Telehealth asthma monitoring	66Yz500
Asthma monitoring SMS text message 1st invitation	9OJB000
Severe asthma exacerbation risk assessment	38B8.00
At risk of severe asthma exacerbation	14Ok000
Asthma monitoring SMS text message 2nd invitation	9OJB100

Asthma monitoring SMS text message 3rd invitation	9OJB200
DESCRIPTION	READ_CODE
Chronic renal failure	K05..00
End stage renal failure	K050.00
Chronic kidney disease stage 4	1Z13.00
Chronic kidney disease stage 3	1Z12.00
Chronic kidney disease stage 5	1Z14.00
Chronic kidney disease stage 2	1Z11.00
Chronic renal impairment	1Z1..00
Except chronic kidney disease qual indic: Patient unsuitable	9hE0.00
Anaemia secondary to renal failure	D215.00
Chronic kidney disease monitoring	66i..00
Anaemia secondary to chronic renal failure	D215000
Chronic kidney disease stage 1	1Z10.00
Chronic kidney disease annual review	6AA..00
Chronic kidney disease monitoring first letter	9Ot0.00
Exc chronic kidney disease quality indicators: Inform dissen	9hE1.00
Exception reporting: chronic kidney disease quality indicato	9hE..00
End stage renal failure	K05..12
[X]Other chronic renal failure	Kyu2100
Chronic kidney disease monitoring telephone invite	9Ot4.00
Chronic kidney disease monitoring administration	9Ot..00
Chronic kidney disease monitoring second letter	9Ot1.00

Chronic kidney disease monitoring third letter	9Ot2.00
Chronic kidney disease monitoring verbal invite	9Ot3.00
Chronic kidney disease stage 1 with proteinuria	1Z17.00
Chronic kidney disease stage 3 with proteinuria	1Z1B.00
Chronic kidney disease stage 3A	1Z15.00
Chronic kidney disease stage 2 without proteinuria	1Z1A.00
Chronic kidney disease stage 4 with proteinuria	1Z1H.00
Chronic kidney disease stage 3 without proteinuria	1Z1C.00
CKD stage 3 with proteinuria	1Z1B.11
Chronic kidney disease stage 2 with proteinuria	1Z19.00
Chronic kidney disease stage 3A without proteinuria	1Z1E.00
CKD stage 3A without proteinuria	1Z1E.11
Chronic kidney disease stage 3B without proteinuria	1Z1G.00
Chronic kidney disease stage 3B with proteinuria	1Z1F.00
Chronic kidney disease stage 3B	1Z16.00
CKD stage 3B with proteinuria	1Z1F.11
CKD stage 3 without proteinuria	1Z1C.11
Chronic kidney disease stage 5 without proteinuria	1Z1L.00
Chronic kidney disease stage 4 without proteinuria	1Z1J.00

Chronic kidney disease stage 3A with proteinuria	1Z1D.00
Did not attend chronic kidney disease monitoring clinic	9Ni9.00
Chronic kidney disease stage 5 with proteinuria	1Z1K.00
CKD stage 3A with proteinuria	1Z1D.11
Chronic kidney disease stage 1 without proteinuria	1Z18.00
CKD stage 4 without proteinuria	1Z1J.11
CKD stage 5 without proteinuria	1Z1L.11
CKD stage 2 without proteinuria	1Z1A.11
CKD stage 2 with proteinuria	1Z19.11
CKD stage 1 with proteinuria	1Z17.11
CKD stage 5 with proteinuria	1Z1K.11
CKD stage 4 with proteinuria	1Z1H.11
Acute-on-chronic renal failure	K0E..00
CKD stage 3B without proteinuria	1Z1G.11
Chronic kidney disease stage 3	K053.00
Chronic kidney disease stage 4	K054.00
Chronic kidney disease	K05..13
Chronic kidney disease stage 5	K055.00
Chronic kidney disease stage 2	K052.00
Chronic kidney disease stage 1	K051.00
Chronic kidney disease self-management plan agreed	661M200
CKD with GFR category G3b & albuminuria category A2	1Z1Y.00
CKD with GFR category G3a & albuminuria category A1	1Z1T.00
CKD with GFR category G3a & albuminuria category A2	1Z1V.00

CKD with GFR category G4 & albuminuria category A2	1Z1b.00
CKD with GFR category G3a & albuminuria category A3	1Z1W.00
CKD with GFR category G3b & albuminuria category A1	1Z1X.00
CKD with GFR category G4 & albuminuria category A1	1Z1a.00
CKD with GFR category G5 & albuminuria category A2	1Z1e.00
CKD with GFR category G3b & albuminuria category A3	1Z1Z.00
CKD with GFR category G1 & albuminuria category A2	1Z1N.00
CKD with GFR category G1 & albuminuria category A1	1Z1M.00
CKD with GFR category G2 & albuminuria category A2	1Z1R.00
CKD with GFR category G5 & albuminuria category A1	1Z1d.00
CKD with GFR category G2 & albuminuria category A3	1Z1S.00
CKD with GFR category G2 & albuminuria category A1	1Z1Q.00
CKD with GFR category G5 & albuminuria category A3	1Z1f.00
CKD with GFR category G1 & albuminuria category A3	1Z1P.00
CKD with GFR category G4 & albuminuria category A3	1Z1c.00
CKD stage 1 without proteinuria	1Z18.11
Chronic kidney disease self-management plan review	661N200

DESCRIPTION	READ_CODE
Depressive disorder NEC	E2B..00
[X]Depression NOS	Eu32z11
Endogenous depression	E112.14
Anxiety with depression	E200300
Agitated depression	E135.00
Neurotic depression reactive type	E204.00
Brief depressive reaction	E290.00
Depressive psychoses	E11..12
Postnatal depression	E204.11
H/O: depression	1465
Puerperal depression	62T1.00
[X]Depressive episode	unspecified
Postviral depression	E2B0.00
[X]Depressive disorder NOS	Eu32z12
[X]Recurrent depressive disorder	Eu33.00
Chronic depression	E2B1.00
[X]Depressive episode	Eu32.00
[X]Postpartum depression NOS	Eu53012
Agitated depression	E112.11
[X] Reactive depression NOS	Eu32z14
Recurrent depression	E113700
Endogenous depression first episode	E112.12
[X]Other depressive episodes	Eu32y00
Endogenous depression - recurrent	E113.11
Endogenous depression first episode	E112.13
Single major depressive episode NOS	E112z00
[X]Single episode of reactive depression	Eu32.13
[X]Neurotic depression	Eu34113
[X]Mild anxiety depression	Eu41211
[X]Dysthymia	Eu34100

Reactive depressive psychosis	E130.00
[X]Depressive neurosis	Eu34111
[X]SAD - Seasonal affective disorder	Eu33.15
[X]Recurrent episodes of depressive reaction	Eu33.11
[X]Recurrent episodes of reactive depression	Eu33.13
[X]Single episode of depressive reaction	Eu32.11
Masked depression	E11z200
[X]Moderate depressive episode	Eu32100
[X]Severe depressive episode without psychotic symptoms	Eu32200
Single major depressive episode	E112.00
[X]Mild depression	Eu32400
[X]Atypical depression	Eu32y11
Seasonal affective disorder	E118.00
[X]Schizoaffective disorder	depressive type
[X]Major depression	recurrent without psychotic symptoms
[X]Endogenous depression without psychotic symptoms	Eu33211
[X]Mild depressive episode	Eu32000
[X]Mixed anxiety and depressive disorder	Eu41200
[X]Severe depressive episode with psychotic symptoms	Eu32300
Depression medication review	9H91.00
Depression annual review	9H90.00
[X]Postnatal depression NOS	Eu53011

Recurrent major depressive episodes	moderate
Recurrent major depressive episode	E113.00
Single major depressive episode	moderate
Single major depressive episode	severe
[X]Persistant anxiety depression	Eu34114
Single major depressive episode	mild
Prolonged depressive reaction	E291.00
[X]Recurrent severe episodes of psychotic depression	Eu33315
Psychotic reactive depression	E130.11
[X]Single episode of psychogenic depression	Eu32.12
Postnatal depression counselling	6G00.00
[X]Recurrent brief depressive episodes	Eu3y111
Depression resolved	212S.00
[X]Recurrent episodes of psychogenic depression	Eu33.12
[X]Post-schizophrenic depression	Eu20400
Senile dementia with depression	E002100
[X]Single episode major depression w'out psychotic symptoms	Eu32212
[X]Endogenous depression with psychotic symptoms	Eu33311
[X]Single episode of psychotic depression	Eu32313
[X]Single episode of major depression and psychotic symptoms	Eu32311
Recurrent major depressive episodes	severe
Recurrent major depressive episode NOS	E113z00
Recurrent major depressive episodes	severe
Atypical depressive disorder	E11y200

Presenile dementia with depression	E001300
[X]Prolonged single episode of reactive depression	Eu32z13
[X]Seasonal depressive disorder	Eu33.14
[X]Single episode of reactive depressive psychosis	Eu32314
Recurrent major depressive episodes	mild
[X]Recurrent depressive disorder	current episode moderate
[D]Postoperative depression	R007z13
[X]Recurrent depressive disorder	current episode mild
Depression interim review	9H92.00
Patient given advice about management of depression	8CAa.00
Depression - enhanced services administration	9k4..00
[X]Recurr severe episodes/psychogenic depressive psychosis	Eu33314
Single major depressive episode	severe
Referral for guided self-help for depression	8HHq.00
[X]Depressive conduct disorder	Eu92000
[X]Recurr severe episodes/major depression+psychotic symptom	Eu33313
[X]Recurr depress disorder cur epi severe without psyc sympt	Eu33200
Single major depressive episode	unspecified
[X]Schizoaffective psychosis	depressive type
Recurrent major depressive episodes	unspecified

Brief depressive reaction NOS	E290z00
[X]Monopolar depression NOS	Eu33z11
[X]Recurrent severe episodes/reactive depressive psychosis	Eu33316
[X]Schizophreniform psychosis	depressive type
Senile dementia with depressive or paranoid features NOS	E002z00
[X]Single episode agitated depressn w'out psychotic symptoms	Eu32211
On depression register	9HA0.00
Arteriosclerotic dementia with depression	E004300
[X]Recurrent depressive disorder	unspecified
Senile dementia with depressive or paranoid features	E002.00
Depression management programme	8BK0.00
Drug-induced depressive state	E02y300
[X]Recurrent depress disorder cur epi severe with psyc symp	Eu33300
[X]Other recurrent depressive disorders	Eu33y00
Depression monitoring administration	9Ov..00
[X]Single episode of psychogenic depressive psychosis	Eu32312
[X]Single episode of masked depression NOS	Eu32y12
[X]Single episode vital depression w'out psychotic symptoms	Eu32213
Depression - enhanced service completed	9k40.00
Depression monitoring first letter	9Ov0.00
Depression monitoring second letter	9Ov1.00

[X]Vital depression	recurrent without psychotic symptoms
Depression monitoring telephone invite	9Ov4.00
Depression monitoring verbal invite	9Ov3.00
Depression monitoring third letter	9Ov2.00
On full dose long term treatment depression - enh serv admin	9kQ..00
[X]Major depression	moderately severe
[X]Major depression	mild
[X]Major depression	severe without psychotic symptoms
[X]Major depression	severe with psychotic symptoms
[X]Single major depr ep	severe with psych
[X]Recurr major depr ep	severe with psych
[X]Antenatal depression	Eu32B00
Referral for guided self-help for depression declined	8IH5200
DESCRIPTION	READ_CODE
Endometriosis	K50..00
Adenomyosis	K50..11
Endometriosis NOS	K50z.00
Laparoscopic laser destruction of endometriosis	7E0D800

Chocolate cyst of ovary	K501.11
Internal endometriosis	K500000
Endometriosis of ovary	K501.00
Endometriosis of the intestine	K505.00
Adenomyosis of endometrium	K500111
Endometriosis of the pelvic peritoneum	K503.00
Endometriosis of the fallopian tube	K502.00
Endometriosis of cervix	K500200
Endometriosis of the bladder	K50y000
Endometriosis of the vagina	K504100
Endometriosis of uterus	K500.00
Endometriosis of uterus NOS	K500z00
Endometriosis of the pelvic peritoneum NOS	K503z00
Endometriosis of the umbilicus	K50y200
Other endometriosis	K50y.00
Endometriosis of the pouch of Douglas	K503100
Endometriosis of the rectovaginal septum	K504000
Endometriosis of the round ligament	K503300
[M]Stromal endometriosis	BBL1.11
Endometriosis in scar of skin	K506.00
Endometriosis of the rectum	K505200
Endometriosis of myometrium	K500100
Endometriosis of the colon	K505100
Endometriosis of the parametrium	K503200
[X]Other endometriosis	Kyu9000
Other endometriosis NOS	K50yz00
Endometriosis of the broad ligament	K503000
Endometriosis of the vulva	K50y300

Endometriosis of the lung	K50y100
Endometriosis of the rectovaginal septum and vagina	K504.00
Endometriosis of the appendix	K505000
Endometriosis of the rectovaginal septum and vagina NOS	K504z00
Endometriosis of the intestine NOS	K505z00
DESCRIPTION	READ_CODE
Hypertensive disease	G2...00
Essential hypertension	G20..00
Benign essential hypertension	G201.00
H/O: hypertension	14A2.00
Hypertension resolved	2126100
On treatment for hypertension	662O.00
Hypertension NOS	G20z.11
Hypertensive encephalopathy	G672.00
Seen in hypertension clinic	9N03.00
Systolic hypertension	G202.00
Hypertensive renal disease	G22..00
Hypertensive retinopathy	F421300
Hypertensive disease NOS	G2z..00
Secondary hypertension	G24..00
Borderline hyperten:yearly obs	6624
BP - hypertensive disease	G2...11
Cardiomegaly - hypertensive	G21z011
Essential hypertension NOS	G20z.00
Patient on maximal tolerated antihypertensive therapy	8BL0.00
Hypertension treatm.stopped	662H.00
Hypertensive treatm.changed	662G.00
Hypertensive renal disease NOS	G22z.00
Malignant essential hypertension	G200.00

Secondary hypertension NOS	G24z.00
Hypertensive heart disease NOS	G21zz00
Hypertensive heart disease	G21..00
Good hypertension control	6627
Antihypertensive therapy	8B26.00
Hypertension six month review	662c.00
Moderate hypertension control	662b.00
Other specified hypertensive disease	G2y..00
Hypertension annual review	662d.00
Hypertension resolved	212K.00
Adverse reaction to antihypertensives NOS	TJC7z00
Adverse reaction to other antihypertensives	TJC7.00
Hypertension treatm. started	662F.00
Hypertensive heart&renal dis wth (congestive) heart failure	G232.00
Hypertension treatment refused	8I3N.00
Secondary benign renovascular hypertension	G241000
Fetus or neonate affected by maternal hypertensive disease	Q000.00
Poor hypertension control	6628
Seen in hypertension clinic	9N1y200
Hypertensive heart and renal disease with renal failure	G233.00
Renal hypertension	G22z.11
[X] Adverse reaction to other antihypertensives	U60C511
Hypertension:follow-up default	6629
Hypertension secondary to drug	G24z100
Secondary renovascular hypertension NOS	G24z000

Hypertensive heart disease NOS	G21z.00
Secondary malignant hypertension	G240.00
Hypertensive crisis	G672.11
Hypertensive renal disease with renal failure	G222.00
Hypertension induced by oral contraceptive pill	6146200
Hypertension secondary to endocrine disorders	G244.00
Blind hypertensive eye	F404200
Malignant hypertensive renal disease	G220.00
Secondary hypertension NOS	G24zz00
Benign hypertensive renal disease	G221.00
[X] Adverse reaction to antihypertensives NOS	U60C51A
Pre-exist hypertension compl preg childbirth and puerperium	L128.00
Malignant hypertensive heart disease	G210.00
Secondary benign hypertension NOS	G241z00
Benign hypertensive heart disease with CCF	G211100
Benign hypertensive heart disease	G211.00
Secondary benign hypertension	G241.00
Hyperten heart&renal dis+both(congestv)heart and renal fail	G234.00
Secondary malignant renovascular hypertension	G240000
Pre-exist hyperten heart dis compl preg childbth+puerperium	L128000
Hypertensive heart disease NOS without CCF	G21z000
Benign hypertensive heart disease without CCF	G211000

Other pre-existing hypertension in preg/childb/puerp NOS	L122z00
Hypertensive heart disease NOS with CCF	G21z100
Benign hypertensive heart and renal disease	G231.00
[X]Oth antihyperten drug caus advers eff in therap use	NEC
Hypertensive heart and renal disease	G23..00
Other pre-existing hypertension in preg/childbirth/puerp	L122.00
Hypertens.monitor deleted	9OI9.00
Malignant hypertensive heart and renal disease	G230.00
Hypertensive heart and renal disease NOS	G23z.00
[X]Hypertensive diseases	Gyu2.00
Other pre-existing hypertension in preg/childb/puerp - deliv	L122100
Other hypertensive agent poisoning	SLC6.00
Malignant hypertensive heart disease with CCF	G210100
Secondary malignant hypertension NOS	G240z00
Other pre-existing hypertension in preg/childb/puerp unspec	L122000
Diastolic hypertension	G203.00
High cost hypertension drugs	7Q01.00
Pre-eclampsia or eclampsia + pre-existing hypertension NOS	L127z00
Malignant hypertensive heart disease without CCF	G210000

Trial withdrawal of antihypertensive therapy	662r.00
Other pre-exist hypertension in preg/childb/puerp-not deliv	L122300
[X]Hypertension secondary to other renal disorders	Gyu2100
Trial reduction of antihypertensive therapy	662q.00
Other specified high cost hypertension drugs	7Q01y00
Hypertension 9 month review	662P000
[X]Other secondary hypertension	Gyu2000
Malignant hypertensive heart disease NOS	G210z00
Stage 2 hypertension (NICE - Nat Ins for Hth Clin Excl 2011)	G28..00
Stage 1 hypertension	G25..11
Stage 1 hypertension (NICE - Nat Ins for Hth Clin Excl 2011)	G25..00
Hypertension resistant to drug therapy	G27..00
Severe hypertension	G26..11
Benign hypertensive heart disease NOS	G211z00
Severe hypertension (Nat Inst for Health Clinical Ex 2011)	G26..00
Trial withdrawal of antihypertensive therapy declined	8IA5.00
Primary hypertension	G20..12
Stage 1 hyperten (NICE 2011) without evidnce end organ damge	G250.00
Stage 1 hyperten (NICE 2011) with evidnce end organ damge	G251.00

Other pre-exist hypertension in preg/childb/puerp + p/n comp	L122400
DESCRIPTION	READ_CODE
Thyrotoxicosis	C02..00
Hyperthyroidism	C02..11
Thyrotoxic exophthalmos	F4G2000
Thyrotoxicosis without mention of goitre	cause with crisis
Graves' disease	C020.12
H/O: hyperthyroidism	1431
Toxic goitre	C02..12
Toxic multinodular goitre	C022.00
Thyrotoxicosis without mention of goitre or other cause	C02z.00
Toxic nodular goitre unspecified	C023.00
Thyrotoxic heart disease	G557500
Toxic diffuse goitre	C020.00
Hyperthyroidism resolved	212P.00
Thyrotoxicosis NOS	C02zz00
Thyrotoxicosis without mention of goitre or cause no crisis	C02z000
Toxic diffuse goitre with no crisis	C020000
Toxic uninodular goitre with no crisis	C021000
Thyrotoxicosis of other specified origin NOS	C02yz00
Thyrotoxicosis of other specified origin	C02y.00
Toxic multinodular goitre with no crisis	C022000
Toxic diffuse goitre NOS	C020z00
Toxic nodular goitre NOS	C023z00
Thyrotoxicosis from ectopic thyroid nodule	C024.00

Thyrotoxicosis of other specified origin with no crisis	C02y000
Toxic uninodular goitre	C021.00
Toxic multinodular goitre NOS	C022z00
Thyrotoxicosis from ectopic thyroid nodule NOS	C024z00
Toxic diffuse goitre with crisis	C020100
Toxic uninodular goitre NOS	C021z00
Thyrotoxicosis from ectopic thyroid nodule with no crisis	C024000
Toxic nodular goitre unspecified with no crisis	C023000
Toxic nodular goitre unspecified with crisis	C023100
Thyrotoxicosis of other specified origin with crisis	C02y100
Toxic multinodular goitre with crisis	C022100
DESCRIPTION	READ_CODE
Crohn's disease	J40..11
Crohn's colitis	J401z11
Crohn's disease of the small bowel NOS	J400z00
Regional enteritis - Crohn's disease	J40..00
Juvenile arthritis in Crohn's disease	N045300
Arthropathy in Crohn's disease	N031100
Crohn's disease of the large bowel NOS	J401z00
Crohn's disease of the terminal ileum	J400200
Orofacial Crohn's disease	J08z900
Exacerbation of Crohn's disease of small intestine	J400500
Exacerbation of Crohn's disease of large intestine	J401200

Crohn's disease of the ileum NOS	J400400
Crohn's disease NOS	J40z.11
Crohn's disease of the ileum unspecified	J400300
[X]Other Crohn's disease	Jyu4000
DESCRIPTION	READ_CODE
Ulcerative colitis	J410100
Ulcerative colitis and/or proctitis	J41..12
H/O: ulcerative colitis	14C4.11
Ulcerative proctocolitis	J410.00
Ulcerative proctitis	J410300
Arthropathy in ulcerative colitis	N031000
Exacerbation of ulcerative colitis	J410400
Ulcerative rectosigmoiditis	J410200
Ulcerative (chronic) enterocolitis	J411.00
Ulcerative proctocolitis NOS	J410z00
[X]Other ulcerative colitis	Jyu4100
Juvenile arthritis in ulcerative colitis	N045400
Ulcerative pancolitis	J413.00
DESCRIPTION	READ_CODE
Discoid lupus erythematosus	M154100
Lupus erythematosus	M154.00
Lupus erythematosus NOS	M154z00
Systemic lupus erythematosus	N000.00
Systemic lupus erythematosus with pericarditis	N000400
Disseminated lupus erythematosus	N000000
Subacute cutaneous lupus erythematosus	M154700
Systemic lupus erythematosus with organ or sys involv	N000300
Lung disease with systemic lupus erythematosus	H57y400

Lupus erythematosus chronicus	M154000
Drug-induced systemic lupus erythematosus	N000200
Lupus erythematosus migrans	M154200
Systemic lupus erythematosus NOS	N000z00
Polyneuropathy in disseminated lupus erythematosus	F371000
Lupus erythematosus tumidus	M154500
Systemic lupus erythematosus disease activity index	ZRq9.00
Lupus erythematosus profundus	M154400
Nephrotic syndrome in systemic lupus erythematosus	K01x400
Systemic lupus activity measure	ZRq8.00
[X]Other forms of systemic lupus erythematosus	Nyu4300
Lupus erythematosus unguium mutilans	M154600
Lupus erythematosus nodularis	M154300
Eyelid discoid lupus erythematosus	F4D3300
[X]Other local lupus erythematosus	Myu7800
SLAM - Systemic lupus activity measure	ZRq8.11
Myopathy due to disseminated lupus erythematosus	F396100
DESCRIPTION	READ_CODE
Insulin dependent diabetes mellitus	C100011
Type 1 diabetes mellitus	C10E.00
Insulin dependent diabetes mellitus	C108.00
Insulin dependent diabetes mellitus with retinopathy	C108700
Insulin dependent diabetes mellitus - poor control	C108800

Type 1 diabetes mellitus with nephropathy	C10ED00
Type 1 diabetes mellitus with ketoacidosis	C10EM00
Type I diabetes mellitus	C10E.11
Type I diabetes mellitus with diabetic cataract	C108F11
Type 1 diabetes mellitus	C108.12
Type 1 diabetes mellitus with neuropathic arthropathy	C108J12
Type 1 diabetes mellitus with retinopathy	C10E700
IDDM-Insulin dependent diabetes mellitus	C108.11
Type 1 diabetes mellitus with arthropathy	C10EH00
Type 1 diabetes mellitus with ulcer	C10E500
Type 1 diabetes mellitus with renal complications	C108012
Type 1 diabetes mellitus with exudative maculopathy	C10EP00
Type I diabetes mellitus	C108.13
Insulin dependent diabetes mellitus with mononeuropathy	C108B00
Unstable insulin dependent diabetes mellitus	C108400
Type 1 diabetes mellitus with persistent microalbuminuria	C10EL00
Type 1 diabetes mellitus with persistent proteinuria	C10EK00
Insulin dependent diabetes maturity onset	C108900

Type 1 diabetes mellitus - poor control	C10E800
Type I diabetes mellitus with retinopathy	C108711
Type 1 diabetes mellitus with hypoglycaemic coma	C10EE00
Insulin dependent diab mell with neuropathic arthropathy	C108J00
Type 1 diabetes mellitus maturity onset	C10E900
Type 1 diabetes mellitus with ketoacidotic coma	C10EN00
Type 1 diabetes mellitus with retinopathy	C108712
Insulin dependent diabetes mellitus with polyneuropathy	C108C00
Type I diabetes mellitus with hypoglycaemic coma	C108E11
Type 1 diabetes mellitus with neurological complications	C10E200
Unstable type 1 diabetes mellitus	C10E400
Insulin dependent diabetes mellitus with diabetic cataract	C108F00
Insulin dependent diabetes mellitus with hypoglycaemic coma	C108E00
Insulin dependent diabetes mellitus with ulcer	C108500
Insulin dependent diabetes mellitus with multiple complicat	C10E312
Type 1 diabetes mellitus - poor control	C108812
Type 1 diabetes mellitus with polyneuropathy	C10EC00

Type I diabetes mellitus - poor control	C108811
Type 1 diabetes mellitus with renal complications	C10E000
Type 1 diabetes mellitus with ophthalmic complications	C10E100
Type 1 diabetes mellitus with multiple complications	C10E300
Type I diabetes mellitus with neurological complications	C108211
Type 1 diabetes mellitus with diabetic cataract	C10EF00
Unstable type I diabetes mellitus	C10E411
Insulin dependent diabetes mellitus	C10E.12
Type I diabetes mellitus with ulcer	C108511
Insulin dependent diabetes mellitus with multiple complicatn	C108300
Type 1 diabetes mellitus with neuropathic arthropathy	C10EJ00
Unstable insulin dependent diabetes mellitus	C10E412
Type 1 diabetes mellitus with gastroparesis	C10EQ00
Insulin dependent diabetes mellitus with nephropathy	C108D00
Unstable type I diabetes mellitus	C108411
Type I diabetes mellitus with neuropathic arthropathy	C108J11
Insulin dependent diabetes mellitus with gangrene	C108600
Type I diabetes mellitus with renal complications	C108011
Type 1 diabetes mellitus with neurological complications	C108212

Type I diabetes mellitus with ketoacidosis	C10EM11
Type I diabetes mellitus with arthropathy	C108H11
Type I diabetes mellitus without complication	C10EA11
Type I diabetes mellitus maturity onset	C108911
Insulin dependent diab mell with peripheral angiopathy	C108G00
Insulin dependent diabetes mellitus with arthropathy	C108H00
Type I diabetes mellitus with ketoacidotic coma	C10EN11
Type I diabetes mellitus with nephropathy	C108D11
Type 1 diabetes mellitus with mononeuropathy	C10EB00
Type 1 diabetes mellitus with ulcer	C108512
Dietary advice for type I diabetes	ZC2C900
Type 1 diabetes mellitus without complication	C10EA00
Type 1 diabetes mellitus with gangrene	C10E600
Type 1 diabetes mellitus with hypoglycaemic coma	C108E12
Insulin dependent diabetes mellitus - poor control	C10E812
Type I diabetes mellitus with multiple complications	C10E311
Type I diabetes mellitus with polyneuropathy	C10EC11

Type 1 diabetes mellitus with peripheral angiopathy	C10EG00
Insulin dependent diabetes mellitus with retinopathy	C10E712
Type I diabetes mellitus with ulcer	C10E511
Type I diabetes mellitus with retinopathy	C10E711
Type I diabetes mellitus without complication	C108A11
Type I diabetes mellitus maturity onset	C10E911
Type 1 diabetes mellitus maturity onset	C108912
Unstable type 1 diabetes mellitus	C108412
Insulin dependent diabetes maturity onset	C10E912
Type I diabetes mellitus with exudative maculopathy	C10EP11
Insulin dependent diabetes mellitus with ulcer	C10E512
Type I diabetes mellitus with mononeuropathy	C108B11
Type I diabetes mellitus with ophthalmic complications	C10E111
Insulin dependent diabetes mellitus with hypoglycaemic coma	C10EE12
Insulin dependent diabetes mellitus with diabetic cataract	C10EF12
Insulin dependent diabetes mellitus with polyneuropathy	C10EC12
Type I diabetes mellitus with gangrene	C10E611

Insulin dependent diabetes mellitus with nephropathy	C10ED12
Type I diabetes mellitus with persistent microalbuminuria	C10EL11
Type 1 diabetes mellitus with ophthalmic complications	C108112
Type 1 diabetic dietary review	66At011
Type I diabetes mellitus - poor control	C10E811
Type I diabetes mellitus with multiple complications	C108311
Type I diabetes mellitus in remission	C10P000
Type I diabetes mellitus with gastroparesis	C10EQ11
Insulin dependent diabetes mellitus with gangrene	C10E612
Type 1 diabetes mellitus in remission	C10P011
Type I diabetes mellitus with renal complications	C10E011
Type 1 diabetes mellitus with diabetic cataract	C108F12
Type 1 diabetes mellitus without complication	C108A12
Type 1 diabetes mellitus with nephropathy	C108D12
Type I diabetes mellitus with nephropathy	C10ED11
Type I diabetes mellitus with polyneuropathy	C108C11
Type 1 diabetes mellitus with gangrene	C108612
DESCRIPTION	READ_CODE
Non-insulin dependent diabetes mellitus	C100112

Type 2 diabetes mellitus	C10F.00
Insulin treated Type 2 diabetes mellitus	C10FJ00
Diabetic on oral treatment	66A4.00
Non-insulin dependent diabetes mellitus	C109.00
NIDDM - Non-insulin dependent diabetes mellitus	C109.11
Diabetic on diet only	66A3.00
Non-insulin dependent diabetes mellitus - poor control	C109700
Type 2 diabetes mellitus with nephropathy	C10FC00
Type 2 diabetes mellitus with gangrene	C10F500
Non-insulin-dependent diabetes mellitus with retinopathy	C109600
Type 2 diabetes mellitus	C109.12
Type II diabetes mellitus with arthropathy	C109G11
Type 2 diabetes mellitus with renal complications	C109012
Type II diabetes mellitus	C109.13
Insulin treated Type II diabetes mellitus	C109J12
Insulin treated Type 2 diabetes mellitus	C109J00
Type 2 diabetes mellitus with persistent microalbuminuria	C10FM00
Type 2 diabetes mellitus with polyneuropathy	C10FB00
Type 2 diabetes mellitus with retinopathy	C10F600

Type 2 diabetes mellitus with renal complications	C10F000
Type II diabetes mellitus	C10F.11
Type II diabetes mellitus - poor control	C109711
Non-insulin dependent diabetes mellitus with arthropathy	C109G00
Type 2 diabetes mellitus with nephropathy	C109C12
Dietary advice for type II diabetes	ZC2CA00
Type 2 diabetes mellitus with exudative maculopathy	C10FQ00
Type 2 diabetes mellitus - poor control	C10F700
Type 2 diabetes mellitus with persistent proteinuria	C10FL00
Non-insulin-dependent diabetes mellitus without complication	C109900
Type 2 diabetes mellitus with ketoacidosis	C10FN00
Type 2 diabetes mellitus with neurological complications	C10F200
Hyperosmolar non-ketotic state in type 2 diabetes mellitus	C10FK00
Non-insulin dependent diabetes mellitus with ulcer	C109400
Type 2 diabetes mellitus with neuropathic arthropathy	C10FH00
Hyperosmolar non-ketotic state in type 2 diabetes mellitus	C109K00
Insulin treated non-insulin dependent diabetes mellitus	C109J11

Type 2 diabetes mellitus with peripheral angiopathy	C10FF00
Non-insulin dependent diabetes mellitus with gangrene	C109500
Non-insulin dependent d m with neuropathic arthropathy	C109H00
Type 2 diabetes mellitus with retinopathy	C109612
Type II diabetes mellitus with multiple complications	C10F311
Non-insulin dependent diabetes mellitus with hypoglyca coma	C109D00
Type 2 diabetes mellitus with diabetic cataract	C109E12
Type 2 diabetes mellitus with diabetic cataract	C10FE00
Non-insulin dependent diabetes mellitus with polyneuropathy	C109B00
Type 2 diabetes mellitus - poor control	C109712
Type 2 diabetes mellitus with neurological complications	C109212
Type 2 diabetes mellitus with gangrene	C109512
Type 2 diabetes mellitus with hypoglycaemic coma	C10FD00
Type II diabetes mellitus - poor control	C10F711
Type 2 diabetes mellitus with ophthalmic complications	C10F100
Type II diabetes mellitus with polyneuropathy	C109B11

Type II diabetes mellitus with neuropathic arthropathy	C109H11
Type 2 diabetes mellitus without complication	C10F900
Type II diabetes mellitus with diabetic cataract	C109E11
Type 2 diabetes mellitus with ulcer	C10F400
Type II diabetes mellitus with retinopathy	C10F611
Type 2 diabetes mellitus with arthropathy	C109G12
Type II diabetes mellitus with renal complications	C109011
Non-insulin-dependent diabetes mellitus with ophthalm comps	C109100
Type II diabetes mellitus with polyneuropathy	C10FB11
Pre-existing diabetes mellitus	non-insulin-dependent
Type II diabetes mellitus with mononeuropathy	C109A11
Type 2 diabetes mellitus with ketoacidotic coma	C10FP00
Non-insulin-dependent diabetes mellitus with renal comps	C109000
Type II diabetes mellitus without complication	C10F911
Non-insulin-dependent d m with peripheral angiopath	C109F00
Type II diabetes mellitus with peripheral angiopathy	C109F11
Type II diabetes mellitus with ulcer	C109411

Non-insulin-dependent diabetes mellitus with neuro comps	C109200
Type II diabetes mellitus with hypoglycaemic coma	C109D11
NIDDM with peripheral circulatory disorder	C107400
Type II diabetes mellitus with renal complications	C10F011
Type II diabetes mellitus with retinopathy	C109611
Type 2 diabetes mellitus with arthropathy	C10FG00
Non-insulin dependent diabetes mellitus with nephropathy	C109C00
Type II diabetes mellitus with ophthalmic complications	C109111
Type 2 diabetes mellitus with peripheral angiopathy	C109F12
Type II diabetes mellitus with persistent proteinuria	C10FL11
Type 2 diabetes mellitus with hypoglycaemic coma	C109D12
Type II diabetes mellitus with gangrene	C109511
Non-insulin-dependent diabetes mellitus with multiple comps	C109300
Type 2 diabetes mellitus with mononeuropathy	C10FA00
Type 2 diabetes mellitus with gastroparesis	C10FR00
Type II diabetes mellitus with nephropathy	C109C11

Insulin treated Type II diabetes mellitus	C10FJ11
Type 2 diabetes mellitus with multiple complications	C10F300
Type 2 diabetes mellitus with ulcer	C109412
Type 2 diabetes mellitus with neuropathic arthropathy	C109H12
Type II diabetes mellitus with neurological complications	C109211
Non-insulin depend diabetes mellitus with diabetic cataract	C109E00
Type 2 diabetes mellitus with ophthalmic complications	C109112
Non-insulin dependent diabetes mellitus with mononeuropathy	C109A00
Type II diabetes mellitus with persistent microalbuminuria	C10FM11
Type II diabetes mellitus with ulcer	C10F411
Type II diabetes mellitus with diabetic cataract	C10FE11
Type II diabetes mellitus with mononeuropathy	C10FA11
Type II diabetes mellitus with neurological complications	C10F211
Type II diabetes mellitus with hypoglycaemic coma	C10FD11
Type II diabetes mellitus with ophthalmic complications	C10F111
Type II diabetes mellitus with nephropathy	C10FC11
Type II diabetes mellitus with arthropathy	C10FG11

Type II diabetes mellitus with gangrene	C10F511
Type II diabetes mellitus with peripheral angiopathy	C10FF11
Type 2 diabetes mellitus without complication	C109912
Type II diabetes mellitus with ketoacidotic coma	C10FP11
Type II diabetes mellitus with ketoacidosis	C10FN11
Hyperosmolar non-ketotic state in type II diabetes mellitus	C10FK11
Type II diabetes mellitus in remission	C10P100
Type 2 diabetes mellitus with multiple complications	C109312
Type II diabetes mellitus without complication	C109911
Type II diabetes mellitus with neuropathic arthropathy	C10FH11
Conversion to non-insulin injectable medication	66AH300
Type 2 diabetes mellitus with polyneuropathy	C109B12
Diabetic on non-insulin injectable medication	66o2.00
Diabetic on oral treatment and glucagon-like peptide 1	66o5.00
Type 2 diabetes mellitus in remission	C10P111
Type II diabetes mellitus with exudative maculopathy	C10FQ11
Type II diabetes mellitus with multiple complications	C109311

Type II diabetes mellitus with gastroparesis	C10FR11
Focal epilepsy	F255011
Status epilepticus	unspecified
[X]Epileptic psychosis NOS	Eu05y11
Epilepsy monitoring	667..00
Absence seizure	2828
Tonic-clonic epilepsy	F251500
Jacksonian	focal or motor epilepsy
Epilepsy NOS	F25z.00
Petit mal status	F252.00
Locl-rlt(foc)(part)idiop epilep&epilptic syn seiz locl onset	F25y200
Other forms of epilepsy NOS	F25yz00
Generalised nonconvulsive epilepsy	F250.00
Complex partial epileptic seizure	F254500
Epilepsy control poor	667D.00
Juvenile absence epilepsy	F250400
Epileptic seizures - clonic	F251200
Benign Rolandic epilepsy	F25y400
Juvenile myoclonic epilepsy	F25A.00
Epilepsy control good	667C.00
Epilepsy does not limit activities	667L.00
Epilepsy treatment stopped	667A.00
Epilepsy confirmed	1O30.00
Tonic-clonic epilepsy	F251011
Salaam attacks	F256100
Psychomotor epilepsy	F254100
Epileptic seizures - atonic	F250200
Complex partial status epilepticus	F25y300

Partial epilepsy without impairment of consciousness	F255.00
Generalised convulsive epilepsy	F251.00
Epilepsy treatment changed	6678
Epilepsy limits activities	667K.00
Epilepsy restricts employment	667G.00
Partial epilepsy without impairment of consciousness OS	F255y00
Partial epilepsy without impairment of consciousness NOS	F255z00
Alcohol-induced epilepsy	F25B.00
Photosensitive epilepsy	F25F.00
Drug-induced epilepsy	F25C.00
Epileptic seizures - akinetic	F250300
[X]Schizophrenia-like psychosis in epilepsy	Eu05212
Partial epilepsy with impairment of consciousness NOS	F254z00
Partial epilepsy with impairment of consciousness	F254.00
Epileptic automatism	F254400
Epilepsy treatment started	6679
Lennox-Gastaut syndrome	F250500
Psychosensory epilepsy	F254200
Epilepsy monitoring NOS	667Z.00
Somatosensory epilepsy	F255200
Progressive myoclonic epilepsy	F132100
Neonatal myoclonic epilepsy	F251100
Early infant epileptic encephalopathy wth suppression bursts	F259.00
Other forms of epilepsy	F25y.00
Transient epileptic amnesia	1B1W.00
West syndrome	F256.12

Simple partial epileptic seizure	F255600
Generalised convulsive epilepsy NOS	F251z00
Epilepsy impairs education	667J.00
[X]Acquired aphasia with epilepsy [Landau - Kleffner]	Eu80300
Generalised nonconvulsive epilepsy NOS	F250z00
Other specified generalised convulsive epilepsy	F251y00
Emergency epilepsy treatment since last appointment	667W.00
Sensory induced epilepsy	F255100
[X]Limbic epilepsy personality	Eu06013
Infantile spasms NOS	F256z00
Otohara syndrome	F251111
Acquired epileptic aphasia	ZS82.00
Epilepsy associated problems	6674
Epilepsy prevents employment	667H.00
Ohtahara syndrome	F259.11
Gelastic epilepsy	F25y100
Cursive (running) epilepsy	F25y000
Limbic system epilepsy	F254300
Visual reflex epilepsy	F255400
Menstrual epilepsy	F25D.00
[X]Other status epilepticus	Fyu5200
Other specified generalised nonconvulsive epilepsy	F250y00
Stress-induced epilepsy	F25E.00
Motor epilepsy	F255012
Lightning spasms	F256.11
Unilateral epilepsy	F255500
[X]Other epilepsy	Fyu5100
Kojevnikov's epilepsy	F257.00

Visceral reflex epilepsy	F255300
Panayiotopoulos syndrome	F25y500
Partial epilepsy with autonomic symptoms	F255311
Pykno-epilepsy	F250100
[X]Other generalized epilepsy and epileptic syndromes	Fyu5000
Dravet syndrome	F25G.11
Severe myoclonic epilepsy in infancy	F25G.00
At risk of sudden unexpected death in epilepsy	14On.00

Drug codes

DESCRIPTION	BNF1
Sumatriptan 50mg tablets Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 100mg tablets Sumatriptan succinate 100mg Tablet Oral	04070401
Migraleve tablets (McNeil Products Ltd) Not applicable Route of administration not applicable	04070200
Migraleve Pink tablets (McNeil Products Ltd) Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
Rizatriptan 10mg oral lyophilisates sugar free Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Imigran 50mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 5mg/0.1ml nasal spray unit dose Zolmitriptan 50mg/1ml Spray Nasal	04070401
Rizatriptan 10mg orodispersible tablets sugar free Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Migard 2.5mg tablets (A. Menarini Farmaceutica Internazionale SRL) Frovatriptan succinate monohydrate 2.5mg Tablet Oral	04070401
Naramig 2.5mg tablets (DE Pharmaceuticals) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401

Imigran 10mg nasal spray (DE Pharmaceuticals) Sumatriptan 100mg/1ml Spray Nasal	04070401
Sumatriptan 50mg tablets (Mylan) Sumatriptan succinate 50mg Tablet Oral	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Actavis UK Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Imigran Radis 50mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Alliance Healthcare (Distribution) Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free Zolmitriptan 5mg Orodispersible tablet Oral	04070401
HealthAid 5-HTP HydroxyTryptoPhan 50mg tablets (HealthAid Ltd) Oxitriptan 50mg Modified-release tablet Oral	09040251
Zomig Rapimelt 2.5mg orodispersible tablets (Grunenthal Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (Accord Healthcare Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 2.5mg tablets (Actavis UK Ltd) Zolmitriptan 2.5mg Tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (Merck Sharp & Dohme Ltd) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Generic Migraleve Pink tablets Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
Sumatriptan 50mg tablets (Pfizer Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Naratriptan 2.5mg tablets (A A H Pharmaceuticals Ltd) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Zolmitriptan 2.5mg tablets Zolmitriptan 2.5mg Tablet Oral	04070401
Imigran 100mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zolmitriptan 2.5mg orodispersible tablets sugar free (Teva UK Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (Teva UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Almotriptan 12.5mg tablets Almotriptan hydrogen malate 12.5mg Tablet Oral	04070401

Sumatriptan 50mg tablets (Dexcel-Pharma Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 100mg tablets (A A H Pharmaceuticals Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Actavis UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Almus Pharmaceuticals Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 100mg tablets (Almus Pharmaceuticals Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zomig 5mg/0.1ml nasal spray 0.1ml unit dose (Waymade Healthcare Plc) Zolmitriptan 50mg/1ml Spray Nasal	04070401
Naramig 2.5mg tablets (GlaxoSmithKline UK Ltd) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Dr Reddy's Laboratories (UK) Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Rizatriptan 5mg tablets (A A H Pharmaceuticals Ltd) Rizatriptan benzoate 5mg Tablet Oral	04070401
Sumatriptan 100mg tablets (Arrow Generics Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free (Zentiva) Zolmitriptan 5mg Orodispersible tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (Mawdsley-Brooks & Company Ltd) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Eletriptan 20mg tablets Eletriptan hydrobromide 20mg Tablet Oral	04070401
Zolmitriptan 2.5mg tablets (Teva UK Ltd) Zolmitriptan 2.5mg Tablet Oral	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Alliance Healthcare (Distribution) Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (Sandoz Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Imigran 10mg nasal spray (Lexon (UK) Ltd) Sumatriptan 100mg/1ml Spray Nasal	04070401
Maxalt 10mg tablets (Merck Sharp & Dohme Ltd) Rizatriptan benzoate 10mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Milpharm Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401

Zolmitriptan 2.5mg orodispersible tablets sugar free (Alliance Healthcare (Distribution) Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Rizatriptan 10mg tablets (A A H Pharmaceuticals Ltd) Rizatriptan benzoate 10mg Tablet Oral	04070401
Imigran 50mg tablets (Lexon (UK) Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Arrow Generics Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Frovatriptan 2.5mg tablets Frovatriptan succinate monohydrate 2.5mg Tablet Oral	04070401
Relpax 20mg tablets (Upjohn UK Ltd) Eletriptan hydrobromide 20mg Tablet Oral	04070401
Zolmitriptan 5mg tablets Zolmitriptan 5mg Tablet Oral	04070401
Migraitan 50mg tablets (Bristol Laboratories Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Bristol Laboratories Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Migraleve Yellow tablets (McNeil Products Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Lamberts 5-HTP 100mg tablets (Lamberts Healthcare Ltd) Oxitriptan 100mg Tablet Oral	09040251
Sumatriptan 100mg tablets (Milpharm Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Imigran Radis 50mg tablets (Waymade Healthcare Plc) Sumatriptan succinate 50mg Tablet Oral	04070401
Imigran 10mg nasal spray (GlaxoSmithKline UK Ltd) Sumatriptan 100mg/1ml Spray Nasal	04070401
Sumatriptan 100mg tablets (Dr Reddy's Laboratories (UK) Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zolmitriptan 2.5mg orodispersible tablets sugar free Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Zomig 5mg/0.1ml nasal spray 0.1ml unit dose (Grunenthal Ltd) Zolmitriptan 50mg/1ml Spray Nasal	04070401
Maxalt 10mg tablets (Waymade Healthcare Plc) Rizatriptan benzoate 10mg Tablet Oral	04070401
Zomig 2.5mg tablets (Grunenthal Ltd) Zolmitriptan 2.5mg Tablet Oral	04070401

Rizatriptan 5mg tablets Rizatriptan benzoate 5mg Tablet Oral	04070401
Imigran 50mg tablets (DE Pharmaceuticals) Sumatriptan succinate 50mg Tablet Oral	04070401
Naratriptan 2.5mg tablets Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Generic Migraleve tablets Not applicable Route of administration not applicable	04070200
Rizatriptan 10mg orodispersible tablets sugar free (A A H Pharmaceuticals Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (A A H Pharmaceuticals Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Migraleve - 1 Tablet (Pfizer Consumer Healthcare Ltd) Buclizine Hydrochloride/Codeine Phosphate/Paracetamol Tablet Oral	03040102
Imigran Recovery 50mg tablets (Forest Laboratories UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free (Teva UK Ltd) Zolmitriptan 5mg Orodispersible tablet Oral	04070401
Maxalt 10mg tablets (DE Pharmaceuticals) Rizatriptan benzoate 10mg Tablet Oral	04070401
Migraleve Ultra 50mg tablets (McNeil Products Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Imigran Radis 100mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zomig Rapimelt 2.5mg orodispersible tablets (Mawdsley-Brooks & Company Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Rizatriptan 5mg orodispersible tablets sugar free Rizatriptan benzoate 5mg Orodispersible tablet Oral	04070401
Sumatriptan 100mg tablets (Waymade Healthcare Plc) Sumatriptan succinate 100mg Tablet Oral	04070401
Naratriptan 2.5mg tablets (Teva UK Ltd) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Sumatriptan 20mg/0.1ml nasal spray unit dose Sumatriptan 200mg/1ml Spray Nasal	04070401
Zomig Rapimelt 5mg orodispersible tablets (Grunenthal Ltd) Zolmitriptan 5mg Orodispersible tablet Oral	04070401
Zolmitriptan 2.5mg orodispersible tablets sugar free (Actavis UK Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401

Eletriptan 40mg tablets Eletriptan hydrobromide 40mg Tablet Oral	04070401
Sumatriptan 10mg/0.1ml nasal spray unit dose Sumatriptan 100mg/1ml Spray Nasal	04070401
Relpax 40mg tablets (Upjohn UK Ltd) Eletriptan hydrobromide 40mg Tablet Oral	04070401
Migraleve - 2 8mg+500mg Tablet (Pfizer Consumer Healthcare Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Maxalt 5mg tablets (Merck Sharp & Dohme Ltd) Rizatriptan benzoate 5mg Tablet Oral	04070401
Zolmitriptan 5mg tablets (Waymade Healthcare Plc) Zolmitriptan 5mg Tablet Oral	04070401
Imigran 20mg nasal spray (GlaxoSmithKline UK Ltd) Sumatriptan 200mg/1ml Spray Nasal	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Mylan) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (Lexon (UK) Ltd) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Aspire Pharma Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (DE Pharmaceuticals) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Almogran 12.5mg tablets (Almirall Ltd) Almotriptan hydrogen malate 12.5mg Tablet Oral	04070401
Imigran 20mg nasal spray (Lexon (UK) Ltd) Sumatriptan 200mg/1ml Spray Nasal	04070401
Rizatriptan 10mg tablets Rizatriptan benzoate 10mg Tablet Oral	04070401
Sumatriptan 100mg tablets (Mylan)Sumatriptan succinate100mgTabletOral	04070401
Sumatriptan 100mg tablets (Dexcel-Pharma Ltd)Sumatriptan succinate100mgTabletOral	04070401
Sumatriptan 50mg tablets (DE Pharmaceuticals)Sumatriptan succinate50mgTabletOral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free (A A H Pharmaceuticals Ltd)Zolmitriptan5mgOrodispersible tabletOral	04070401
Maxalt 5mg tablets (Mawdsley-Brooks & Company Ltd)Rizatriptan benzoate5mgTabletOral	04070401
Sumatriptan 100mg tablets (Pfizer Ltd)Sumatriptan succinate100mgTabletOral	04070401
Imigran 20mg nasal spray (Dowelhurst Ltd)Sumatriptan200mg/1mlSprayNasal	04070401

DESCRIPTION	BNF1
Topiramate 25mg capsules Topiramate 25mg Capsule Oral	04070402
Topiramate 50mg capsules Topiramate 50mg Capsule Oral	04070402
Topamax 25mg sprinkle capsules (Mawdsley-Brooks & Company Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 25mg capsules (Phoenix Healthcare Distribution Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 100mg tablets (Teva UK Ltd) Topiramate 100mg Tablet Oral	04070402
Topiramate 30mg/5ml oral solution Topiramate 6mg/1ml Oral solution Oral	04070402
Topiramate 12.5mg/5ml oral solution Topiramate 2.5mg/1ml Oral solution Oral	04070402
Topiramate 25mg capsules (A A H Pharmaceuticals Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 25mg capsules (Alliance Healthcare (Distribution) Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 10mg/5ml oral solution Topiramate 2mg/1ml Oral solution Oral	04070402
Topiramate 50mg capsules (A A H Pharmaceuticals Ltd) Topiramate 50mg Capsule Oral	04070402
Topiramate 25mg tablets (Sandoz Ltd) Topiramate 25mg Tablet Oral	04070402
Topiramate 25mg capsules (Actavis UK Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 50mg tablets (Accord Healthcare Ltd) Topiramate 50mg Tablet Oral	04070402
Topiramate 30mg/5ml oral suspension Topiramate 6mg/1ml Oral suspension Oral	04070402
Topamax 200mg tablets (Janssen-Cilag Ltd) Topiramate 200mg Tablet Oral	04070402
Topiramate 100mg/5ml oral solution Topiramate 20mg/1ml Oral solution Oral	04070402
Topiramate 50mg capsules (Teva UK Ltd) Topiramate 50mg Capsule Oral	04070402
Topamax 15mg sprinkle capsules (Waymade Healthcare Plc) Topiramate 15mg Capsule Oral	04070402
Topiramate 50mg capsules (Phoenix Healthcare Distribution Ltd) Topiramate 50mg Capsule Oral	04070402
Topamax 100mg tablets (Janssen-Cilag Ltd) Topiramate 100mg Tablet Oral	04070402
Topiramate 50mg tablets Topiramate 50mg Tablet Oral	04070402

Topamax 15mg sprinkle capsules (Janssen-Cilag Ltd) Topiramate 15mg Capsule Oral	04070402
Topiramate 50mg tablets (A A H Pharmaceuticals Ltd) Topiramate 50mg Tablet Oral	04070402
Topiramate 125mg/5ml oral suspension Topiramate 25mg/1ml Oral suspension Oral	04070402
Topiramate 50mg tablets (Teva UK Ltd) Topiramate 50mg Tablet Oral	04070402
Topiramate 20mg/5ml oral suspension Topiramate 4mg/1ml Oral suspension Oral	04070402
Topamax 50mg sprinkle capsules (Janssen-Cilag Ltd) Topiramate 50mg Capsule Oral	04070402
Topiramate 25mg/5ml oral solution Topiramate 5mg/1ml Oral solution Oral	04070402
Topiramate 200mg tablets Topiramate 200mg Tablet Oral	04070402
Topiramate 12mg/5ml oral suspension Topiramate 2.4mg/1ml Oral suspension Oral	04070402
Topiramate 50mg/5ml oral suspension sugar free Topiramate 10mg/1ml Oral suspension Oral	04070402
Topiramate 100mg/5ml oral suspension sugar free Topiramate 20mg/1ml Oral suspension Oral	04070402
Topiramate 15mg capsules Topiramate 15mg Capsule Oral	04070402
Topiramate 15mg/5ml oral solution Topiramate 3mg/1ml Oral solution Oral	04070402
Topamax 25mg tablets (Janssen-Cilag Ltd) Topiramate 25mg Tablet Oral	04070402
Topiramate 25mg capsules (Sandoz Ltd) Topiramate 25mg Capsule Oral	04070402
Topamax 25mg sprinkle capsules (Janssen-Cilag Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 50mg capsules (Waymade Healthcare Plc) Topiramate 50mg Capsule Oral	04070402
Topiramate 15mg capsules (A A H Pharmaceuticals Ltd) Topiramate 15mg Capsule Oral	04070402
Topiramate 200mg tablets (Actavis UK Ltd) Topiramate 200mg Tablet Oral	04070402
Topiramate 25mg tablets (Accord Healthcare Ltd) Topiramate 25mg Tablet Oral	04070402
Topiramate 100mg/5ml oral suspension Topiramate 20mg/1ml Oral suspension Oral	04070402
Topiramate 25mg tablets (Actavis UK Ltd) Topiramate 25mg Tablet Oral	04070402

Topiramate 15mg capsules (DE Pharmaceuticals) Topiramate 15mg Capsule Oral	04070402
Topiramate 25mg tablets (Teva UK Ltd) Topiramate 25mg Tablet Oral	04070402
Topamax 50mg tablets (Janssen-Cilag Ltd) Topiramate 50mg Tablet Oral	04070402
Topiramate 25mg capsules (DE Pharmaceuticals) Topiramate 25mg Capsule Oral	04070402
Topiramate 5mg/5ml oral solution Topiramate 1mg/1ml Oral solution Oral	04070402
Topiramate 25mg tablets Topiramate 25mg Tablet Oral	04070402
Topiramate 25mg/5ml oral suspension Topiramate 5mg/1ml Oral suspension Oral	04070402
Topiramate 20mg/5ml oral solution Topiramate 4mg/1ml Oral solution Oral	04070402
Topiramate 50mg/5ml oral suspension Topiramate 10mg/1ml Oral suspension Oral	04070402
Topiramate 12mg/5ml oral solution Topiramate 2.4mg/1ml Oral solution Oral	04070402
Topamax 50mg sprinkle capsules (Lexon (UK) Ltd) Topiramate 50mg Capsule Oral	04070402
Topiramate 25mg capsules (Teva UK Ltd) Topiramate 25mg Capsule Oral	04070402
Topiramate 12.5mg/5ml oral suspension Topiramate 2.5mg/1ml Oral suspension Oral	04070402
Topiramate 50mg capsules (Sandoz Ltd) Topiramate 50mg Capsule Oral	04070402
Topiramate 25mg capsules (Sigma Pharmaceuticals Plc) Topiramate 25mg Capsule Oral	04070402
Topiramate 15mg/5ml oral suspension Topiramate 3mg/1ml Oral suspension Oral	04070402
Topiramate 100mg tablets Topiramate 100mg Tablet Oral	04070402
Topiramate 100mg tablets (Milpharm Ltd)Topiramate100mgTabletOral	04070402
Topiramate 200mg tablets (Milpharm Ltd)Topiramate200mgTabletOral	04070402
Topiramate 50mg capsules (DE Pharmaceuticals)Topiramate50mgCapsuleOral	04070402
Topiramate 15mg capsules (Sandoz Ltd)Topiramate15mgCapsuleOral	04070402

DESCRIPTION	BNF1
Prochlorperazine 5mg tablets Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg/5ml oral solution Prochlorperazine mesilate 1mg/1ml Oral solution Oral	04020101

Proziere 5mg tablets (Ashbourne Pharmaceuticals Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (Teva UK Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg tablets (Waymade Healthcare Plc) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg/5ml syrup (Sanofi) Prochlorperazine mesilate 1mg/1ml Oral solution Oral	04020101
Prochlorperazine 5mg tablets (Bristol Laboratories Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg Tablet (Teva UK Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020100
Stemetil 5mg tablets (Sanofi) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg tablets (Mawdsley-Brooks & Company Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (Mylan) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg Tablet (Castlemead Healthcare Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020100
Prochlorperazine 5mg tablets (Actavis UK Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg tablets (Sigma Pharmaceuticals Plc) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (IVAX Pharmaceuticals UK Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (Medreich Plc) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (Waymade Healthcare Plc) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg/5ml Oral solution (Castlemead Healthcare Ltd) Prochlorperazine mesilate 1mg/1ml Oral solution Oral	04020100
Prochlorperazine 5mg tablets (Sigma Pharmaceuticals Plc) Prochlorperazine maleate 5mg Tablet Oral	04020101

Prochlorperazine 5mg tablets (Genesis Pharmaceuticals Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (A A H Pharmaceuticals Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg tablets (DE Pharmaceuticals) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine maleate 10mg modified release capsule Prochlorperazine Maleate 10mg Modified Release Capsules Oral	04020100
Prochlorperazine 5mg tablets (DE Pharmaceuticals) Prochlorperazine maleate 5mg Tablet Oral	04020101
Stemetil 5mg tablets (Lexon (UK) Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (Dr Reddy's Laboratories (UK) Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Prochlorperazine 5mg tablets (Almus Pharmaceuticals Ltd) Prochlorperazine maleate 5mg Tablet Oral	04020101
Vertigon spansule 10 10mg Spansule (GlaxoSmithKline Consumer Healthcare) Prochlorperazine Maleate 10mg Spansule Oral	04020100
Prochlorperazine 5mg tablets (Phoenix Healthcare Distribution Ltd)Prochlorperazine maleate5mgTabletOral	04020101

DESCRIPTION	BNF1
Metoclopramide 10mg tablets Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Maxolon 5mg/5ml Oral solution (Shire Pharmaceuticals Ltd) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	01020300
Metoclopramide 5mg/5ml oral solution sugar free (Sandoz Ltd) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500
Metoclopramide 10mg tablets (Almus Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 10mg tablets (Alliance Healthcare (Distribution) Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 5mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500

Metoclopramide 10mg tablets (A A H Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Maxolon 5mg/5ml syrup (Amdipharm Plc) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500
Metoclopramide 10mg Tablet (C P Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	01020300
Metoclopramide 10mg tablets (Actavis UK Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclomex 10mg tablets (Actavis UK Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 1mg/ml sugar free Oral solution Metoclopramide Hydrochloride 1mg/ml Oral Solution Oral	01020300
Maxolon 10mg Tablet (Shire Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	01020300
Metoclopramide 5mg/5ml oral solution sugar free (A A H Pharmaceuticals Ltd) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500
Maxolon Paediatric 5mg/5ml liquid (Amdipharm Plc) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500
Primperan 10mg Tablet (Berk Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	01020300
Metoclopramide 5mg/5ml oral solution sugar free (Alliance Healthcare (Distribution) Ltd) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500
Metoclopramide 10mg tablets (Crescent Pharma Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 10mg tablets (Accord Healthcare Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 10mg Tablet (Celltech Pharma Europe Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	01020300
Gastroflux 10mg tablets (Ashbourne Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 10mg tablets (Waymade Healthcare Plc) Metoclopramide hydrochloride 10mg Tablet Oral	04065500

Metoclopramide 10mg tablets (DE Pharmaceuticals) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metox 10mg Tablet (M A Steinhard Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	01020300
Maxolon 10mg tablets (Advanz Pharma) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 5mg/5ml Oral solution Metoclopramide Hydrochloride 5mg/5ml Oral Solution Oral	01020300
Primperan 5mg/5ml Oral solution sugar free (Berk Pharmaceuticals Ltd) Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	01020300
Metoclopramide 5mg/5ml oral solution sugar free Metoclopramide hydrochloride 1mg/1ml Oral solution Oral	04065500
Metoclopramide 10mg tablets (Kent Pharmaceuticals Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 10mg tablets (Sigma Pharmaceuticals Plc) Metoclopramide hydrochloride 10mg Tablet Oral	04065500
Metoclopramide 10mg tablets (Teva UK Ltd) Metoclopramide hydrochloride 10mg Tablet Oral	04065500

DESCRIPTION	BNF1
Motilium 30mg suppositories (Zentiva) Domperidone 30mg Suppository Rectal	04065500
Domperidone 10mg tablets (Zentiva) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 1mg/ml oral suspension sugar free Domperidone 1mg/1ml Oral suspension Oral	04065500
Domperidone 1mg/ml oral suspension sugar free (A A H Pharmaceuticals Ltd) Domperidone 1mg/1ml Oral suspension Oral	04065500
Domperidone 1mg/ml oral suspension sugar free (Waymade Healthcare Plc) Domperidone 1mg/1ml Oral suspension Oral	04065500
Motilium Instants 10mg orodispersible tablets (McNeil Products Ltd) Domperidone 10mg Orodispersible tablet Oral	04065500
Motilium 1mg/ml oral suspension (Zentiva) Domperidone 1mg/1ml Oral suspension Oral	04065500

Domperidone 10mg tablets (PLIVA Pharma Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Vivadone 10mg tablets (Lexon (UK) Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets (Sandoz Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets (A A H Pharmaceuticals Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 1mg/ml oral suspension sugar free (DE Pharmaceuticals) Domperidone 1mg/1ml Oral suspension Oral	04065500
Domperidone 800micrograms/5ml oral suspension Domperidone 160microgram/1ml Oral suspension Oral	04065500
Domperidone 10mg tablets (Strides Pharma UK Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets (Almus Pharmaceuticals Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Evoxin 10mg Tablet (Sanofi-Synthelabo Ltd) Domperidone maleate 10mg Tablet Oral	01020300
Motilium 10mg tablets (Waymade Healthcare Plc) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets (Actavis UK Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets (Mylan) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg tablets (Bristol Laboratories Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Motilium 10 tablets (McNeil Products Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 10mg orodispersible tablets sugar free Domperidone 10mg Orodispersible tablet Oral	04065500
Domperidone 10mg/5ml oral suspension Domperidone 2mg/1ml Oral suspension Oral	04065500
Domperidone 10mg Tablet (Manx Pharma Ltd) Domperidone maleate 10mg Tablet Oral	01020300
Motilium 10mg tablets (Zentiva) Domperidone maleate 10mg Tablet Oral	04065500

Evoxin 30mg Suppository (Sanofi-Synthelabo Ltd) Domperidone 30mg Suppository Rectal	01020300
Domperidone 1.9mg/5ml oral suspension Domperidone 380microgram/1ml Oral suspension Oral	04065500
Domperidone 10mg tablets (Wockhardt UK Ltd) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 50mg/5ml oral suspension Domperidone 10mg/1ml Oral suspension Oral	04065500
Domperidone 10mg/2ml solution for injection ampoules Domperidone 5mg/1ml Solution for injection Intravenous	04065500
Domperidone 1mg/ml oral suspension sugar free (Alliance Healthcare (Distribution) Ltd) Domperidone 1mg/1ml Oral suspension Oral	04065500
Domperidone 10mg tablets (Sigma Pharmaceuticals Plc) Domperidone maleate 10mg Tablet Oral	04065500
Domperidone 1mg/ml oral suspension sugar free (Zentiva) Domperidone 1mg/1ml Oral suspension Oral	04065500
Domperidone 10mg tablets (Medreich Plc)Domperidone maleate10mgTabletOral	04065500

DESCRIPTION	BNF1
Cyclizine 50mg tablets Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 50mg tablets (DE Pharmaceuticals) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 50mg tablets (A A H Pharmaceuticals Ltd) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 50mg tablets (Morningside Healthcare Ltd) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Valoid 50mg tablets (Amdipharm Plc) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 50mg tablets (Actavis UK Ltd) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 5mg/5ml oral suspension Cyclizine hydrochloride 1mg/1ml Oral suspension Oral	04060000
Cyclizine 50mg suppositories Cyclizine hydrochloride 50mg Suppository Rectal	04060000

Cyclizine 12.5mg/5ml oral solution Cyclizine hydrochloride 2.5mg/1ml Oral solution Oral	04060000
Cyclizine 50mg tablets (Alliance Healthcare (Distribution) Ltd) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 50mg/1ml solution for injection ampoules (Hameln Pharmaceuticals Ltd) Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 25mg/5ml oral suspension Cyclizine hydrochloride 5mg/1ml Oral suspension Oral	04060000
Cyclizine 50mg/1ml solution for injection ampoules (Martindale Pharmaceuticals Ltd) Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 50mg tablets (Phoenix Healthcare Distribution Ltd) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 12.5mg/5ml oral suspension Cyclizine hydrochloride 2.5mg/1ml Oral suspension Oral	04060000
Cyclizine 50mg/1ml solution for injection ampoules (Alliance Healthcare (Distribution) Ltd) Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 50mg/1ml solution for injection ampoules Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 50mg/1ml solution for injection ampoules (A A H Pharmaceuticals Ltd) Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 50mg tablets (Sigma Pharmaceuticals Plc) Cyclizine hydrochloride 50mg Tablet Oral	04060000
Cyclizine 50mg/5ml oral suspension Cyclizine hydrochloride 10mg/1ml Oral suspension Oral	04060000
Cyclizine 50mg/5ml oral solution Cyclizine hydrochloride 10mg/1ml Oral solution Oral	04060000
Cyclizine 5mg/5ml oral solution Cyclizine hydrochloride 1mg/1ml Oral solution Oral	04060000
Valoid 50mg/1ml solution for injection ampoules (Advanz Pharma) Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 10mg/5ml oral solution Cyclizine hydrochloride 2mg/1ml Oral solution Oral	04060000
Cyclizine 50mg tablets (Advanz Pharma) Cyclizine hydrochloride 50mg Tablet Oral	04060000

Cyclizine 25mg suppositories Cyclizine hydrochloride 25mg Suppository Rectal	04060000
Cyclizine 50mg/1ml solution for injection ampoules (Advanz Pharma) Cyclizine lactate 50mg/1ml Solution for injection Intravenous/Intramuscular	04060000
Cyclizine 10mg/5ml oral suspension Cyclizine hydrochloride 2mg/1ml Oral suspension Oral	04060000
Cyclizine 50mg tablets (Teva UK Ltd) Cyclizine hydrochloride 50mg Tablet Oral	04060000

DESCRIPTION	BNF1
Tolfenamic acid 200mg Capsule Tolfenamic Acid 200mg Capsule Oral	04070401
Clotam Rapid 200mg tablets (Galen Ltd) Tolfenamic acid 200mg Tablet Oral	04070401
Tolfenamic acid 200mg tablets (A A H Pharmaceuticals Ltd) Tolfenamic acid 200mg Tablet Oral	04070401
Tolfenamic acid 200mg tablets Tolfenamic acid 200mg Tablet Oral	04070401
Clotam 200mg Capsule (Thames Laboratories Ltd) Tolfenamic Acid 200mg Capsule Oral	04070401

DESCRIPTION	BNF1
Epilim Chrono 500 tablets (Sanofi) Sodium valproate 500mg Modified-release tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Epilim Chrono 300 tablets (Sanofi) Sodium valproate 300mg Modified-release tablet Oral	04080100
Epilim ec 200mg Gastro-resistant tablet (Sanofi) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Epilim Chrono 200 tablets (Sanofi) Sodium valproate 200mg Modified-release tablet Oral	04080100
Sodium valproate 500mg gastro-resistant tablets Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Epilim 500 gastro-resistant tablets (Sanofi) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100

Depakote 250mg gastro-resistant tablets (Sanofi) Valproate semisodium 250mg Gastro-resistant tablet Oral	04020300
Valproic acid 500mg gastro-resistant tablets Valproate semisodium 500mg Gastro-resistant tablet Oral	04020300
Valproic acid 250mg gastro-resistant tablets Valproate semisodium 250mg Gastro-resistant tablet Oral	04020300
Sodium valproate 200mg/5ml oral solution Sodium valproate 40mg/1ml Oral solution Oral	04080100
Epilim 200mg/5ml syrup (Sanofi) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate with valproic acid 200mg modified release tablets Sodium Valproate 200mg Modified Release Tablet Oral	04080100
Episenta 300mg modified-release capsules (Desitin Pharma Ltd) Sodium valproate 300mg Modified-release capsule Oral	04080100
Epilim Chronosphere MR 750mg granules sachets (Sanofi) Sodium valproate 750mg Modified-release granules Oral	04080100
Valproate sodium 500mg Gastro-resistant tablet (IVAX Pharmaceuticals UK Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Valproic acid 500mg/5ml oral suspension Valproate semisodium 100mg/1ml Oral suspension Oral	04020300
Epilim Chronosphere MR 500mg granules sachets (Sanofi) Sodium valproate 500mg Modified-release granules Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Teva UK Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Epilim Chrono 300 tablets (Lexon (UK) Ltd) Sodium valproate 300mg Modified-release tablet Oral	04080100
Sodium valproate 500mg modified-release tablets Sodium valproate 500mg Modified-release tablet Oral	04080100
Sodium valproate 500mg gastro-resistant tablets (Zentiva) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Epilim ec 500mg Gastro-resistant tablet (Sanofi) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Sodium valproate 200mg/5ml oral solution sugar free (Wockhardt UK Ltd) Sodium valproate 40mg/1ml Oral solution Oral	04080100

Convulex 500mg gastro-resistant capsules (Pfizer Ltd) Valproic acid 500mg Gastro-resistant capsule Oral	04070402
Sodium valproate 500mg modified-release tablets (J M McGill Ltd) Sodium valproate 500mg Modified-release tablet Oral	04080100
Sodium valproate with valproic acid 500mg modified release tablets Sodium Valproate 500mg Modified Release Tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Valproic acid 500mg/5ml oral solution Valproate semisodium 100mg/1ml Oral solution Oral	04020300
Epilim Chrono 300 tablets (DE Pharmaceuticals) Sodium valproate 300mg Modified-release tablet Oral	04080100
Epilim Chrono 300 tablets (Waymade Healthcare Plc) Sodium valproate 300mg Modified-release tablet Oral	04080100
Epilim Chrono 200 tablets (Lexon (UK) Ltd) Sodium valproate 200mg Modified-release tablet Oral	04080100
Epilim 200 gastro-resistant tablets (Sanofi) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Convulex 300mg gastro-resistant capsules (Pfizer Ltd) Valproic acid 300mg Gastro-resistant capsule Oral	04070402
Orlept SF 200mg/5ml liquid (Wockhardt UK Ltd) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate CR 300mg Tablet (Hillcross Pharmaceuticals Ltd) Sodium Valproate 300mg Tablet	04080100
Epilim Chrono 500 tablets (Lexon (UK) Ltd) Sodium valproate 500mg Modified-release tablet Oral	04080100
Sodium valproate 750mg modified-release granules sachets sugar free Sodium valproate 750mg Modified-release granules Oral	04080100
Epilim Chronosphere MR 250mg granules sachets (Sanofi) Sodium valproate 250mg Modified-release granules Oral	04080100
Sodium valproate 500mg gastro-resistant tablets (Wockhardt UK Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100

Sodium valproate 200mg/5ml Oral solution (Sterwin Medicines) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate 300mg suppositories Sodium valproate 300mg Suppository Rectal	04080100
Epilim Chrono 500 tablets (Waymade Healthcare Plc) Sodium valproate 500mg Modified-release tablet Oral	04080100
Belvo 250mg gastro-resistant tablets (Consilient Health Ltd) Valproate semisodium 250mg Gastro-resistant tablet Oral	04020300
Epilim Chrono 200 tablets (Waymade Healthcare Plc) Sodium valproate 200mg Modified-release tablet Oral	04080100
Sodium valproate 500mg modified-release granules sachets sugar free Sodium valproate 500mg Modified-release granules Oral	04080100
Epilim Chrono 500 tablets (DE Pharmaceuticals) Sodium valproate 500mg Modified-release tablet Oral	04080100
Sodium valproate 500mg gastro-resistant tablets (Arrow Generics Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Depakote 500mg gastro-resistant tablets (Sanofi) Valproate semisodium 500mg Gastro-resistant tablet Oral	04020300
Orlept 200mg gastro-resistant tablets (Wockhardt UK Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Syonell 250mg gastro-resistant tablets (Lupin Healthcare (UK) Ltd) Valproate semisodium 250mg Gastro-resistant tablet Oral	04020300
Sodium valproate 200mg/5ml oral solution sugar free (A A H Pharmaceuticals Ltd) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Episenta 1000mg modified-release granules sachets (Desitin Pharma Ltd) Sodium valproate 1gram Modified-release granules Oral	04020300
Sodium valproate oral solution Sodium Valproate Oral Liquid Oral	04080100
Valproate sodium 200mg Gastro-resistant tablet (IVAX Pharmaceuticals UK Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Epilim 200mg/5ml syrup (Lexon (UK) Ltd) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Orlept 500mg gastro-resistant tablets (Wockhardt UK Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100

Epival CR 500mg tablets (Healthcare Pharma Ltd) Sodium valproate 500mg Modified-release tablet Oral	04080100
Sodium valproate 150mg modified-release capsules Sodium valproate 150mg Modified-release capsule Oral	04080100
Sodium valproate 500mg Tablet (Sterwin Medicines) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Sodium valproate with valproic acid 300mg modified release tablets Sodium Valproate 300mg Modified Release Tablet Oral	04080100
Sodium valproate CR 500mg Tablet (Hillcross Pharmaceuticals Ltd) Sodium Valproate 500mg Tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Zentiva) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Epilim Chrono 200 tablets (DE Pharmaceuticals) Sodium valproate 200mg Modified-release tablet Oral	04080100
Sodium valproate with valproic acid 750mg modified release granules Sodium Valproate 750mg Modified Release Granules Oral	04080100
Valproic acid 250mg/5ml oral suspension Valproate semisodium 50mg/1ml Oral suspension Oral	04020300
Sodium valproate 500mg/5ml oral suspension Sodium valproate 100mg/1ml Oral suspension Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Wockhardt UK Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Sodium valproate 200mg/5ml Oral solution (IVAX Pharmaceuticals UK Ltd) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate 250mg modified-release granules sachets sugar free Sodium valproate 250mg Modified-release granules Oral	04080100
Sodium valproate 1g modified-release granules sachets sugar free Sodium valproate 1gram Modified-release granules Oral	04080100
Sodium valproate with valproic acid 500mg modified release granules Sodium Valproate 500mg Modified Release Granules Oral	04080100
Sodium valproate 500mg gastro-resistant tablets (Teva UK Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100

Sodium valproate 300mg modified-release capsules Sodium valproate 300mg Modified-release capsule Oral	04080100
Sodium valproate 200mg Tablet (Sterwin Medicines) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Sodium valproate 200mg/5ml oral solution sugar free (Zentiva) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Syonell 500mg gastro-resistant tablets (Lupin Healthcare (UK) Ltd) Valproate semisodium 500mg Gastro-resistant tablet Oral	04020300
Sodium valproate 600mg/5ml oral solution Sodium valproate 120mg/1ml Oral solution Oral	04080100
Valproic acid 250mg/5ml oral solution Valproate semisodium 50mg/1ml Oral solution Oral	04020300
Epilim 500 gastro-resistant tablets (Waymade Healthcare Plc) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Sodium valproate 500mg modified-release tablets (Alliance Healthcare (Distribution) Ltd) Sodium valproate 500mg Modified-release tablet Oral	04080100
Epilim Chrono 200 tablets (Sigma Pharmaceuticals Plc) Sodium valproate 200mg Modified-release tablet Oral	04080100
Sodium valproate 300mg modified-release tablets (Sigma Pharmaceuticals Plc) Sodium valproate 300mg Modified-release tablet Oral	04080100
Epilim Chronosphere MR 1000mg granules sachets (Sanofi) Sodium valproate 1gram Modified-release granules Oral	04080100
Sodium valproate 200mg modified-release tablets Sodium valproate 200mg Modified-release tablet Oral	04080100
Episenta 500mg modified-release granules sachets (Desitin Pharma Ltd) Sodium valproate 500mg Modified-release granules Oral	04020300
Epilim 200mg/5ml syrup (DE Pharmaceuticals) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate with valproic acid 250mg modified release granules Sodium Valproate 250mg Modified Release Granules Oral	04080100

Sodium valproate 500mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Sodium valproate 500mg Gastro-resistant tablet (C P Pharmaceuticals Ltd) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Sodium valproate 500mg gastro-resistant tablets (Mylan) Sodium valproate 500mg Gastro-resistant tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Mylan) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Waymade Healthcare Plc) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Sodium valproate 500mg modified-release tablets (DE Pharmaceuticals) Sodium valproate 500mg Modified-release tablet Oral	04080100
Epilim 200mg/5ml liquid (Sanofi) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate with valproic acid 1000mg modified release granules Sodium Valproate 1000mg Modified Release Granules Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Epival CR 300mg tablets (Healthcare Pharma Ltd) Sodium valproate 300mg Modified-release tablet Oral	04080100
Sodium valproate 200mg/5ml oral solution sugar free Sodium valproate 40mg/1ml Oral solution Oral	04080100
Sodium valproate 200mg/5ml Oral solution (Hillcross Pharmaceuticals Ltd) Sodium valproate 40mg/1ml Oral solution Oral	04080100
Belvo 500mg gastro-resistant tablets (Consilient Health Ltd) Valproate semisodium 500mg Gastro-resistant tablet Oral	04020300
Sodium valproate 300mg modified-release tablets Sodium valproate 300mg Modified-release tablet Oral	04080100
Sodium valproate 200mg gastro-resistant tablets (Actavis UK Ltd) Sodium valproate 200mg Gastro-resistant tablet Oral	04080100
Sodium valproate 500mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd)Sodium valproate500mgGastro-resistant tabletOral	04080100
Sodium valproate 500mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd)Sodium valproate500mgGastro-resistant tabletOral	04080100

Sodium valproate 300mg modified-release tablets (Colorama Pharmaceuticals Ltd)Sodium valproate300mgModified-release tabletOral	04080100
Sodium valproate 200mg modified-release tablets (DE Pharmaceuticals)Sodium valproate200mgModified-release tabletOral	04080100
Sodium valproate 300mg modified-release tablets (Ennogen Healthcare Ltd)Sodium valproate300mgModified-release tabletOral	04080100
Sodium valproate 200mg modified-release tablets (Ennogen Healthcare Ltd)Sodium valproate200mgModified-release tabletOral	04080100
Epilim 200mg/5ml liquid (Waymade Healthcare Plc)Sodium valproate40mg/1mlOral solutionOral	04080100

DESCRIPTION	BNF1
Amitriptyline 10mg tablets Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg modified-release capsules Amitriptyline hydrochloride 25mg Modified-release capsule Oral	00000000
Lentizol 50mg modified-release capsules (Pfizer Ltd) Amitriptyline hydrochloride 50mg Modified-release capsule Oral	00000000
Amitriptyline 10mg tablets (Teva UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Perphenazine 2mg with Amitriptyline 25mg tablet Amitriptyline Hydrochloride/Perphenazine 2mg + 25mg Tablets Oral	04020100
Amitriptyline 25mg / Perphenazine 2mg tablets Amitriptyline hydrochloride/Perphenazine 25mg + 2mg Tablet Oral	04030100
Tryptizol mr 75mg Modified-release capsule (Merck Sharp & Dohme Ltd) Amitriptyline Hydrochloride 75mg Modified-Release Capsule Oral	04030100
Amitriptyline 10mg tablets (Almus Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml Oral solution (Rosemont Pharmaceuticals Ltd) Amitriptyline Hydrochloride 10mg/5ml Oral Solution Oral	04030100

Amitriptyline 50mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg/1ml Oral solution Oral	04030100
AMITRIPTYLINE	00000000
Amitriptyline 25mg tablets (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 75mg modified-release capsules Amitriptyline Hydrochloride 75mg Modified Release Capsules Oral	04030100
Amitriptyline 50mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg tablets (DE Pharmaceuticals) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Crescent Pharma Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg Tablet (Sussex Pharmaceutical Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
AMITRIPTYLINE 100 MG TAB	00000000
Amitriptyline 25mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Almus Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Lentizol 25mg modified-release capsules (Pfizer Ltd) Amitriptyline hydrochloride 25mg Modified-release capsule Oral	00000000
Amitriptyline 25mg tablets (Phoenix Healthcare Distribution Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Arrow Generics Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Teva UK Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Almus Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100

Amitriptyline 5mg/5ml oral suspension Amitriptyline hydrochloride 1mg/1ml Oral suspension Oral	04030100
Amitriptyline 10mg Tablet (Sussex Pharmaceutical Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 100mg/5ml oral solution Amitriptyline hydrochloride 20mg/1ml Oral solution Oral	04030100
Amitriptyline 50mg/5ml oral solution sugar free Amitriptyline hydrochloride 10mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg tablets (Genesis Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Tryptizol 10mg/5ml sugar free Oral solution (Merck Sharp and Dohme Ltd) Amitriptyline Hydrochloride 10mg/5ml Oral Solution Oral	04030100
AMITRIPTYLINE S/R	00000000
Triptafen m 2mg+10mg Tablet (Goldshield Pharmaceuticals Ltd) Amitriptyline hydrochloride/Perphenazine 10mg + 2mg Tablet Oral	04020100
Amitriptyline 10mg tablets (Actavis UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Kent Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Teva UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 75mg/5ml oral solution Amitriptyline hydrochloride 15mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg tablets (IVAX Pharmaceuticals UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Wockhardt UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	00000000
Domical 25mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100

Domical 50mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Sigma Pharmaceuticals Plc) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
AMITRIPTYLINE S/F	00000000
Tryptizol 10mg Tablet (Merck Sharp & Dohme Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Ranbaxy (UK) Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
AMITRIPTYLINE S/F 25 MG/5ML SYR	00000000
Amitriptyline oral solution Amitriptyline Hydrochloride Oral Liquid Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg tablets (Arrow Generics Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets (DE Pharmaceuticals) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Waymade Healthcare Plc) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 12.5mg / Chlordiazepoxide 5mg capsules Amitriptyline Hydrochloride/Chlordiazepoxide 12.5mg + 5mg Capsules Oral	04030100
Domical 10mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral suspension Amitriptyline hydrochloride 2mg/1ml Oral suspension Oral	04030100
Limbitrol 10 Capsule (Roche Products Ltd) Amitriptyline Hydrochloride/Chlordiazepoxide Capsule Oral	04030100
Amitriptyline 10mg tablets (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg Tablet (Regent Laboratories Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Actavis UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100

Amitriptyline 25mg Tablet (Crosspharma Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free (DE Pharmaceuticals) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
TRYPTIZOL	00000000
Amitriptyline 10mg tablets (Phoenix Healthcare Distribution Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Accord Healthcare Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 50mg/5ml oral solution sugar free (Wockhardt UK Ltd) Amitriptyline hydrochloride 10mg/1ml Oral solution Oral	04030100
Amitriptyline 50mg tablets (Accord Healthcare Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg tablets (NorthStar Healthcare Unlimited Company) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
AMITRIPTYLINE 75 MG TAB	00000000
Limbitrol 5 Capsule (Roche Products Ltd) Amitriptyline Hydrochloride/Chlordiazepoxide Capsule Oral	04030100
Amitriptyline 2.5mg/5ml oral solution Amitriptyline hydrochloride 500microgram/1ml Oral solution Oral	04030100
Amitriptyline 10mg/5ml sugar free oral solution Amitriptyline Hydrochloride 10mg/5ml Oral Solution Sugar-Free Oral	04030100
Amitriptyline 25mg tablets (DE Pharmaceuticals) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Tryptizol 50mg Tablet (Merck Sharp & Dohme Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 50mg tablets (IVAX Pharmaceuticals UK Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Elavil 10mg Tablet (DDSA Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100

Amitriptyline 50mg modified-release capsules Amitriptyline hydrochloride 50mg Modified-release capsule Oral	00000000
Amitriptyline 50mg tablets (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Kent Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Sandoz Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 10mg tablets (IVAX Pharmaceuticals UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Kent Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 5mg/5ml oral solution Amitriptyline hydrochloride 1mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg / Perphenazine 2mg tablets Amitriptyline hydrochloride/Perphenazine 10mg + 2mg Tablet Oral	00000000
Amitriptyline 25mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg tablets (Mawdsley-Brooks & Company Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free (Wockhardt UK Ltd) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg tablets (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Wockhardt UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Triptafen-M tablets (Mercury Pharma Group Ltd) Amitriptyline hydrochloride/Perphenazine 10mg + 2mg Tablet Oral	00000000
Amitriptyline 25mg / Chlordiazepoxide 10mg capsules Amitriptyline Hydrochloride/Chlordiazepoxide 25mg + 10mg Capsules Oral	04030100

Amitriptyline 10mg/5ml oral solution sugar free (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
AMITRIPTYLINE 300 MG TAB	00000000
Amitriptyline 25mg Tablet (Celltech Pharma Europe Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Accord Healthcare Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Sigma Pharmaceuticals Plc) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Sigma Pharmaceuticals Plc) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Tryptizol 25mg Tablet (Merck Sharp & Dohme Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Wockhardt UK Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg tablets (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Genesis Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Perphenazine 2mg with Amitriptyline 10mg tablet Amitriptyline Hydrochloride/Perphenazine 2mg + 10mg Tablets Oral	04020100
Amitriptyline 10mg tablets (Mawdsley-Brooks & Company Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (Wockhardt UK Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Triptafen tablets (Advanz Pharma) Amitriptyline hydrochloride/Perphenazine 25mg + 2mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Arrow Generics Ltd)Amitriptyline hydrochloride50mgTabletOral	04030100

DESCRIPTION	BNF1
Diclofenac sodium 50mg gastro-resistant tablets Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg Tablet (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets Diclofenac Sodium 50mg EC Tablets Oral	10010100
Voltarol 50mg gastro-resistant tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 25mg Tablet (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 25mg gastro-resistant tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Lofensaid 50mg gastro-resistant tablets (Opus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg Gastro-resistant tablet (Genus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Alliance Healthcare (Distribution) Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Phoenix Healthcare Distribution Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Dicloflex 25mg gastro-resistant tablets (Dexcel-Pharma Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (A A H Pharmaceuticals Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Voltarol 50mg dispersible tablets (DE Pharmaceuticals) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac 50mg dispersible tablets sugar free (DE Pharmaceuticals) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Voltarol Rapid 50mg tablets (Lexon (UK) Ltd) Diclofenac potassium 50mg Tablet Oral	10010100

Diclofenac sodium 50mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Waymade Healthcare Plc) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg capsules Diclofenac Sodium	10010100
Diclofenac sodium 25mg tablets Diclofenac Sodium 25mg Tablets Oral	10010100
Voltarol Pain-eze Extra Strength 25mg tablets (Novartis Consumer Health UK Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
DICLOFENAC SODIUM S/R	00000000
Diclofenac 10mg/5ml oral suspension Diclofenac sodium 2mg/1ml Oral suspension Oral	10010100
Dicloflex 50mg Gastro-resistant tablet (Ratiopharm UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
First Resort Double Action Pain Relief 12.5mg tablets (Actavis UK Ltd) Diclofenac potassium 12.5mg Tablet Oral	10010100
Valenac ec 50mg Gastro-resistant tablet (Shire Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Sterwin Medicines) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Focus Pharmaceuticals Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Mylan) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (DE Pharmaceuticals) Diclofenac potassium 50mg Tablet Oral	10010100
Dicloflex 25mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100

Diclofenac sodium 50mg gastro-resistant tablets (Waymade Healthcare Plc) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Dicloflex 50mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg Tablet (C P Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Gastro-resistant tablet (Genus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Sterwin Medicines) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Medreich Plc) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets Diclofenac potassium 50mg Tablet Oral	10010100
Voltarol Rapid 25mg tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Sandoz Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Waymade Healthcare Plc) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 25mg tablets (Accord Healthcare Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac 50mg/5ml oral solution Diclofenac sodium 10mg/1ml Oral solution Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Crescent Pharma Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg Tablet (Regent Laboratories Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg/5ml oral suspension Diclofenac sodium 10mg/1ml Oral suspension Oral	10010100
Diclofenac potassium 50mg tablets (DE Pharmaceuticals) Diclofenac potassium 50mg Tablet Oral	10010100

Diclofenac 12.5mg/5ml oral solution Diclofenac sodium 2.5mg/1ml Oral solution Oral	10010100
Diclofenac 50mg Gastro-resistant tablet (Pharmacia Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 12.5mg tablets Diclofenac potassium 12.5mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Actavis UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Waymade Healthcare Plc) Diclofenac potassium 50mg Tablet Oral	10010100
Flamrase 50 EC tablets (Teva UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Teva UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Medreich Plc) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 25mg tablets (DE Pharmaceuticals) Diclofenac potassium 25mg Tablet Oral	10010100
Fenactol 50mg gastro-resistant tablets (Dexcel-Pharma Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 10mg dispersible tablets Diclofenac sodium 10mg Dispersible tablet Oral	10010100
Valenac ec 25mg Gastro-resistant tablet (Shire Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Teva UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Lexon (UK) Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Defanac 25mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets Diclofenac Sodium 25mg EC Tablets Oral	10010100

Diclofenac 50mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Rhumalgan 25mg Tablet (Lagap) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Dicloflex 50mg gastro-resistant tablets (Dexcel-Pharma Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Mawdsley-Brooks & Company Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Flamrase 25 EC tablets (Teva UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Volraman 25mg gastro-resistant tablets (LPC Medical (UK) Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Sigma Pharmaceuticals Plc) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Sigma Pharmaceuticals Plc) Diclofenac potassium 50mg Tablet Oral	10010100
Fenactol 25mg gastro-resistant tablets (Discovery Pharmaceuticals) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Mawdsley-Brooks & Company Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Defanac 50mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Pain-eze 12.5mg tablets (Novartis Consumer Health UK Ltd) Diclofenac potassium 12.5mg Tablet Oral	10010100
Diclofenac 50mg Tablet (Approved Prescription Services Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Isclofen 50mg Gastro-resistant tablet (Isis Products Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (DE Pharmaceuticals) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100

Diclofenac sodium 50mg gastro-resistant tablets (Actavis UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclovol 50mg gastro-resistant tablets (Arun Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Dicloflex 25mg gastro-resistant tablets (Teva UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Genesis Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Dicloflex 25mg Gastro-resistant tablet (Ratiopharm UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 25mg tablets Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg dispersible tablets sugar free Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac 25mg Tablet (Berk Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Lofensaid 25mg gastro-resistant tablets (Opus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Gastro-resistant tablet (Pharmacia Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac potassium 25mg tablets (A A H Pharmaceuticals Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac 50mg dispersible tablets sugar free (Sigma Pharmaceuticals Plc) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Mylan) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Rhumalgan 50mg Tablet (Lagap) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 10mg/5ml oral solution Diclofenac sodium 2mg/1ml Oral solution Oral	10010100
Diclofenac sodium 50mg tablets Diclofenac Sodium 50mg Tablets Oral	10010100

Diclofenac 50mg Tablet (Berk Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Tablet (C P Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Acoflam 50mg gastro-resistant tablets (Mercury Pharma Group Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Accord Healthcare Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac 12.5mg/5ml oral suspension Diclofenac sodium 2.5mg/1ml Oral suspension Oral	10010100
Diclovol 25mg gastro-resistant tablets (Arun Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (DE Pharmaceuticals) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Sandoz Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Stephar (U.K.) Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclozip 25mg gastro-resistant tablets (Ashbourne Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Volraman 50mg gastro-resistant tablets (LPC Medical (UK) Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Sigma Pharmaceuticals Plc) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclozip 50mg gastro-resistant tablets (Ashbourne Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Stephar (U.K.) Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100

Diclofenac 15mg/5ml oral suspensionDiclofenac sodium3mg/1mlOral suspensionOral	10010100
Diclofenac potassium 50mg tablets (Medihealth (Northern) Ltd)Diclofenac potassium50mgTabletOral	10010100
Diclofenac sodium 25mg capsulesDiclofenac Sodium	10010100

DESCRIPTION	BNF1
Nurofen Maximum Strength Migraine Pain 684mg caplets (Reckitt Benckiser Healthcare (UK) Ltd) Ibuprofen lysine 400mg Tablet Oral	4070100
Galprofen 200mg tablets (Galpharm International Ltd) Ibuprofen 200mg Tablet Oral	10010100
Nurofen Migraine Pain 342mg tablets (Reckitt Benckiser Healthcare (UK) Ltd) Ibuprofen lysine 200mg Tablet Oral	4070100
Galprofen 100mg/5ml oral suspension (Galpharm International Ltd) Ibuprofen 20mg/1ml Oral suspension Oral	10010100
Galprofen Long Lasting 300mg capsules (Galpharm International Ltd) Ibuprofen 300mg Modified-release capsule Oral	10010100
Galprofen Long Lasting 200mg capsules (Galpharm International Ltd) Ibuprofen 200mg Modified-release capsule Oral	10010100

DESCRIPTION	BNF1
Naproxen 500mg tablets Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg tablets Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Tablet (M & A Pharmachem Ltd) Naproxen 500mg Tablet Oral	10010100
Valrox 250mg Tablet (Shire Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	10010100

Naproxen 250mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (IVAX Pharmaceuticals UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg effervescent tablets sugar free Naproxen 250mg Effervescent tablet Oral	10010100
Timpron 250mg Gastro-resistant tablet (Berk Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	10010100
Rheuflex 500mg Tablet (Goldshield Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (Teva UK Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Stirlescent 250mg effervescent tablets (Stirling Anglian Pharmaceuticals Ltd) Naproxen 250mg Effervescent tablet Oral	10010100
Naprosyn 500mg tablets (Atnahs Pharma UK Ltd) Naproxen 500mg Tablet Oral	04070100
Nycopren 250mg gastro-resistant tablets (Ardern Healthcare Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (DE Pharmaceuticals) Naproxen 250mg Tablet Oral	04070100
Timpron 500mg Gastro-resistant tablet (Berk Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	10010100
Naprosyn EC 250mg tablets (Atnahs Pharma UK Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg tablets (Noumed Life Sciences Ltd) Naproxen 500mg Tablet Oral	04070100
Feminax Ultra 250mg gastro-resistant tablets (Bayer Plc) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Gastro-resistant tablet (Sterwin Medicines) Naproxen 500mg Gastro-resistant tablet Oral	10010100
Naproxen 500mg tablets (A A H Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg tablets (Waymade Healthcare Plc) Naproxen 250mg Tablet Oral	04070100
Timpron 500mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100

Naproxen 500mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Teva UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (Teva UK Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg tablets (Sigma Pharmaceuticals Plc) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Mylan) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg/5ml oral suspension Naproxen 50mg/1ml Oral suspension Oral	04070100
Naproxen 500mg tablets (Mylan) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg Tablet (Almus Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naprosyn EC 500mg tablets (Atnahs Pharma UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (DE Pharmaceuticals) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Timpron 250mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg tablets (Genesis Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Arthrosin EC 500 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Mylan) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Arthrosin EC 250 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naprosyn 250mg tablets (Atnahs Pharma UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Genesis Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Genesis Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
NAPROXEN SODIUM	00000000

NAPROXEN 250 MG CAP	00000000
Naproxen Oral solution Naproxen Oral Solution Oral	10010100
Naproxen 500mg tablets (Kent Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg tablets (Sigma Pharmaceuticals Plc) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 500mg Tablet Oral	04070100
Prosaid 250mg Tablet (BHR Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (Accord Healthcare Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
NAPROXEN	00000000
NAPROXEN	00000000
Naproxen 500mg gastro-resistant tablets (Mylan) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Almus Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naprosyn S/R 500mg tablets (Roche Products Ltd) Naproxen sodium 500mg Modified-release tablet Oral	10010100
Arthroxen 250mg Tablet (C P Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg tablets (Accord Healthcare Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Actavis UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Sovereign Medical Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Rheuflex 250mg Tablet (Goldshield Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 500mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Crescent Pharma Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (Wockhardt UK Ltd) Naproxen 500mg Tablet Oral	04070100
Boots Period Pain Relief 250mg gastro-resistant tablets (The Boots Company Plc) Naproxen 250mg Gastro-resistant tablet Oral	04070100

Naproxen 250mg tablets (Milpharm Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg tablets (Wockhardt UK Ltd) Naproxen 250mg Tablet Oral	04070100
Prosaid 500mg Tablet (BHR Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 500mg tablets (Pfizer Ltd) Naproxen 500mg Tablet Oral	04070100
Pranoxen continus 500mg Tablet (Napp Pharmaceuticals Ltd) Naproxen sodium 500mg Modified-release tablet Oral	10010100
Arthrosin 250 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (Accord Healthcare Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Teva UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 250mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Gastro-resistant tablet (Galen Ltd) Naproxen 500mg Gastro-resistant tablet Oral	10010100
Naproxen 250mg tablets (Phoenix Healthcare Distribution Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg tablets (A A H Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg Gastro-resistant tablet (Galen Ltd) Naproxen 250mg Gastro-resistant tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (Sigma Pharmaceuticals Plc) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg tablets (Milpharm Ltd) Naproxen 500mg Tablet Oral	04070100
Nycopren 500mg gastro-resistant tablets (Ardern Healthcare Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 500mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100

Naproxen 250mg tablets (Kent Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Sigma Pharmaceuticals Plc) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Waymade Healthcare Plc) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Valrox 500mg Tablet (Shire Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 250mg tablets (Actavis UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (DE Pharmaceuticals) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Granules Naproxen 500mg Granules Oral	10010100
Arthroxen 500mg Tablet (C P Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 500mg tablets (Actavis UK Ltd) Naproxen 500mg Tablet Oral	04070100
Naprosyn 500mg Granules (Roche Products Ltd) Naproxen 500mg Granules Oral	10010100
Naproxen 250mg tablets (Mawdsley-Brooks & Company Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (DE Pharmaceuticals) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Arthrosin 500 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg modified-release tablets Naproxen sodium 500mg Modified-release tablet Oral	00000000
Naproxen 250mg tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Medreich Plc)Naproxen500mgGastro-resistant tabletOral	04070100
Naproxen 500mg tablets (Almus Pharmaceuticals Ltd)Naproxen500mgTabletOral	04070100

Naproxen 500mg tablets (Bristol Laboratories Ltd)Naproxen500mgTabletOral	04070100

DESCRIPTION	BNF1
Mefenamic acid 500mg tablets Mefenamic acid 500mg Tablet Oral	10010100
Ponstan Forte 500mg tablets (Chemidex Pharma Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 500mg tablets (Alliance Healthcare (Distribution) Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Capsule (Teva UK Ltd) Mefenamic acid 250mg Capsule Oral	10010100
PONSTAN	00000000
Opustan 250mg Capsule (Opus Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg Capsule (Sandoz Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Zentiva) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (Essential Generics Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Actavis UK Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 500mg tablets (A A H Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Capsule (Berk Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Dysman 500 tablets (Ashbourne Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mendys 250mg Capsule (Kent Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
MEFENAMIC ACID DISPERSIBLE	00000000
PONSTAN FORTE	00000000
Mefenamic acid 250mg capsules Mefenamic acid 250mg Capsule Oral	10010100

Mefenamic acid 500mg tablets (Sigma Pharmaceuticals Plc) Mefenamic acid 500mg Tablet Oral	10010100
Ponstan 50mg/5ml paediatric Liquid (Chemidex Pharma Ltd) Mefenamic acid 10mg/1ml Oral suspension Oral	10010100
Meflam 500mg Tablet (Trinity Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 500mg Tablet (Berk Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Dispersible tablet Mefenamic Acid 250mg Dispersible Tablet Oral	10010100
Ponstan 250mg Dispersible tablet (Chemidex Pharma Ltd) Mefenamic Acid 250mg Dispersible Tablet Oral	10010100
Mefenamic acid 250mg/5ml oral suspension Mefenamic acid 50mg/1ml Oral suspension Oral	10010100
Opustan 500mg Tablet (Opus Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Meflam 250mg Capsule (Trinity Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg capsules (Advanz Pharma) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg Capsule (Actavis UK Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Dysman 250 capsules (Ashbourne Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg capsules (Mylan) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg/5ml oral suspension Mefenamic acid 100mg/1ml Oral suspension Oral	10010100
Mefenamic acid 500mg tablets (IVAX Pharmaceuticals UK Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 50mg/5ml oral suspension Mefenamic acid 10mg/1ml Oral suspension Oral	10010100
Mefenamic acid 500mg tablets (Almus Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100

Dysman 250mg Capsule (Ashbourne Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Contraflam 250mg Capsule (Berk Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg capsules (Zentiva) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Teva UK Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (A A H Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Waymade Healthcare Plc) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Capsule (IVAX Pharmaceuticals UK Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Ponstan 250mg capsules (Chemidex Pharma Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Contraflam 500mg Tablet (Berk Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (Waymade Healthcare Plc) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Essential Generics Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (Alliance Healthcare (Distribution) Ltd) Mefenamic acid 250mg Capsule Oral	10010100

DESCRIPTION	BNF1
Tolfenamic acid 200mg Capsule Tolfenamic Acid 200mg Capsule Oral	04070401
Clotam Rapid 200mg tablets (Galen Ltd) Tolfenamic acid 200mg Tablet Oral	04070401
Tolfenamic acid 200mg tablets (A A H Pharmaceuticals Ltd) Tolfenamic acid 200mg Tablet Oral	04070401
Tolfenamic acid 200mg tablets Tolfenamic acid 200mg Tablet Oral	04070401
Clotam 200mg Capsule (Thames Laboratories Ltd) Tolfenamic Acid 200mg Capsule Oral	04070401

DESCRIPTION	BNF1
Atenolol 50mg tablets Atenolol 50mg Tablet Oral	02040000
Atenolol 100mg tablets Atenolol 100mg Tablet Oral	02040000
Propranolol 80mg modified-release capsules Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Half Inderal LA 80mg capsules (AstraZeneca UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Propranolol 160mg modified-release capsules Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Tenormin LS 50mg tablets (AstraZeneca UK Ltd) Atenolol 50mg Tablet Oral	02040000
Tenormin 100mg tablets (AstraZeneca UK Ltd) Atenolol 100mg Tablet Oral	02040000
Propranolol 80mg tablets Propranolol hydrochloride 80mg Tablet Oral	02040000
Inderal LA 160mg capsules (AstraZeneca UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Metoprolol 100mg tablets Metoprolol tartrate 100mg Tablet Oral	02040000
Propranolol 160mg tablets Propranolol hydrochloride 160mg Tablet Oral	02040000
Betaloc-SA 200mg tablets (AstraZeneca UK Ltd) Metoprolol tartrate 200mg Modified-release tablet Oral	02040000
Inderal 80mg tablets (AstraZeneca UK Ltd) Propranolol hydrochloride 80mg Tablet Oral	02040000
Betaloc 100mg tablets (AstraZeneca UK Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Corgard 40mg tablets (Sanofi-Synthelabo Ltd) Nadolol 40mg Tablet Oral	02040000
Rapranol SR 80mg capsules (Ranbaxy (UK) Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Inderal LA 160mg capsules (Waymade Healthcare Plc) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Propranolol LA 80mg Modified-release capsule (Approved Prescription Services Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (Mylan) Atenolol 50mg Tablet Oral	02040000
Bedranol SR 160mg capsules (Sandoz Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
PROPRANOLOL S/R	00000000

Berkolol 160mg Tablet (Berk Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Tablet Oral	02030202
Atenolol 50mg tablets (Crescent Pharma Ltd) Atenolol 50mg Tablet Oral	02040000
Nadolol 40mg/5ml oral solution Nadolol 8mg/1ml Oral solution Oral	02040000
Bedranol 80mg tablets (Ennogen Pharma Ltd) Propranolol hydrochloride 80mg Tablet Oral	02040000
Metoprolol 100mg tablets (IVAX Pharmaceuticals UK Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Metoprolol tartrate Oral solution Metoprolol Tartrate Oral Solution Oral	02040000
Corgard 80mg tablets (Sanofi) Nadolol 80mg Tablet Oral	02040000
Beta-Prograne 160mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (Sandoz Ltd) Atenolol 50mg Tablet Oral	02040000
Betim 10mg Tablet (ICN Pharmaceuticals France S.A.) Timolol maleate 10mg Tablet Oral	02040000
Atenolol 50mg tablets (Alliance Healthcare (Distribution) Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 80mg modified-release capsules (Mawdsley-Brooks & Company Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (Actavis UK Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 80mg/5ml oral solution Propranolol Hydrochloride 80mg/5ml Oral Solution Oral	02030202
Atenamin 50mg Tablet (OPD Pharm) Atenolol 50mg Tablet Oral	02040000
Propranolol 160mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Vasaten 50mg Tablet (Shire Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Atenolol 100mg tablets (Kent Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	02040000
Atenolol 100mg tablets (A A H Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	02040000
Atenix 50 tablets (Ashbourne Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Lopresor SR 200mg tablets (Recordati Pharmaceuticals Ltd) Metoprolol tartrate 200mg Modified-release tablet Oral	02040000
Half Inderal LA 80mg capsules (Necessity Supplies Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000

Propranolol SR 160mg Modified-release capsule (C P Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Propanix 160mg Tablet (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Tablet Oral	02030202
Propranolol SR 160mg Modified-release capsule (Hillcross Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Propranolol 80mg tablets (Actavis UK Ltd) Propranolol hydrochloride 80mg Tablet Oral	02040000
Atenolol 50mg tablets (Teva UK Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 160mg tablets (Actavis UK Ltd) Propranolol hydrochloride 160mg Tablet Oral	02040000
Angilol 80mg Tablet (DDSA Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	02030202
Slo-Pro 160mg capsules (Mylan) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (DE Pharmaceuticals) Atenolol 50mg Tablet Oral	02040000
Atenolol 50mg tablets (Boston Healthcare Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 80mg Capsule (IVAX Pharmaceuticals UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenolol 100mg Tablet (Celltech Pharma Europe Ltd) Atenolol 100mg Tablet Oral	02040000
Metoprolol 200mg modified-release tablets Metoprolol tartrate 200mg Modified-release tablet Oral	00000000
Propranolol LA 160mg Capsule (Approved Prescription Services Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Nadolol 40mg tablets Nadolol 40mg Tablet Oral	02040000
Half Beta-Prograne 80mg modified-release capsules (Actavis UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Propranolol 80mg Modified-release capsule (Actavis UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Probeta LA 160mg Capsule (Trinity Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenix 100 tablets (Ashbourne Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	02040000

Apsolol 160mg Tablet (Approved Prescription Services Ltd) Propranolol hydrochloride 160mg Tablet Oral	02030202
Bedranol SR 80mg capsules (Sandoz Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Betadur cr 160mg Modified-release capsule (Monmouth Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Propranolol 160mg modified-release capsules (A A H Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
BEDRANOL SR 80 MG CAP	00000000
Lopranol la 160mg Capsule (Opus Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 100mg tablets (Almus Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	02040000
Propranolol 80mg tablets (Ranbaxy (UK) Ltd) Propranolol hydrochloride 80mg Tablet Oral	02040000
Bedranol SR 80mg capsules (Almus Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	00000000
Atenolol 50mg tablets (A A H Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Blocadren 10mg Tablet (Merck Sharp & Dohme Ltd) Timolol maleate 10mg Tablet Oral	02040000
Timolol 10mg tablets Timolol maleate 10mg Tablet Oral	02040000
Berkolol 80mg Tablet (Berk Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	02030202
Propranolol 80mg tablets (Mylan) Propranolol hydrochloride 80mg Tablet Oral	02040000
Propanix 160mg Modified-release capsule (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 100mg tablets (Wockhardt UK Ltd) Atenolol 100mg Tablet Oral	02040000
Nadolol 40mg/5ml oral suspension Nadolol 8mg/1ml Oral suspension Oral	02040000
Atenolol 50mg tablets (Zentiva) Atenolol 50mg Tablet Oral	02040000
Mepranix 100mg Tablet (Ashbourne Pharmaceuticals Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Propranolol 80mg Modified-release capsule (Lagap) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000

Half Beta-Prograne 80mg modified-release capsules (Actavis UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	00000000
Propranolol 160mg tablets (Mylan) Propranolol hydrochloride 160mg Tablet Oral	02040000
Atenolol 50mg tablets (Phoenix Healthcare Distribution Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 160mg Modified-release capsule (Actavis UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (Kent Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Atenolol 100mg tablets (Sandoz Ltd) Atenolol 100mg Tablet Oral	02040000
Half-betadur cr 80mg Capsule (Monmouth Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Metoprolol 100mg tablets (Waymade Healthcare Plc) Metoprolol tartrate 100mg Tablet Oral	02040000
Half Beta-Prograne 80mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Metoprolol 100mg tablets (Alliance Healthcare (Distribution) Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Propranolol 80mg tablets (Teva UK Ltd) Propranolol hydrochloride 80mg Tablet Oral	02040000
Antipressan 100mg tablets (Teva UK Ltd) Atenolol 100mg Tablet Oral	02040000
Antipressan 50mg tablets (Teva UK Ltd) Atenolol 50mg Tablet Oral	02040000
ATENOLOL	00000000
Atenolol 50mg tablets (Tillomed Laboratories Ltd) Atenolol 50mg Tablet Oral	02040000
Atenolol 50mg Tablet (Celltech Pharma Europe Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 160mg Modified-release capsule (Sandoz Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
HALF-INDERAL LA	00000000
Bedranol SR 160mg capsules (Almus Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Inderal 160mg Tablet (AstraZeneca UK Ltd) Propranolol hydrochloride 160mg Tablet Oral	02030202
Half Beta-Prograne 80mg modified-release capsules (Tillomed Laboratories Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000

Rapranol SR 160mg capsules (Ranbaxy (UK) Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
METOPROLOL FUMARATE 190 MG TAB	00000000
Atenolol 50mg tablets (Almus Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Atenolol 50mg tablets (IVAX Pharmaceuticals UK Ltd) Atenolol 50mg Tablet Oral	02040000
Beta-Prograne 160mg modified-release capsules (Tillomed Laboratories Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Nadolol Oral solution Nadolol Oral Solution	02040000
Atenolol 50mg tablets (Accord Healthcare Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol SR 80mg Modified-release capsule (C P Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Propanix 80mg Tablet (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	02030202
Beta-Prograne 160mg modified-release capsules (Actavis UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (Wockhardt UK Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 80mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
ATENOLOL	00000000
Propranolol 80mg modified-release capsules (DE Pharmaceuticals) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Metoprolol 100mg tablets (Actavis UK Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Betim 10mg tablets (Meda Pharmaceuticals Ltd) Timolol maleate 10mg Tablet Oral	02040000
Sloprolol 160mg Capsule (C P Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Propranolol 80mg modified-release capsules (Kent Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenamin 100mg Tablet (OPD Pharm) Atenolol 100mg Tablet Oral	02040000
Metoprolol 100mg tablets (Teva UK Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Half Inderal LA 80mg capsules (DE Pharmaceuticals) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenolol 50mg Tablet (Berk Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Corgard 80mg tablets (Lexon (UK) Ltd) Nadolol 80mg Tablet Oral	02040000

Propranolol oral solution Propranolol Hydrochloride	02030202
Half propanix la 80mg Modified-release capsule (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Nadolol 80mg tablets Nadolol 80mg Tablet Oral	02040000
Lopresor 100mg tablets (Recordati Pharmaceuticals Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Atenolol 100mg tablets (Teva UK Ltd) Atenolol 100mg Tablet Oral	02040000
Bedranol SR 80mg capsules (Almus Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenolol 50mg tablets (Sigma Pharmaceuticals Plc) Atenolol 50mg Tablet Oral	02040000
Propranolol 80mg modified-release capsules (A A H Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Atenolol 100mg tablets (Mylan) Atenolol 100mg Tablet Oral	02040000
Metoprolol 100mg tablets (A A H Pharmaceuticals Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Propanix LA 160mg Modified-release capsule (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Propranolol 160mg Modified-release capsule (Lagap) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Totamol 50mg Tablet (C P Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	02040000
Bedranol sr 160mg Capsule (Lagap) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 100mg tablets (Phoenix Healthcare Distribution Ltd) Atenolol 100mg Tablet Oral	02040000
Propranolol 80mg tablets (A A H Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	02040000
Inderal LA 160mg capsules (Sigma Pharmaceuticals Plc) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 100mg tablets (Crescent Pharma Ltd) Atenolol 100mg Tablet Oral	02040000
Atenolol 100mg tablets (IVAX Pharmaceuticals UK Ltd) Atenolol 100mg Tablet Oral	02040000
Atenolol 50mg tablets (Strides Pharma UK Ltd) Atenolol 50mg Tablet Oral	02040000
Totamol 100mg Tablet (C P Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	02040000

Propranolol 160mg tablets (DE Pharmaceuticals) Propranolol hydrochloride 160mg Tablet Oral	02040000
Metoprolol 100mg tablets (Mylan) Metoprolol tartrate 100mg Tablet Oral	02040000
Propranolol 80mg modified-release capsules (Waymade Healthcare Plc) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Propranolol 160mg Capsule (IVAX Pharmaceuticals UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	02040000
Atenolol 100mg tablets (Actavis UK Ltd) Atenolol 100mg Tablet Oral	02040000
Atenolol 50mg tablets (Waymade Healthcare Plc) Atenolol 50mg Tablet Oral	02040000
Nadolol 80mg/5ml oral suspension Nadolol 16mg/1ml Oral suspension Oral	02040000
Half propatard la 80mg Modified-release capsule (Galen Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	02040000
Lopresor 100mg Tablet (Novartis Pharmaceuticals UK Ltd) Metoprolol tartrate 100mg Tablet Oral	02040000
Atenolol 50mg tablets (Bristol Laboratories Ltd) Atenolol 50mg Tablet Oral	02040000
Propranolol 80mg tablets (Alliance Healthcare (Distribution) Ltd)Propranolol hydrochloride80mgTabletOral	02040000
Propranolol 80mg Tablet (Celltech Pharma Europe Ltd)Propranolol hydrochloride80mgTabletOral	02030202
Inderal LA 160mg capsules (DE Pharmaceuticals)Propranolol hydrochloride160mgModified-release capsuleOral	02040000
Half Inderal LA 80mg capsules (Waymade Healthcare Plc)Propranolol hydrochloride80mgModified-release capsuleOral	02040000
Propranolol 80mg tablets (Relonchem Ltd)Propranolol hydrochloride80mgTabletOral	02040000
INDERAL	00000000

DESCRIPTION	BNF1
Aimovig 70mg/1ml solution for injection pre-filled pens (Novartis Pharmaceuticals UK Ltd) Erenumab 70mg/1ml Solution for injection Subcutaneous	04070402

Aimovig 140mg/1ml solution for injection pre-filled pens (Novartis Pharmaceuticals UK Ltd) Erenumab 140mg/1ml Solution for injection Subcutaneous	04070402
Erenumab 70mg/1ml solution for injection pre-filled disposable devicesErenumab70mg/1mlSolution for injectionSubcutaneous	04070402
Ajovy 225mg/1.5ml solution for injection pre-filled syringes (Teva UK Ltd)Fremanezumab150mg/1mlSolution for injectionSubcutaneous	04070402

DESCRIPTION	BNF1
Candesartan 16mg tablets (Consilient Health Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Tillomed Laboratories Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Mylan) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (A A H Pharmaceuticals Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Amias 16mg tablets (Takeda UK Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Mawdsley-Brooks & Company Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Teva UK Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Alliance Healthcare (Distribution) Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Actavis UK Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Genesis Pharmaceuticals Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Waymade Healthcare Plc) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg tablets (Sandoz Ltd) Candesartan cilexetil 16mg Tablet Oral	02050502
Candesartan 16mg/5ml oral solutionCandesartan cilexetil3.2mg/1mlOral solutionOral	02050502
Candesartan 16mg tablets (Zentiva)Candesartan cilexetil16mgTabletOral	02050502

Amias 16mg tablets (Lexon (UK) Ltd)Candesartan cilexetil16mgTabletOral	02050502

DESCRIPTION	BNF1
Sibelium 5mg tablets (Imported (Ireland)) Flunarizine dihydrochloride 5mg Tablet Oral	04065400
Flunarizine 5mg tablets Flunarizine dihydrochloride 5mg Tablet Oral	04065400
Flunarizine 5mg capsules Flunarizine dihydrochloride 5mg Capsule Oral	04065400
Flunarizine 10mg tablets Flunarizine dihydrochloride 10mg Tablet Oral	04065400

DESCRIPTION	BNF1
Migraleve tablets (McNeil Products Ltd) Not applicable Route of administration not applicable	04070200
Migraleve Pink tablets (McNeil Products Ltd) Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
Paramax tablets (Sanofi) Metoclopramide hydrochloride/Paracetamol 5mg + 500mg Tablet Oral	04070401
Paramax sachets (Sanofi) Paracetamol/Metoclopramide hydrochloride 500mg + 5mg Effervescent powder Oral	04070401
Paracetamol 500mg / Metoclopramide 5mg effervescent powder sachets sugar free Paracetamol/Metoclopramide hydrochloride 500mg + 5mg Effervescent powder Oral	04070401
Migravess forte 5mg+450mg Effervescent tablet (Bayer Plc) Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg+450mg Effervescent Tablet Oral	04065500
Paracetamol 500mg with codeine phosphate 8mg & buclizine 6.25mg Buclizine Hydrochloride/Codeine Phosphate/Paracetamol 500mg+8mg+6.25mg Tablets Oral	03040102
Metoclopramide with aspirin 5mg + 450mg Effervescent tablet Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg + 450mg Effervescent Tablet Oral	04065500

Codeine phosphate 8mg with paracetamol 500mg with buclizine 6.25mg tablets Buclizine Hydrochloride/Codeine Phosphate/Paracetamol 8mg+500mg+6.25mg Tablets Oral	03040102
Midrid (rpr) Capsule (Rhone-Poulenc Rorer Ltd) Paracetamol/Isometheptene mucate 325mg + 65mg Capsule Oral	04070100
Generic Migraleve Pink tablets Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
MigraMax oral powder sachets (Zentiva) Metoclopramide hydrochloride/Aspirin DL-Lysine 10mg + 900mg Powder Oral	04070100
Metoclopramide with paracetamol 5mg + 500mg Tablet Metoclopramide Hydrochloride/Paracetamol 5mg + 500mg Tablet Oral	04065500
Paracetamol 500mg / Domperidone 10mg tablets Paracetamol/Domperidone maleate 500mg + 10mg Tablet Oral	00000000
Domperamol tablets (Servier Laboratories Ltd) Paracetamol/Domperidone maleate 500mg + 10mg Tablet Oral	00000000
Ergotamine tartrate with cyclizine and caffeine tablets Caffeine/Cyclizine Hydrochloride/Ergotamine Tartrate Tablets Oral	03040103
Metoclopramide with aspirin 5mg + 325mg Effervescent tablet Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg + 325mg Effervescent Tablet Oral	04065500
Metoclopramide with paracetamol 5mg + 500mg Sachets Metoclopramide Hydrochloride/Paracetamol 5mg + 500mg Sachets Oral	04065500
Paracetamol 325mg / Isometheptene 65mg capsules Paracetamol/Isometheptene mucate 325mg + 65mg Capsule Oral	04070100
Migraleve Yellow tablets (McNeil Products Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Aspirin 900mg / Metoclopramide 10mg oral powder sachets sugar free Metoclopramide hydrochloride/Aspirin DL-Lysine 10mg + 900mg Powder Oral	04070100
Migravess 5mg+325mg Effervescent tablet (Bayer Plc) Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg+325mg Effervescent Tablet Oral	04065500
Midrid 325mg/65mg capsules (DHP Healthcare Ltd) Paracetamol/Isometheptene mucate 325mg + 65mg Capsule Oral	04070100
Generic Migraleve tablets Not applicable Route of administration not applicable	04070200

Migraleve - 1 Tablet (Pfizer Consumer Healthcare Ltd) Buclizine Hydrochloride/Codeine Phosphate/Paracetamol Tablet Oral	03040102
Isometheptene mucate with paracetamol 65mg+325mg Capsule Paracetamol/Isometheptene Mucate 65mg+325mg Capsule Oral	04070100
Migril tablets (Wockhardt UK Ltd) Caffeine hydrate/Cyclizine hydrochloride/Ergotamine tartrate 100mg + 50mg + 2mg Tablet Oral	04070401
Migraleve Ultra 50mg tablets (McNeil Products Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Generic Migril tablets Caffeine hydrate/Cyclizine hydrochloride/Ergotamine tartrate 100mg + 50mg + 2mg Tablet Oral	04070401
Paracetamol 500mg / Metoclopramide 5mg tablets Metoclopramide hydrochloride/Paracetamol 5mg + 500mg Tablet Oral	04070401
Migraleve - 2 8mg+500mg Tablet (Pfizer Consumer Healthcare Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Metoclopramide with lysine acetylsalicylate 10mg + 900mg Oral solution Metoclopramide Hydrochloride/Aspirin Lysine 10mg + 900mg Oral Solution Oral	04065500
Paracetamol with codeine & buclizine tablet Buclizine Hydrochloride/Codeine Phosphate/Paracetamol Tablets Oral	03040102
Solpadeine Migraine Ibuprofen & Codeine tablets (Omega Pharma Ltd) Ibuprofen/Codeine phosphate 200mg + 12.8mg Tablet Oral	04070200
Femigraine Effervescent tablet (Nicholas Laboratories Ltd)Cyclizine Hydrochloride/AspirinEffervescent Tablet	03040103

DESCRIPTION	BNF1
Paracetamol 500mg tablets Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg soluble tablets Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric sugar free Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 250mg/5ml oral suspension Paracetamol 50mg/1ml Oral suspension Oral	04070100

Paracetamol 250mg/5ml oral suspension sugar free Paracetamol 250mg/5ml Suspension Sugar-Free Oral	04070100
Paracetamol 120mg/5ml oral suspension Paracetamol 120mg/5ml Oral Suspension Paediatric Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg caplets (A A H Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric Paracetamol 24mg/1ml Oral suspension Oral	04070100
Disprol 120mg/5ml Oral suspension (Reckitt Benckiser Healthcare (UK) Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg/5ml oral suspension sugar free Paracetamol 500mg/5ml Suspension Sugar-Free Oral	04070100
Calpol infant 120mg/5ml Oral suspension (McNeil Products Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg Tablet (Teva UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Zentiva) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Rusco Ltd) Paracetamol 500mg Tablet Oral	04070100
PARACETAMOL 125 MG MIX	00000000
PARACETAMOL 30 MG SUP	00000000
Panasorb 500mg Tablet (Sanofi-Synthelabo Ltd) Paracetamol 500mg Tablet Oral	04070100
Medinol For Children 120mg/5ml oral suspension (SSL International Plc) Paracetamol 24mg/1ml Oral suspension Oral	04070100

PARACETAMOL 1 GM SUP	00000000
Paracetamol 500mg caplets (Phoenix Healthcare Distribution Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg soluble tablets (A A H Pharmaceuticals Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 500mg tablets (Zanza Specials International Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules (Almus Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg tablets (Actavis UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Panaleve plus 120mg/5ml Oral suspension sugar free (Pinewood Healthcare) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paravict 500mg tablets (Ecogen Europe Ltd) Paracetamol 500mg Tablet Oral	04070100
PARACETAMOL	00000000
Calpol Infant 120mg/5ml oral suspension 5ml sachets (McNeil Products Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
PARACETAMOL	00000000
PARACETAMOL 125 MG TAB	00000000
Paracetamol 500mg soluble tablets (Fannin UK Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 500mg capsules (DE Pharmaceuticals) Paracetamol 500mg Capsule Oral	04070100
Disprol Paracetamol 120mg/5ml oral suspension (Reckitt Benckiser Healthcare (UK) Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Junior Parapaed 120mg/5ml oral suspension sugar free colour free (Pinewood Healthcare) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Panadol ActiFast Soluble tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol 500mg Effervescent tablet Oral	04070100

Paracetamol 500mg caplets (Bristol Laboratories Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric (Rosemont Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml Oral solution (Teva UK Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Calpol Six Plus Fastmelts 250mg tablets (McNeil Products Ltd) Paracetamol 250mg Orodispersible tablet Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free (A A H Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric sugar free (Alliance Healthcare (Distribution) Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 500mg soluble tablets (Kent Pharmaceuticals Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
PARACETAMOL SOLUBLE TAB	00000000
Calpol infant 120mg/5ml Oral suspension (McNeil Products Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Panadol Extra tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol/Caffeine 500mg + 65mg Tablet Oral	04070100
Paracetamol 120 mg capsule Paracetamol 120mg Capsules Oral	04070100
PARACETAMOL 250 MG TAB	00000000
DISPROL PARACETAMOL SF	00000000
Paracetamol 500mg/5ml oral solution Paracetamol 100mg/1ml Oral solution Oral	04070100
Paracetamol 500mg caplets (Icarus Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Mandanol Infant paracetamol 120mg/5ml oral suspension (M & A Pharmachem Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100

Paracetamol 500mg Tablet (Nucare Plc) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric sugar free (Pinewood Healthcare) Paracetamol 24mg/1ml Oral solution Oral	04070100
Mandanol 500mg tablets (M & A Pharmachem Ltd) Paracetamol 500mg Tablet Oral	04070100
PARACETAMOL 500 MG SUP	00000000
Paracetamol 500mg/50ml solution for infusion vials Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paracetamol 250mg/5ml oral suspension sugar free Paracetamol 250mg/5ml Oral Suspension Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free (Vantage) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Calpol Six Plus 250mg/5ml oral suspension 5ml sachets sugar free (McNeil Products Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg caplets (J M McGill Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric (A A H Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 500mg tablets (A A H Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Medinol Paediatric paracetamol 120mg/5ml oral suspension (SSL International Plc) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg tablets (Teva UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules (Teva UK Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg caplets (Kent Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
PARACETAMOL CO TAB	00000000

Paracetamol 240mg oral powder sachets sugar free Paracetamol 240mg Powder Oral	04070100
Paracetamol 1g oral powder sachets Paracetamol 1gram Powder Oral	04070100
Paracetamol 120mg/5ml Oral suspension (Co-Pharma Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Mandanol 500mg caplets (M & A Pharmachem Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg tablets (IVAX Pharmaceuticals UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules (Zentiva) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg caplets (Vantage) Paracetamol 500mg Tablet Oral	04070100
PARACETAMOL	00000000
PARACETAMOL 60 MG SUP	00000000
Disprol Paracetamol 120mg soluble tablets (Reckitt Benckiser Healthcare (UK) Ltd) Paracetamol 120mg Soluble tablet Oral	04070100
Paracetamol 500mg soluble tablets (Almus Pharmaceuticals Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 500mg caplets (Sigma Pharmaceuticals Plc) Paracetamol 500mg Tablet Oral	04070100
Panadol OA 1000mg tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol 1gram Tablet Oral	04070100
Paracetamol 500mg soluble tablets (Actavis UK Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
Lloydspharmacy Paracetamol 120mg/5ml oral suspension sugar free (Lloyds Pharmacy Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
PARACETAMOL 100 MG SUP	00000000
PARACETAMOL 240 MG SUS	00000000
Galpamol 120mg/5ml Oral suspension (Galpharm International Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100

Paracetamol 500mg Tablet (Thornton & Ross Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg Tablet (Family Health) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Teva UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Infadrops 100mg/ml liquid (Mercury Pharma Group Ltd) Paracetamol 100mg/1ml Oral solution Oral	00000000
Paracetamol 500mg caplets (IVAX Pharmaceuticals UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Calpol Six Plus 250mg/5ml oral suspension (McNeil Products Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Panadol Extra Advance 500mg/65mg tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol/Caffeine 500mg + 65mg Tablet Oral	04070100
Panadol 500mg Soluble tablet (GlaxoSmithKline Consumer Healthcare) Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 500mg capsules (Wockhardt UK Ltd) Paracetamol 500mg Capsule Oral	04070100
Perfalgan 500mg/50ml solution for infusion vials (Bristol-Myers Squibb Pharmaceuticals Ltd) Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paracetamol 500mg soluble tablets (Teva UK Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
Calpol Infant 120mg/5ml oral suspension sugar free (McNeil Products Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg soluble tablets sugar free (Ennogen Healthcare Ltd) Paracetamol 120mg Soluble tablet Oral	04070100
Paracetamol 120mg/5ml oral suspension 5ml sachets Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 1g tablets Paracetamol 1gram Tablet Oral	04070100
Paracetamol 500mg caplets (Numark Ltd) Paracetamol 500mg Tablet Oral	04070100

Calpol Infant 120mg/5ml oral suspension 5ml sachets sugar free (McNeil Products Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric sugar free (Sigma Pharmaceuticals Plc) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 120mg/5ml oral suspension sugar free Paracetamol 120mg/5ml Oral Suspension Paediatric Sugar-Free Oral	04070100
Paracetamol 500mg tablets (Aspar Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Calpol Paediatric 120mg/5ml oral suspension sugar free (McNeil Products Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml Oral solution (Celltech Pharma Europe Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 500mg capsules (Kent Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	04070100
Panadol baby & infant 120mg/5ml Oral suspension (GlaxoSmithKline Consumer Healthcare) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg Tablet (M & A Pharmachem Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules (Sigma Pharmaceuticals Plc) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg capsules (Actavis UK Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg capsules (Waymade Healthcare Plc) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 1g/100ml solution for infusion vials (A A H Pharmaceuticals Ltd) Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paracetamol 500mg caplets (Mawdsley-Brooks & Company Ltd) Paracetamol 500mg Tablet Oral	04070100

Paracetamol 250mg/5ml oral suspension sugar free (Vantage) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Anadin Paracetamol 500mg tablets (Pfizer Consumer Healthcare Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol Capsule (Co-operative) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg/5ml oral suspension (Royal Preston Hospital mucilage formula) (Special Order) Paracetamol 100mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg tablets (Vantage) Paracetamol 500mg Tablet Oral	04070100
Calpol infant 120mg/5ml Liquid (McNeil Products Ltd) Paracetamol 120mg/5ml Liquid Oral	04070100
Paracetamol 120mg/5ml Oral suspension sugar free (Pinewood Healthcare) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg tablets (The Boots Company Plc) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Almus Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free (Pinewood Healthcare) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Calpol 120mg/5ml Liquid (Pfizer Consumer Healthcare Ltd) Paracetamol 120mg/5ml Liquid Oral	04070100
Paracetamol 120mg/5ml Oral solution (Rosemont Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 500mg tablets (Kent Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Waymade Healthcare Plc) Paracetamol 500mg Tablet Oral	04070100
Medised plain 120mg/5ml Oral suspension (SSL International Plc) Paracetamol 120mg/5ml Oral Suspension	04070100
Medinol 120mg/5ml Oral suspension (SSL International Plc) Paracetamol 120mg/5ml Oral Suspension Oral	04070100

Paracetamol 500mg/50ml solution for infusion bottles Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paracetamol 500mg/5ml oral suspension sugar free Paracetamol 100mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg soluble tablets (Waymade Healthcare Plc) Paracetamol 500mg Effervescent tablet Oral	04070100
Perfalgan 1g/100ml solution for infusion vials (Bristol-Myers Squibb Pharmaceuticals Ltd) Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paracetamol 120mg/5ml oral solution paediatric sugar free (Waymade Healthcare Plc) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 500mg Tablet (Co-operative) Paracetamol 500mg Tablet Oral	04070100
Tixymol 120mg/5ml Oral suspension (Novartis Consumer Health UK Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg soluble tablets (Zentiva) Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 500mg soluble tablets (Alliance Healthcare (Distribution) Ltd) Paracetamol 500mg Effervescent tablet Oral	04070100
Children's Lemsip Cold & Flu Blackcurrant oral powder sachets (Reckitt Benckiser Healthcare (UK) Ltd) Paracetamol 240mg Powder Oral	04070100
Paracetamol 500mg/5ml oral solution sugar free Paracetamol 100mg/1ml Oral solution Oral	04070100
PARACETAMOL SOLUBLE TAB	00000000
Paracetamol 120mg/5ml Oral solution (William Ransom) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paldesic paracetamol 120mg/5ml oral suspension (Rosemont Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
PARACETAMOL 300 MG TAB	00000000

Paracetamol 500mg tablets (DE Pharmaceuticals) Paracetamol 500mg Tablet Oral	04070100
Lloydspharmacy Paracetamol Six Plus 250mg/5ml oral suspension sugar free (Lloyds Pharmacy Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Panadol 500mg tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free Paracetamol 250mg/5ml Suspension Sugar-Free Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric (Alliance Healthcare (Distribution) Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 50mg oral powder sachets sugar free Paracetamol 50mg Powder Oral	04070100
Medinol 120mg/5ml Oral suspension (SSL International Plc) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Medinol Under 6 paracetamol 120mg/5ml oral suspension (SSL International Plc) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg capsules (A A H Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg caplets (Ennogen Healthcare Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 1g effervescent tablets sugar free Paracetamol 1gram Effervescent tablet Oral	04070100
Paradote 100mg/500mg tablets (Sinclair IS Pharma Plc) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free (A A H Pharmaceuticals Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
PARACETAMOL 240 MG ELI	00000000
Paracetamol 500mg tablets (Wockhardt UK Ltd) Paracetamol 500mg Tablet Oral	04070100

Paracetamol 500mg caplets (Accord Healthcare Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules (Mawdsley-Brooks & Company Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg Tablet (M & A Pharmachem Ltd) Paracetamol 500mg Tablet Oral	04070100
Calpol Infant 120mg/5ml oral suspension (McNeil Products Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free (Kent Pharmaceuticals Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg Capsule (A A H Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	04070100
Medinol for children 120mg/5ml Oral suspension (SSL International Plc) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg tablets (Sigma Pharmaceuticals Plc) Paracetamol 500mg Tablet Oral	04070100
Panadol 500mg capsules (GlaxoSmithKline Consumer Healthcare) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg tablets (Alliance Healthcare (Distribution) Ltd) Paracetamol 500mg Tablet Oral	04070100
Panadol Advance 500mg tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Actavis UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Calpol Infant Sugar Free Colour Free 120mg/5ml oral suspension (McNeil Products Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free (Pinewood Healthcare) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg caplets (Alliance Healthcare (Distribution) Ltd) Paracetamol 500mg Tablet Oral	04070100

Numark Paracetamol 500mg capsules (Numark Ltd) Paracetamol 500mg Capsule Oral	04070100
PARACETAMOL 75 MG SUS	00000000
Paracetamol 500mg caplets (AM Distributions (Yorkshire) Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 250mg/5ml oral suspension (Rosemont Pharmaceuticals Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 650mg oral powder sachets Paracetamol 650mg Powder Oral	04070100
Disprol 120mg/5ml Oral suspension (Reckitt Benckiser Healthcare (UK) Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg capsules (Bristol Laboratories Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg Tablet (Aspar Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 1g/100ml solution for infusion vials Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Placidex 120mg/5ml Oral solution (E C De Witt) Paracetamol 24mg/1ml Oral solution Oral	04070100
Galpamol for Children 120mg/5ml oral suspension 5ml sachets sugar free (Galpharm International Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 1g/100ml solution for infusion bottles (B.Braun Melsungen AG) Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paracetamol 250mg/5ml oral suspension 5ml sachets sugar free Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free (Alliance Healthcare (Distribution) Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100

Paracetamol 500mg/5ml Oral suspension sugar free (Rosemont Pharmaceuticals Ltd) Paracetamol 500mg/5ml Oral Suspension Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free (Thornton & Ross Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Calpol Six Plus 250mg/5ml oral suspension sugar free (McNeil Products Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg capsules (Aspar Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 125mg/5ml syrup Paracetamol 125mg/5ml Syrup Oral	04070100
Paracetamol 500mg tablets (Galpharm International Ltd) Paracetamol 500mg Tablet Oral	04070100
Panadol ActiFast 500mg tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 100mg/ml oral solution sugar free Paracetamol 100mg/1ml Oral solution Oral	00000000
Paracetamol 120mg/5ml Oral suspension (Nucare Plc) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
PARACETAMOL 150 MG SUP	00000000
Paracetamol 250mg/5ml oral solution Paracetamol 50mg/1ml Oral solution Oral	04070100
Femerital Tablet (Boehringer Mannheim UK Ltd) Paracetamol/Ambucetamide Tablet Oral	04070100
Paracetamol 500mg Tablet (Celltech Pharma Europe Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg capsules (Focus Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	04070100
PARACETAMOL 125 MG ELI	00000000
Paracetamol 120mg/5ml oral suspension paediatric (A A H Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100

Paracetamol 500mg effervescent tablets Paracetamol 500mg Effervescent tablet Oral	04070100
Paracetamol 100mg/10ml solution for infusion ampoules Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Paraclear 500mg Soluble tablet (Roche Consumer Health) Paracetamol 500mg Effervescent tablet Oral	04070100
PARACETAMOL 500 MG ELI	00000000
Paracetamol 120mg/5ml Oral suspension sugar free (IVAX Pharmaceuticals UK Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 120mg soluble tablets sugar free Paracetamol 120mg Soluble tablet Oral	00000000
PARACETAMOL 20 MG SUP	00000000
Paracetamol 500mg Tablet (Almus Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Medinol Over 6 paracetamol 250mg/5ml oral suspension (SSL International Plc) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Boots Paracetamol 500mg caplets (The Boots Company Plc) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric (Thornton & Ross Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Hedex 500mg tablets (Omega Pharma Ltd) Paracetamol 500mg Tablet Oral	04070100
Calpol six plus 250mg/5ml Oral suspension sugar free (McNeil Products Ltd) Paracetamol 250mg/5ml Oral Suspension Oral	04070100
Paracetamol 250mg/5ml oral suspension (A A H Pharmaceuticals Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free (Alliance Healthcare (Distribution) Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg capsules (Almus Pharmaceuticals Ltd) Paracetamol 500mg Capsule Oral	00000000

Paracetamol 500mg/5ml oral suspension Paracetamol 100mg/1ml Oral suspension Oral	04070100
Paracetamol powder Paracetamol Powder	50000000
Paracetamol 500mg caplets (Lloyds Pharmacy Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 250mg/5ml Liquid (Co-Pharma Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg tablets (Zentiva) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg tablets (Accord Healthcare Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracets 500mg capsules (Sussex Pharmaceutical Ltd) Paracetamol 500mg Capsule Oral	04070100
Paldesic paracetamol 250mg/5ml oral suspension (Rosemont Pharmaceuticals Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol oral liquid Paracetamol Oral Liquid Oral	04070100
Panadol Ultra 12.8mg/500mg tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol/Codeine phosphate 500mg + 12.8mg Tablet Oral	04070100
Paracetamol 500mg capsules (Galpharm International Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg/5ml oral suspension sugar free (A A H Pharmaceuticals Ltd) Paracetamol 100mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral suspension 5ml sachets sugar free Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 1g/100ml solution for infusion bottles Paracetamol 10mg/1ml Solution for infusion Intravenous	04070100
Panadol Extra soluble tablets (GlaxoSmithKline Consumer Healthcare) Paracetamol/Caffeine 500mg + 65mg Effervescent tablet Oral	04070100

Paracetamol 500mg caplets (Ethigen Ltd) Paracetamol 500mg Tablet Oral	04070100
Flu strength hot lemon 1g Powder (A A H Pharmaceuticals Ltd) Paracetamol 1gram Powder Oral	04070100
Paracetamol 120mg/5ml Oral solution sugar free (A A H Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Disprol paracetamol 120mg/5ml Oral suspension (Reckitt Benckiser Healthcare (UK) Ltd) Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Flu Strength Hot Lemon Powders 1g oral powder sachets (Bell	Sons & Co (Druggists) Ltd) Paracetamol 1gram Powder Oral
Paracetamol 500mg caplets (Wockhardt UK Ltd) Paracetamol 500mg Tablet Oral	04070100
Tramil 500mg Capsule (Wyeth Consumer Healthcare) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 500mg Tablet (OBG Pharmaceuticals Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 500mg caplets (Galpharm International Ltd) Paracetamol 500mg Tablet Oral	04070100
Boots Paracetamol 500mg capsules (The Boots Company Plc) Paracetamol 500mg Capsule Oral	04070100
Paracets 500mg Tablet (Sussex Pharmaceutical Ltd) Paracetamol 500mg Tablet Oral	04070100
Medinol 250mg/5ml Oral suspension (SSL International Plc) Paracetamol 250mg/5ml Oral Suspension Oral	04070100
Paracetamol 250mg orodispersible tablets sugar free Paracetamol 250mg Orodispersible tablet Oral	04070100
PARACETAMOL 1 GM TAB	00000000
Obimol 500mg Tablet (Ayrton Saunders Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 250mg/5ml oral suspension sugar free (DE Pharmaceuticals) Paracetamol 50mg/1ml Oral suspension Oral	04070100

Mandanol 6+ paracetamol 250mg/5ml oral suspension (M & A Pharmachem Ltd) Paracetamol 50mg/1ml Oral suspension Oral	04070100
Paracetamol 500mg caplets (Crescent Pharma Ltd) Paracetamol 500mg Tablet Oral	04070100
Paracetamol 120mg/5ml oral suspension paediatric sugar free (Kent Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral suspension Oral	04070100
Paracetamol 120mg/5ml oral solution paediatric sugar free (A A H Pharmaceuticals Ltd) Paracetamol 24mg/1ml Oral solution Oral	04070100
Paracetamol 120mg/5ml oral suspension sugar free Paracetamol 120mg/5ml Oral Suspension Oral	04070100
Paracetamol 500mg capsules (Lloyds Pharmacy Ltd) Paracetamol 500mg Capsule Oral	04070100
Paracetamol 1g/5ml oral suspension Paracetamol 200mg/1ml Oral suspension Oral	04070100
Panadol Period Pain 500mg/65mg tablets (GlaxoSmithKline Consumer Healthcare)Paracetamol/Caffeine500mg + 65mgTabletOral	04070100
Paracetamol 500mg tablets (Genesis Pharmaceuticals Ltd)Paracetamol500mgTabletOral	04070100
Paracetamol 500mg/5ml oral solution sugar free (Advanz Pharma)Paracetamol100mg/1mlOral solutionOral	04070100
Paracetamol 1g/5ml oral solutionParacetamol200mg/1mlOral solutionOral	04070100
Paracetamol 500mg/5ml oral suspension sugar free (DE Pharmaceuticals)Paracetamol100mg/1mlOral suspensionOral	04070100
Altridexamol 1000mg effervescent tablets (TriOn Pharma Ltd)Paracetamol1gramEffervescent tabletOral	04070100
Paracetamol 250mg/5ml oral suspension sugar free (Dowelhurst Ltd)Paracetamol50mg/1mlOral suspensionOral	04070100

DESCRIPTION	BNF1
Pizotifen 1.5mg tablets Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Pizotifen 500microgram tablets Pizotifen hydrogen malate 500microgram Tablet Oral	04070402
Pizotifen 250micrograms/5ml oral solution sugar free Pizotifen hydrogen malate 50microgram/1ml Oral solution Oral	04070402
Pizotifen 1.5mg tablets (Teva UK Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
SANOMIGRAN	00000000
Sanomigran 500microgram tablets (Novartis Pharmaceuticals UK Ltd) Pizotifen hydrogen malate 500microgram Tablet Oral	04070402
Pizotifen 1.5mg tablets (Almus Pharmaceuticals Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Sanomigran 1.5mg tablets (Novartis Pharmaceuticals UK Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Pizotifen 500micrograms/5ml oral suspension Pizotifen hydrogen malate 100microgram/1ml Oral suspension Oral	04070402
Pizotifen 1.5mg Tablet (Neo Laboratories Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Sanomigran 0.25mg/5ml elixir (Novartis Pharmaceuticals UK Ltd) Pizotifen hydrogen malate 50microgram/1ml Oral solution Oral	04070402
Pizotifen 250micrograms/5ml oral suspension Pizotifen hydrogen malate 50microgram/1ml Oral suspension Oral	04070402
PIZOTIFEN	00000000
Pizotifen 500microgram tablets (Teva UK Ltd) Pizotifen hydrogen malate 500microgram Tablet Oral	04070402
Pizotifen 1.5mg tablets (Actavis UK Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Pizotifen 1mg/5ml oral suspension Pizotifen hydrogen malate 200microgram/1ml Oral suspension Oral	04070402
Pizotifen 500microgram tablets (Almus Pharmaceuticals Ltd) Pizotifen hydrogen malate 500microgram Tablet Oral	04070402

Pizotifen 0.5mg Tablet (Neo Laboratories Ltd) Pizotifen hydrogen malate 500microgram Tablet Oral	04070402
Pizotifen 250micrograms/5ml oral solution Pizotifen hydrogen malate 50microgram/1ml Oral solution Oral	04070402
Pizotifen 500microgram tablets (A A H Pharmaceuticals Ltd) Pizotifen hydrogen malate 500microgram Tablet Oral	04070402
SANOMIGRAN	00000000
Pizotifen 1.5mg tablets (A A H Pharmaceuticals Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Sanomigran 1.5mg tablets (Mawdsley-Brooks & Company Ltd) Pizotifen hydrogen malate 1.5mg Tablet Oral	04070402
Pizotifen 500microgram tablets (Actavis UK Ltd) Pizotifen hydrogen malate 500microgram Tablet Oral	04070402
Pizotifen 1.5mg tablets (Phoenix Healthcare Distribution Ltd)Pizotifen hydrogen malate1.5mgTabletOral	04070402

Supplementary Table 3.2: Prevalence of migraine in the CPRD Gold pregnancy register 2000-2018 with 95% confidence intervals

Year	Prevalence	Lower CI	Upper CI
2000	11.45	11.15	11.76
2001	11.35	11.08	11.63
2002	11.53	11.27	11.79
2003	11.39	11.16	11.63
2004	11.70	11.47	11.93
2005	12.00	11.78	12.22
2006	12.19	11.97	12.41
2007	12.62	12.41	12.84
2008	12.85	12.64	13.07

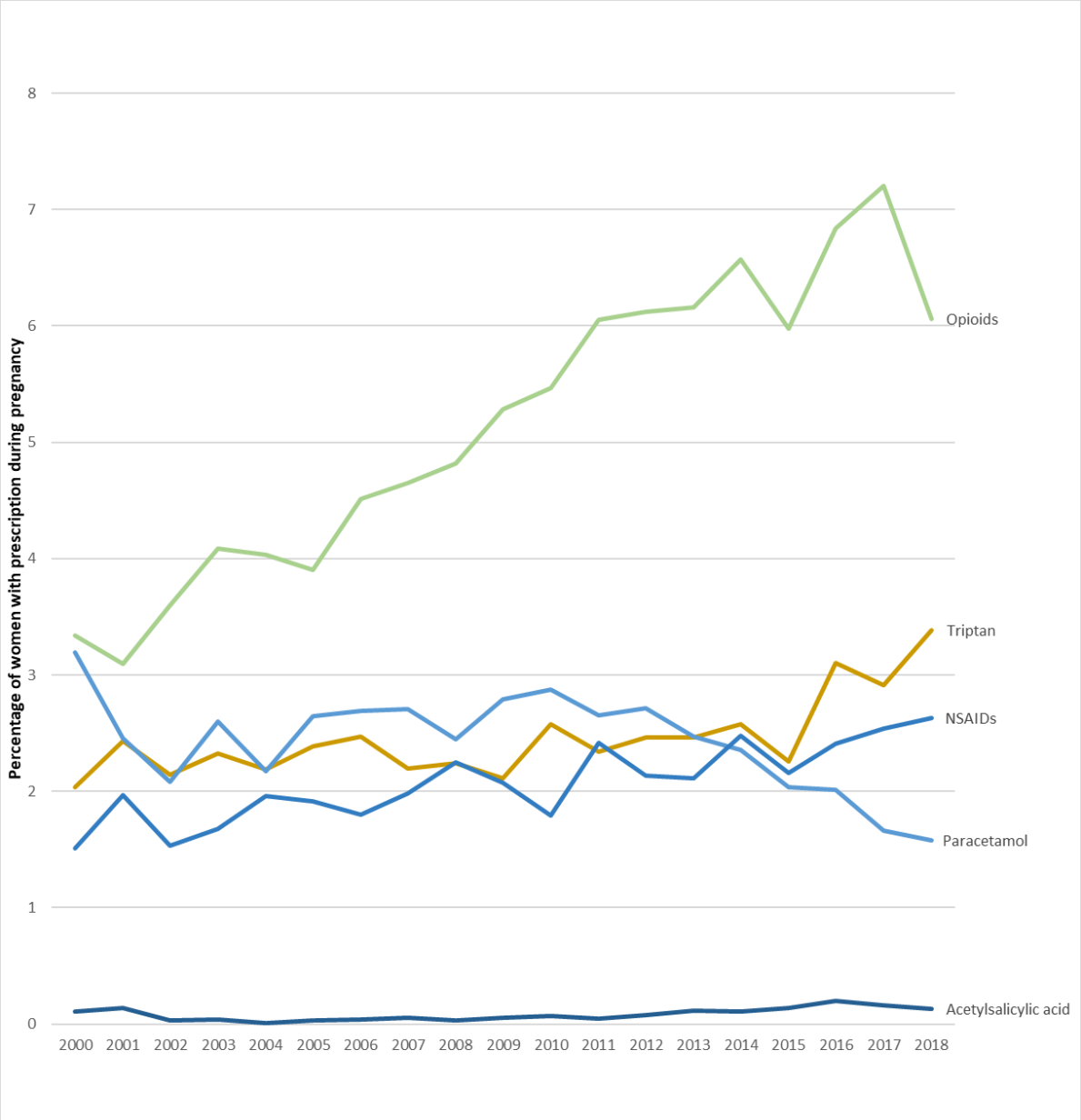
2009	13.09	12.87	13.30
2010	13.86	13.64	14.08
2011	14.36	14.13	14.59
2012	14.91	14.67	15.15
2013	15.28	15.03	15.53
2014	15.76	15.50	16.03
2015	16.26	15.97	16.55
2016	16.52	16.19	16.84
2017	16.78	16.44	17.13
2018	17.11	16.75	17.49

Supplementary Table 3.3: Age standardised prevalence of migraine in the CPRD Gold pregnancy register 2000-2018 with 95% confidence intervals

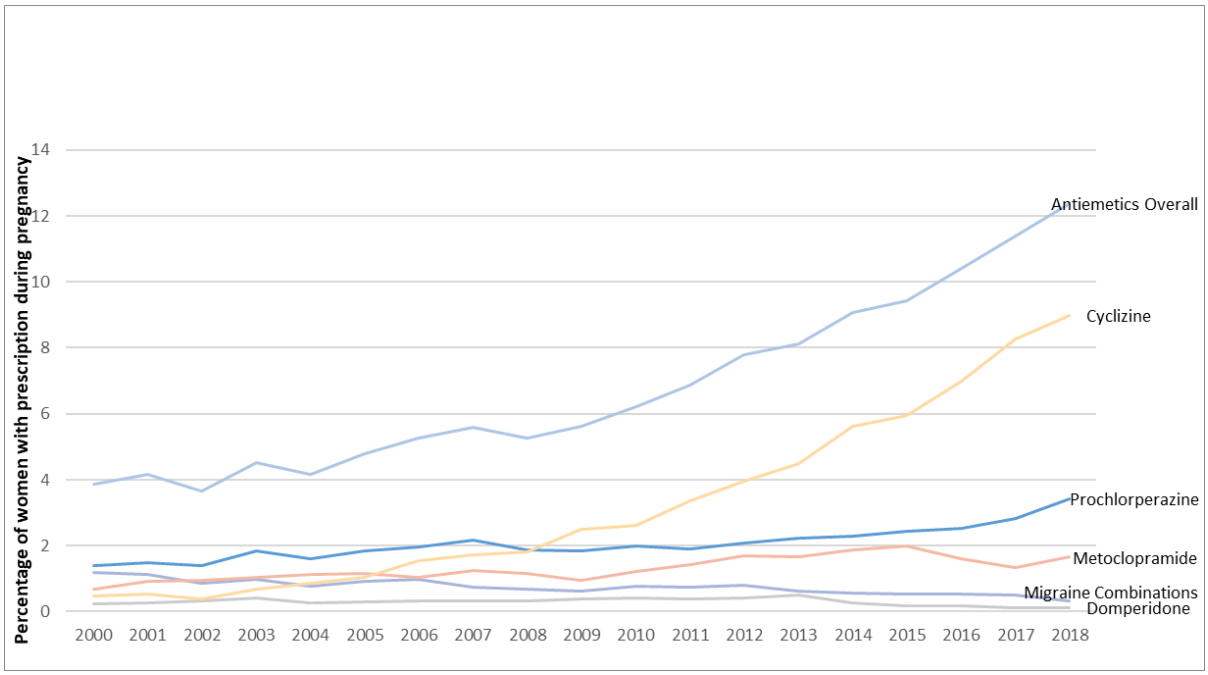
Year	Age Standardised Prevalence	LCI	UCI
2000	11.40%	10.29%	12.51%
2001	11.81%	10.88%	12.74%
2002	12.54%	11.57%	13.50%
2003	11.17%	10.39%	11.95%
2004	12.34%	11.49%	13.19%
2005	12.94%	12.12%	13.76%
2006	12.50%	11.71%	13.29%
2007	12.64%	11.91%	13.37%
2008	12.26%	11.64%	12.88%
2009	12.69%	12.02%	13.36%
2010	13.90%	13.19%	14.60%
2011	14.53%	13.75%	15.31%
2012	15.17%	14.41%	15.92%
2013	16.00%	15.18%	16.82%
2014	15.80%	15.00%	16.59%
2015	16.44%	15.53%	17.35%

2016	16.89%	15.88%	17.91%
2017	16.75%	15.74%	17.77%
2018	17.18%	16.15%	18.20%

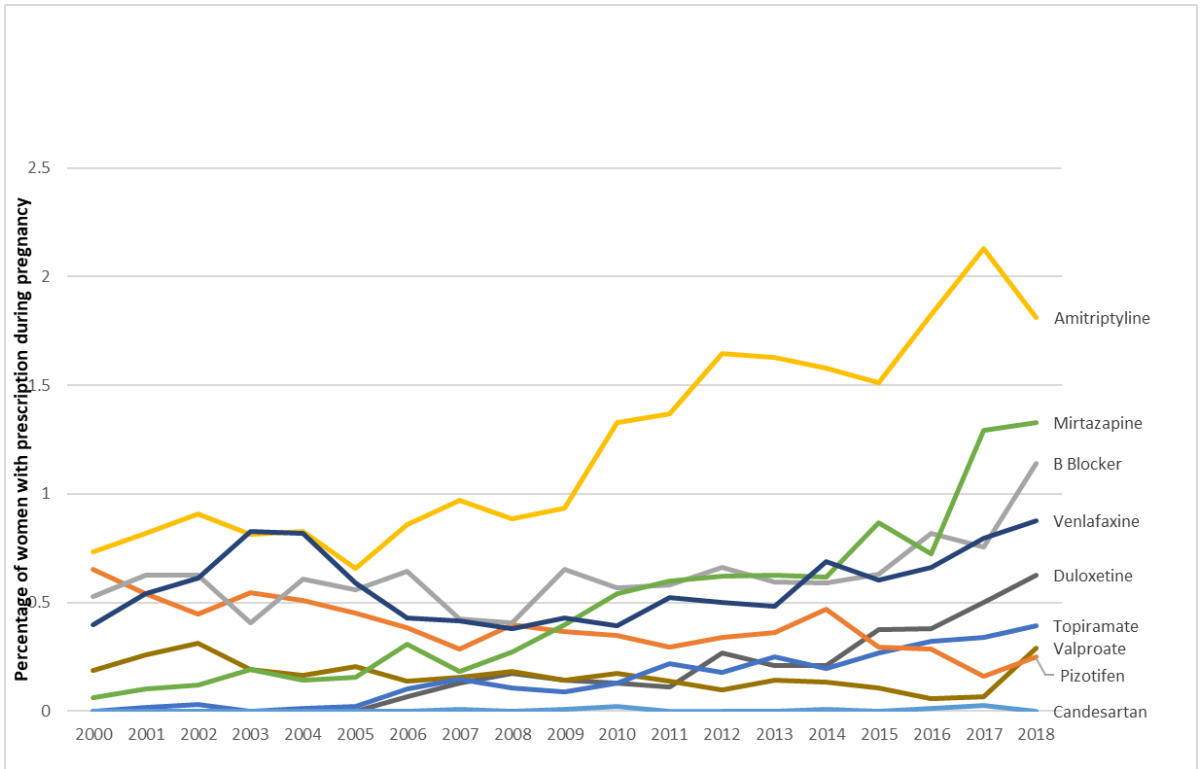
Supplementary Figure 3.1: Prevalence of prescriptions for the acute management of migraine during the first trimester 2000-2018



Supplementary Figure 3.2: Prevalence of prescriptions for anti-emetics for patients with migraine during the first trimester 2000-2018



Supplementary Figure 3.3: Prevalence of prescriptions for the prophylactic management of migraine during the first trimester 2000-2018



Chapter 4

Supplementary Table 4.1: Outcomes considered in Umbrella Review

Outcome
Pregnancy loss (miscarriage, recurrent miscarriage, spontaneous pregnancy loss, stillbirths)
Hypertensive disorders of pregnancy (pre-eclampsia, recurrent pre-eclampsia, eclampsia, HELLP (Haemolysis, Elevated Liver enzymes and Low Platelets) syndrome, gestational hypertension) Placental disorders (placenta previa, placental abruption, placenta accreta, placenta percreta)
Hyperemesis gravidarum
Gestational diabetes mellitus

Ectopic pregnancy
Molar pregnancy/ choriocarcinoma
Obstetric haemorrhage
Preterm birth
Mode of delivery (caesarean section, instrumental)
Low birth weight (small for gestational age, intra-uterine growth restriction, fetal growth restriction)
Post-partum depression
Perineal trauma (3^{rd} and 4^{th} degree)
Obstetric cholestasis
Venous thromboembolism
Acute myocardial infarction
Cerebrovascular event
Neurological outcomes (pituitary apoplexy, sinus thrombosis; posterior reversible encephalopathy syndrome, reversible cerebral vasoconstriction syndrome, subarachnoid haemorrhage)
Maternal death

Supplementary Section 4.1: Example search strategy: MEDLINE

1 exp Pregnancy/

2 exp Pregnant Women/

3 exp Gravidity/

4 exp Mothers/

5 exp Obstetrics/

6 exp Delivery, Obstetric/

7 exp Parturition/

8 exp Maternal Health/

9 exp Maternal Health Services/

10 exp Pregnancy Complications/

11 exp Pregnancy Outcome/

12 pregnan*.ti,ab.

13 gravid*.ti,ab.

14 gestation*.ti,ab.

15 'pregnant wom#n'.ti,ab.

16 matern*.ti,ab.

17 mother*.ti,ab.

18 obstetric*.ti,ab.

19 (child adj3 bearing).ti,ab.

20 childbearing.ti,ab.

21 parturition.ti,ab.

22 childbirth.ti,ab.

23 child-birth.ti,ab.

24 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23

25 exp Migraine Disorders/

26 migrain*.ti,ab.

27 25 or 26

28 24 and 27

29 systematic review.mp.

30 (systematic$ adj2 (review$ or overview)).ti,ab.

31 (systematic$ adj5 review$).tw,sh.

32 meta-analysis.mp. or exp meta-analysis/

33 29 or 30 or 31 or 32

34 exp Abortion, Spontaneous/ or ((recurrent adj3 miscarr$) or miscarr$ or early pregnancy loss$).mp.

35 (stillbirth or still birth).mp. or exp Stillbirth/ or exp Fetal Death/ or (f?etal death$ or f?etal demise$).mp.

36 Hypertension, Pregnancy-Induced/ or (gestational hypertension or (pregnancy adj3 hypertensi$)).mp.

37 (preeclampsia or pre-eclampsia).mp. or exp Pre-Eclampsia/

38 exp Eclampsia/ or (eclampsia or tox?emia).mp.

39 HELLP.mp. or exp HELLP Syndrome/

40 placenta accreta.mp. or exp Placenta Accreta/ or placenta percreta.mp. or placenta increta.mp. or morbidly adherent placenta.mp. or abnormally invasiveplacenta.mp.

41 Placenta$ abruption.mp. or exp Abruptio Placentae/

42 placenta pr?eia.mp. or exp placenta previa/ or exp low lying placenta/

43 Hyperemesis Gravidarum.mp. or Hyperemesis Gravidarum/ or morning sickness.mp. or exp Morning Sickness/

44 (((pregnan$ or gestation$ or prenatal$ or antenatal$ or pre-natal$ or ante-natal$ or maternal$) adj2 diabet$) or gestational diabetes).mp. or exp Diabetes, Gestational/ or GDM.mp.

45 ectopic pregnancy.mp. or exp Pregnancy, Ectopic/ or ((tub$$ adj3 pregnanc$) or (cornual adj3 pregnanc$) or (heterotopic adj3 pregnanc$) or (abdomin$ adj3 pregnanc$) or (extrauterine adj3 pregnanc$) or (interstitial adj3 pregnanc$) or (cervi$ adj3 pregnanc$) or (ovar$ adj3 pregnanc$) or (cesarean scar adj3 pregnanc$)).mp.

46 exp Gestational Trophoblastic Disease/ or gestational trophoblastic.mp. or exp Hydatidiform Mole/ or ((hydatid? adj2 mole?) or (molar adj2 pregnanc?)).mp.

47 exp Choriocarcinoma/ or choriocarcinoma.mp.

48 exp Pregnancy, Multiple/ or ((pregnanc* or gestation*) adj (twin* or triplet* or quadruplet* or quintuplet* or multiple or multi?f?et*)).mp. or (Monochorionic or dichorionic).mp.

49 exp Postpartum Hemorrhage/ or (postpartum hemorrhage or post partum hemorrhage or postpartumhaemorrhage or post partum haemorrhage).ti,ab. or obstetric haemorrhage.mp.

50 obstetric labor, premature.mp. or exp Obstetric Labor, Premature/ or (premature labor or premature labour or preterm labor or preterm labour or preterm birth).mp.

51 exp Cesarean Section, Repeat/ or cesarean.mp. or exp Cesarean Section/ or (caesarean or cesarean or caesarian or cesarian or cesarien or caesarien or c-section or c section).mp.

52 exp Extraction, Obstetrical/ or exp Obstetrical Forceps/ or ((operative or instrumental or assisted or forcep* or ventouse* or vacuum*) adj1 (deliver* or birth*)).mp.

53 low birth weight.mp. or exp Infant, Low Birth Weight/ or (low birth weight* adj4 very low birth weight*).mp.

54 exp Infant, Small for Gestational Age/ or small for gestational age.mp. or (small adj3 gestational age).mp.

55 (intra?uterine growth adj2 (restriction* or retardation)).mp. or iugr.ti,ab.

56 fetal growth retardation.mp. or exp Fetal Growth Retardation/ or (fetal growth adj2 (restriction? or retardation)).mp.

57 postpartum depression.mp. or exp Depression, Postpartum/

58 ((postpartum* or post partum* or post-partum* or postnatal* or post natal* or post-natal* or perinatal* or peri natal* or peri-natal* or puerp*) and (depress* or dysthymi* or adjustment disorder* or mood disorder* or affective disorder*)).mp.

59 (((postpartum* or post partum* or post-partum* or postnatal* or post natal* or post-natal or perinatal* or peri natal* or peri-natal* or puerp*) and (psychos#s or psychotic)) or psychosis after childbirth).mp.

60 (((third or fourth or 3rd or 4th) adj degree) and tear*).mp.

61 (((anal near adj2 sphincter) or (rectal adj mucosa) or rectum or (anal adj epithelium) or anus or (recto?vaginal adj2 fistulae) or (anorectal adj mucosa) or analadj skin) and (tear* or injur* or damage* or lacerat* or rupture* or trauma)).mp.

62 ((obstetric* and anal and sphincter and injur*) or (anal and sphincter and injur*)).mp.

63 (exp Pregnancy/ or exp Obstetrics/ or (pregnan* or obstetric*).mp.) and (exp Cholestasis/ or exp Cholestasis, Intrahepatic/)

64 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63

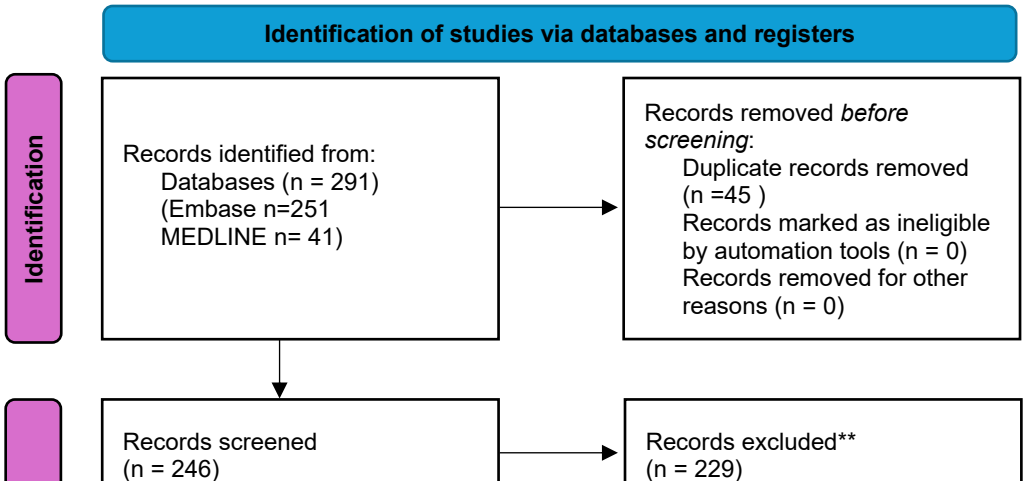
65 27 and 64

66 33 and 65

67 28 and 33

68 66 or 67

Supplementary figure 4.1: PRISMA Flow Diagram



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020

Study	Reason for Exclusion
Abdelnour	Wrong comparator
Adeney et al	Review article (not meeting definition of systematic review)
Chen et al	Umbrella review
Fox et al	Systematic review methodology not reported
Hilaire et al	Review article (not meeting definition of systematic review)
Loder et al	Review article (not meeting definition of systematic review)
Negro et al	Review article (not meeting definition of systematic review)
Nkuna et al	Protocol
Rapoport et al	Review article, abstract only
Saldanha et al	All primary headache, not just migraine included
Sen	Abstract only
Tanos et al	Systematic review methodology not reported
Wabnitz et al	Systematic review methodology not reported

Supplementary table 4.2: Reasons for exclusions of studies from Umbrella Review

Supplementary table 4.3

Study characteristic	**Aukes et al**	**Brown et al**	**Dudman et al**	**Marchenko et al**
Title	Associations Between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis	Chronic Medical Conditions and Peripartum Mental Illness: A Systematic Review and Meta-Analysis	A systematic review and meta-analyses on the prevalence of pregnancy outcomes in migraine treated patients: a contribution from the IMI2 ConcePTION project	Pregnancy Outcome Following Prenatal Exposure to Triptan Medications: A Meta-Analysis
Publication year	2019	2018	2021	2015
Author	Annet M. Aukes, MD, PhD, Feyza N. Yurtsever, BSc, Amélie Boutin, PhD, Marieke C. Visser, MD, PhD,	Hilary K. Brown, Amna Qazilbash, Nedda Rahim, Cindy-Lee Dennis, and Simone N. Vigod	Daniel C. Dudman, Fatima Tauqeer, Moninder Kaur, Mary E. Ritchey, Hu Li, Sandra Lopez-Leon	Alexander Marchenko, MD; Fatma Etwel, MSc; Olukayode Olutunfese, MD; Cheri

	and Christianne J. M. de Groot, MD, PhD			Nickel, BSW; Gideon Koren, MD; Irena Nulman, MD
Geographical Area	The Netherlands	Canada	USA, Norway, UK	Canada
Aim of review	To determine the association of adverse pregnancy outcomes including pre-eclampsia, preterm birth, low birth weight, small for gestational age, and placental abruption with a history of migraine through a systematic review and meta-analysis.	To examine the association between maternal chronic conditions and peripartum mental illness.	To summarise the safety profile of the medications used to treat migraine during pregnancy by performing a systematic review and meta-analysis	To determine the reproductive safety of triptan medications by performing a literature review and a meta-analysis

Databases searched	Medline (Pubmed), Embase, Cochrane Library	MEDLINE, Embase, CINAHL, Psych-INFO	Embase, PubMed, PsychInfo, Scopus, Web of Science	Medical Literature Analysis and Retrieval System Online (via Object, View and Interaction Design [OVID]), Excerpta Medica Database, SCOPUS, Toxicology Information Online Special (via Toxicology Data Network), DART: Developmental and Reproductive Toxicology, ReproTox, Teratogen Information System, OVID International Pharmaceutical Abstracts, Cumulative Index to

				Nursing and Allied Health Literature, Shepard's Citations, Google Scholar, Cochrane Library, World Cat, Digital Dissertations, Global Health, Institute for Scientific Information Proceedings, and Biosciences Information Service Previews.
Search period	Inception to 11th November 2018	Inception to September 2017	Inception to 31st Dec 2020	1991 (when triptans first introduced) to Dec 2013
Population	Pregnant women	Pregnant women	Pregnant women	Pregnant women
Exposures	History of migraine	Chronic medical conditions of which one was migraine	Exposure to antimigraine medications anytime during pregnancy	Triptan medications during at least the first trimester of pregnancy
Comparator	No history of migraine	No chronic medical condition	Untreated migraine patients or general population	Women with migraine who were not treated

				with triptans or healthy controls
Outcomes	Pre-eclampsia, low birth weight, small for gestational age, premature birth, placental abruption	Peri-partum mental illness	All pregnancy outcomes	Major congenital malformations, prematurity, spontaneous abortion
Covariates	All studies adjusted for maternal age. Other confounders adjusted for were parity, adiposity or body mass index, ethnicity, education, marital status, income, chronic hypertension, diabetes mellitus, hyperlipidemia, coronary heart disease, a family history of hypertension in pregnancy, smoking, physical exercise during pregnancy, and	One study adjusted for age and ethnicity	Alcohol, BMI, concomitant medications, delivery method, age, education, comorbidities, parity, previous children with birth defects, miscarriages, smoking were considered, but most only adjusted for maternal age, parity and smoking.	None

	sex of the neonate.			
Study designs	Case-controls, cohorts	Cross-sectional, prospective cohort	Retrospective and prospective cohorts	RCT, case-control, observational cohort
Definition of Exposure	Varied: questionnaires or structured interviews (ranging from asking if diagnosed to meeting diagnostic criteria from International Society of Headache (ISH); recorded in medical notes	Unclear	Any medication for the management of migraine as ascertained by prescription records or interview	Prescription or dispensing of triptans
Definition of Outcome	Pre-eclampsia: any definition but considered blood pressure of ≥140/90 mm Hg combined with proteinuria >300 mg/24 hours or	Depression via Patient Health Questionnaire	Unclear. Sources of outcomes included birth registry data, obstetrician or physician reports or medical records	Unclear.

	>30 mg/dL after 20 weeks of gestation as most valid definition, premature birth (<37 weeks or 259 days' gestational age), LBW (≤2500 g), SGA (birth weight below the 10th percentile for gestational age),			
Data synthesis method	Meta-analysis: random effects model	Meta-analysis: random effects model	Meta-analysis: random effects model	Meta-analysis: random effects model
Quality assessment tool	ROBINS-1	Effective Public Health Practice Project Quality Assessment tool	Newcastle Ottawa Scale (NOS)	Newcastle Ottawa Scale (NOS)
Quality of the included primary studies as assessed by review authors	2 low risk, 2 unclear risk, 10 high risk	1 moderate, 1 weak	Average score high (7.2), Five out of six included were high-quality cohort studies	Not reported fully. All six studies met the quality threshold
Number of studies included in qualitative analysis	Fourteen	Two	Three	Six

(narrative synthesis where meta-analysis was not done / possible by the review authors				
Number of meta-analyses	Four meta-analyses looking at: pre-eclampsia, preterm birth, low birth weight, small for gestational age	One	Three: major malformations, low birth weight, preterm birth	Eight: major congenital malformations (triptan exposed vs non-triptan exposed migraine, triptan exposed vs healthy controls, non-triptan exposed migraine v healthy controls), spontaneous abortion (triptan exposed vs non-triptan exposed migraine, triptan exposed vs healthy controls), prematurity (triptan exposed vs non-triptan

				exposed migraine, triptan exposed vs healthy controls, non-triptan exposed migraine v healthy controls)
Number of studies included in each meta-analysis	Pre-eclampsia: 9 Preterm birth: 5 Low birth weight: 3 Small for gestational age: 2	Migraine: 2	Women taking triptan vs general population Major malformations: 2 Low birth weight: 2 Preterm birth: 2	Major congenital malformations (triptan v non-triptan migraine): 3 Major congenital malformations (triptan v healthy control): 4 Major congenital malformations (non-triptan v healthy control): 3 Spontaneous abortion (triptan v non-triptan):2 Spontaneous abortion (triptan vs healthy control): 2

				Prematurity (triptan vs non-triptan): 3 Prematurity (triptan vs health control): 4 Prematurity (non-triptan v healthy control): 3
Summary estimates of each meta-analysis and its related 95% CI	Pre-eclampsia: Pooled crude OR 2.07 (95% CI: 1.51-2.84), Pooled adjusted OR 1.94 (1.37-2.76) Preterm birth: Pooled crude OR 1.23 (0.97-1.55), adjusted OR 1.25 (1.13-1.38)	Pooled OR 1.75 (1.20-2.54)	Major malformations: adjusted OR 1.07 (0.83-1.39) Low birth weight: adjusted OR 1.18 (0.94-1.48) Preterm birth: 1.49 (0.37-6.08)	Major congenital malformations (triptan v non-triptan migraine): 0.84 (0.61-1.16 Major congenital malformations (triptan v healthy control):

	Low birth weight: Pooled crude OR 1.18 (1.03-1.34), adjusted OR 1.27 (0.89-1.82) Small for gestational age: Pooled crude OR 1.06 (0.98-1.15), adjusted OR 1.06 (0.99-1.14)			1.18 (0.97-1.44) Major congenital malformations (non-triptan v healthy control): 1.41 (1.11-1.80) Spontaneous abortion (triptan v non-triptan): 1.27 (0.58-2.79) Spontaneous abortion (triptan vs healthy control): 3.54 (2.24-5.59) Prematurity (triptan vs non-triptan): 0.90 (0.35-2.30) Prematurity (triptan vs health control): 1.16 (0.67-1.99) Prematurity (non-triptan v healthy control): 1.44 (0.66-3.16)

Author's conclusion	A history of migraine is associated with a significantly increased risk of pre-eclampsia and low birth weight	Migraine is associated with peripartum mental illness	Triptans do not appear to increase the risk of pregnancy outcomes when compared to the general population. It was not possible to assess other migraine medications	Exposure to triptans during pregnancy does not appear to increase the risk of major congenital malformation or preterm birth. However, there were increased rates of miscarriage in the triptan exposed group when compared to healthy controls
Review limitations	High risk of bias and misclassification in a number of included studies. Unable to perform sensitivity analysis as only two studies at low risk of bias. Not all studies adjusted for confounders. High	Some studies not controlling for variables that could be on causal pathway (such as pregnancy complications), heterogeneity, use of screening tools for depression rather than clinical diagnosis. Studies not distinguishing	Few studies evaluating patients treated with newer migraine medication. No studies evaluating prophylactic migraine medication. Low number of studies included in meta-analysis, confounding by indication, indication for medication not known,	Use of prescribing or dispensing data as proxy for drug consumption, incomplete data regarding dose, duration and timing of medications, confounding effect of concomitant medication use

	heterogeneity particularly in pre-eclampsia analysis Inclusion of case-control studies which overestimated association between migraine and pre-eclampsia	between new and ongoing mental illness.		
Additional comments		Note that migraine was among several conditions considered as an exposure during pregnancy. Only data regarding migraine as an exposure are presented here		

Supplementary section 4.2: Aukes et al update

Methods

A systematic review was performed based on the methods used in Aukes et al.

Search strategy

MEDLINE, EMBASE and Cochrane library were searched between 11th November 2018 (the last date Aukes et al performed their search) and 15th November 2023. The search strategy used by Aukes et was replicated. The search is shown below:

1. exp pregnancy complication/
2. pregnan*.ti,ab.
3. complication*.ab,ti.
4. 2 and 3
5. exp hypertension/
6. hypertensi*.ti,ab.

7. 5 or 6

8. exp pregnancy/

9. gestation*.ti,ab.

10. 2 or 8 or 9

11. 7 and 10

12. preeclampsi*.ti,ab.

13. eclampsi*.ti,ab.

14. pih.ti,ab.

15. eph.ti,ab.

16. exp prematurity/

17. exp low birth weight/

18. "small for gestational age".ti,ab.

19. prematur*.ti,ab.

20. vlbw.ti,ab.

21. elbw.ti,ab.

22. "low birth weight".ti,ab.

23. preterm*.ti,ab.

24. "placental insufficien*".ti,ab.

25. abrupt*.ti,ab.

26. placent*.ti,ab.

27. 4 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

28. 25 and 26

29. 27 or 28

30. primary headache/

31. exp migraine/

32. migrain*.ti,ab.

33. 30 or 31 or 32

34. 29 and 33

Study selection

Title and abstracts were screened by two reviewers independently. Full texts were retrieved for abstracts found to be eligible and reviewed by two authors independently.

Data collection and risk of bias

One author collected data and data extraction was checked by a second author. Risk of bias was assessed using a modified version of the ROBINS-1 tool by two reviewers.

Risk of publication bias was assessed using funnel plots.

Statistical analysis

Where available, adjusted odds ratios were used in meta-analyses (crude odds ratios if unavailable). Crude odds ratios were calculated where other summary measures were reported. Where studies reported adjusted risk ratios, these were pooled in additional meta-analyses. Effect estimates and 95% confidence intervals were pooled using Mantel-Haenszel and random-effects models. All statistical analyses were performed using Stata statistical software, version 17 (StataCorp, College Station, Texas, USA).

Results

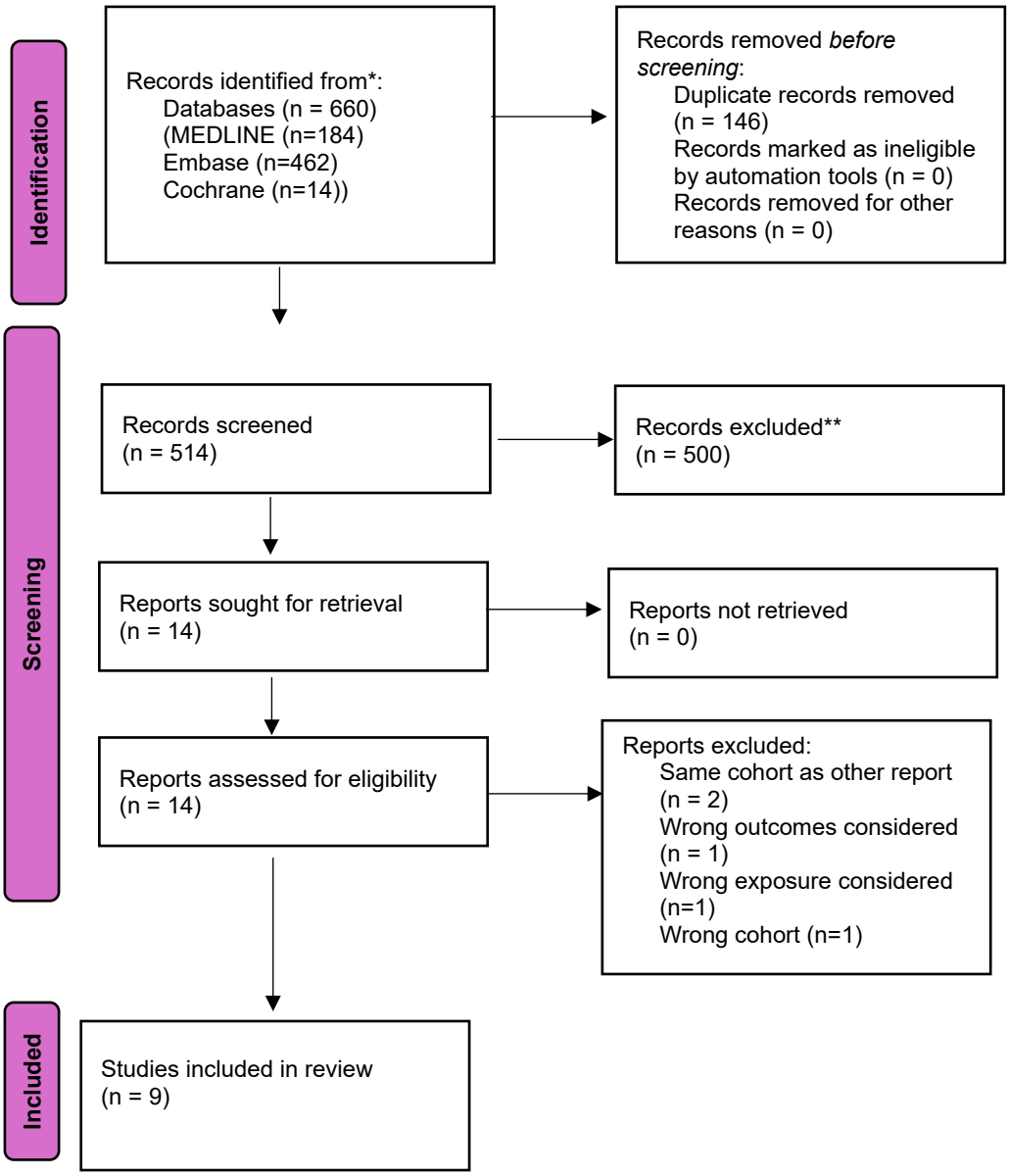
Following the removal of duplicates, 660 titles and abstracts were screened for eligibility. Fourteen full reports were retrieved, of which nine were deemed eligible for inclusion. Three studies were retrospective cohorts[125] [210] [55] [211], four were prospective cohorts [171] [212] [170] and two were case-control studies [213] [214]. Six studies were published in peer reviewed journals, two were conference abstracts and one was a peer reviewed letter.

Odds ratios could not be calculated for one study [213], therefore eight studies were included in meta-analyses. For the primary analysis, only peer-reviewed articles were

included, all studies were included in a sensitivity analysis. For the primary analysis,the studies investigated a total of 1,419,856 women, of which 192,988 had migraine.

Migraine was captured using a variety of methods. Three studies used the presence of ICD-9/10 in hospital records [125, 210] [55], three studies relied on self-report of the women [171] [170] [214]and three studies used validated questionnaires (one was conducted via interview, the other did not report how the questionnaire was conducted)[212] [213, 214]. The pregnancy complications were also measured in different ways. Four studies relied on health records [125, 211, 212], one interviewed patients up two weeks after delivery [213], and four studies did not make the collection of their outcome definitions clear [210] [55] [55, 170, 214]. With regards to outcomes, seven studies considered preterm birth [125, 210] [55, 171] [212] [170] [213], three considered small for gestational age[125] [171] [212], seven considered preeclampsia [125] [55] [211] [171] [170] [213] [214], three considered low birth weight[125] [170] [213] and two considered placental abruption [125] [212]. Two studies provided adjusted odds ratios[171, 214], one study provided adjusted ORs for low birth weight only [212], so crude odds ratios were calculated for the other outcomes. Four studies provided adjusted prevalence ratios, so odds ratios were calculated. [125] [55] [170, 211] and one study did not provide sufficient information to calculate odds ratios [213], so was not included in the meta-analyses, but a narrative review of this study is included.

PRISMA flow diagram



Supplementary section table 1: Reason for exclusion of studies after full text screening

	Reason for exclusion
Lev et al	Wrong outcome
Mammadli et al	Same cohort as another report
Myers et al	Wrong exposure
Spielman et al	Wrong cohort

Tzur et al	Same cohort as another report

Supplementary section table 2: Characteristics of studies included in update of Aukes et al

Reference	Year	Publication Type	Time period	Population	Study design	No. participants (No. with migraine)	Diagnosis of migraine	Pregnancy outcome variable	Diagnosis of outcome variable	Covariates
Adam et al (9)	2021	Journal article	2021	Women giving birth at a single maternity hospital in Central Sudan	Case-control study	444 (76)	Self-reported physician diagnosis	Preeclampsia	ACOG criteria used, unclear how collected	Age, History of Preeclampsia, BMI
Bandoli et al (210)	**2020**	Abstract	2007-2012	California birth cohort	Retrospective cohort	2,892,756 (26,440)	ICD-9 codes in emergency department or hospital discharge records	Preterm birth	Unclear	Year of birth, race/ethnicity, payer source, maternal age, parity, maternal BMI, WIC participation, maternal nativity, maternal hypertension, diabetes, asthma, autoimmune conditions, mental illness, drug or alcohol abuse or dependence, and pregnancy smoking.
Crowe et al (4)	**2023**	Journal article	2023	United Kingdom Primary Care Electronic Health Records	Prospective Cohort Study	1,049,839 (132,623)	Diagnosis code in primary care or prescription for migraine-specific medication	Preeclampsia	Diagnosis code in primary care	Smoking, history of asthma, history of diabetes, history of mood disorder, early pregnancy mood disorder, parity, age, BMI, calendar year

Miller et al (171)	**2022**	Letter	2010-2015	Nulliparous US participants with singleton pregnancy	Prospective cohort study	10,038 (1752)	Self-report	Preeclampsia, small for gestational age, preterm birth,	Outcome defined using standardised definitions and adjudicated by maternal-fetal medicine	race or ethnicity, chronic hypertension, renal disease, autoimmune disorders (systemic lupus erythematosus or antiphospholipid syndrome), smoking in the 3 months before pregnancy, and family history of preeclampsia in mother or sister.
Neri et al (212)	**2021**	Journal article	June 2018-Dec 2019	Consecutive women with singleton pregnancies attending first trimester screening at a hospital in Northern Italy	Prospective cohort study	515 (99)	ID migraine questionnaire and visual aura rating scale (VARS)	Small for gestational age Stillbirth Abruptio placentae Gestational Hypertension Preterm delivery	Hospital maternity records or directly from patients	Maternal age ≥35, multiparity,high BMI, Mean Arterial Pressure >90mmmHg,uterine artery doppler PI >90th, PAPP-A MoM PLGF MoM, inhibin-A, migraine without aura, migraine with aura
Purdue-Smithe et al (6)	**2022**	Abstract	1989-2009	Women in the Nurses' Health Study, US	Prospective cohort study	30,555 (3,361)	Self-reported physician diagnosis	Preterm birth Preeclampsia Low birth weight	Unclear	Age, adiposity, and other behavioral and health factors
Shoaib et al (213)	**2021**	Journal article	1st August 2018-31st August 2021	Pregnant women attending obstetrics department at a single hospital in Pakistan	Case control study	100 (50)	Interviewed using ICHD-2 criteria	Pre-eclampsia Low birth weight Preterm	Patients followed up two weeks after delivery	Maternal age, gestational age,employment, BMI

Skajaa et al (125)	**2019**	Journal article	2005-2012	Danish population registry	Nationwide population-based retrospective cohort study	251,165 (22,841)	Women with an ICD 10 diagnosis of migraine during a hospital encounter or outpatient dispensing of migraine medication	Preeclampsia Placental abruption Preterm Low birth weight Small for gestational ages	Danish National Patient Registry and Danish Medical Birth Registry records	Maternal age, preconception history of diabetes, hypertension, depression, asthma, infertility, pregnancy-associated hypertension disorders, parity, miscarriage, elective pregnancy termination, pregnancy with fetal abnormality, use of NSAIDs, smoking, and obesity
Wood et al (55)	**2021**	Abstract	2011-2015	Commercially insured women in the US	Retrospective cohort	904,609 (7085)	ICD-9 codes	Preterm birth Preeclampsia Placental abruption	Unclear	Chronic hypertension, obesity, depression, epilepsy, diabetes

Risk of bias

Three studies were at low risk of bias [125] [211] [170], four were at high risk of bias[170] [210] [171, 213] [214] and two had an unclear risk of bias [55, 212].

Supplementary section table 3: Quality of studies included in updated review as assessed using Risk of Bias in Non-intervention studies (ROBINs-1) tool

Study	Selection bias	Missing data	Information bias-exposure	Information bias-outcome	Confounding	Summary
Adam et al	?	?	+	?	-	+
Bandoli et al	+	?	+	?	+	+
Crowe et al	-	-	?	-	-	-

Miller et al	+	-	+	+	+	+
Neri et al	+	?	+	?	-	?
Purdue-Smithe et al	-	-	+	?	+	-
Shoaib et al	?	?	?	?	+	-
Skajaa et al	+	?	?	+	+	+
Wood et al	?	?	?	?	+	?

Key: + low risk of bias. – high risk of bias, ? unclear risk of bias

There were sufficient studies to construct funnel plots for studies of preterm birth and pre-eclampsia. Visual inspection of the plots indicated potential publication bias, particularly for pre-eclampsia.

Results

Meta-analyses were carried out using the selected studies and studies included in the original systematic review by Aukes et al. Sensitivity analyses were carried out on articles that were published in peer reviewed journals only and studies at low risk of bias only.

Pre-eclampsia

In total, fourteen studies investigating a total of 2,360,451 women, reported on the association between migraine and preeclampsia. Compared to women without migraine, women with migraine had more than double the odds of pre-eclampsia (pooled crude OR was 2.05 (1.47-2.84)), and the pooled OR was also statistically significantly higher for migraine for studies that included adjustment for confounding (pooled aOR 2.22 (1.34-3.68) 6 studies, n=44,356) (Supplementary Figure 2a). The OR remained significant in a sensitivity analysis , of studies at those at low risk of bias reporting

unadjusted odds ratios (pooled unadjusted OR 1.28 (1.10-1.50) but not in the one study reporting adjusted ORs (1.18 (0.98-1.42)) (Supplementary Figure 4.3B).

Heterogeneity was high for both the crude (I^2=98%) and adjusted analyses (I^2=93%). Sensitivity analysis was conducted to examine the effect of study design on heterogeneity. For cohort studies, the pooled crude OR was 1.38 (1.20-1.58, I^2=82%) and the pooled adjusted OR was 1.27 (1.11-1.47, I^2=0.2%) (Supplementary Figure 4.3C). For case-control studies, the pooled crude OR was 3.05 (1.78-5.231, I^2=89%) and the pooled adjusted OR was 3.39 (1.73-6.64, I^2=86%) (Supplementary Figure 4.3D). This suggests some, but not all, heterogeneity can be attributed to differences in study design.

The OR were higher and remained significant in a sensitivity analysis that included the abstract not publishes in a peer reviewed (Supplementary Figure 4.3A) journal. In a sensitivity analysis of studies at low risk of bias, the pooled crude OR was 1.36 (1.13-1.64) (2 studies, n=139,957).

Three studies reported adjusted risk ratios for pre-eclampsia. The pooled adjusted risk ratio was 1.31 (1.14-1.50) (Supplementary Figure 4.3E).

There were sufficient studies to construct a funnel plot. Visual inspection of the plot indicated potential publication bias (Supplementary Figure 4.4).

Preterm Birth

Ten studies, including a total of 364,079 women, investigated the association between migraine and preterm birth; compared to women without migraine, women with migraine had a 33% higher odds of pre-term birth with a pooled odds ratio of 1.33 (1.17-1.51). Three studies also reported adjusted odds ratios (pooled aOR 1.32 (1.15-1.51) n=39,601) (Figure 4.2b). The odds ratios remained significant in sensitivity analyses which included only the six studies with low risk of bias (Supplementary Figure 4.5B) and when abstracts were included (Supplementary Figure 4.5A).

Heterogeneity was moderate for the adjusted analysis (I^2=31.5%) and low for the crude analysis (I^2=0%). In a sensitivity analysis conducted to explore the effect of study

design on heterogeneity, restricting the meta-analysis to only prospective cohort studies did not impact the heterogeneity observed (Supplementary Figure 4.5C).

The meta-analysis of studies that reported adjusted risk ratios showed that women with migraine had a 20% significantly higher risk of preterm birth with a pooled aRR of 1.20 (1.13-1.27) (Supplementary Figure 4.5D). Shoaib et, who did not provide sufficient information in their paper to calculate ORs, also reported a higher prevalence of preterm birth in women with migraine.

Placental abruption

The 2 studies that were included in the meta-analysis included a total of 251,908 women. The odds of placental abruption were more than 50% higher in women with migraine, but this was not statistically significant (OR 1.51 (0.81-2.84)) (Figure 2c). When the abstract was included, the odds of placental abruption was more than one third higher in women with migraine, which was statistically significant (OR 1.35(1.05-1.75) (Supplementary Figure 4.7).

Low birth weight

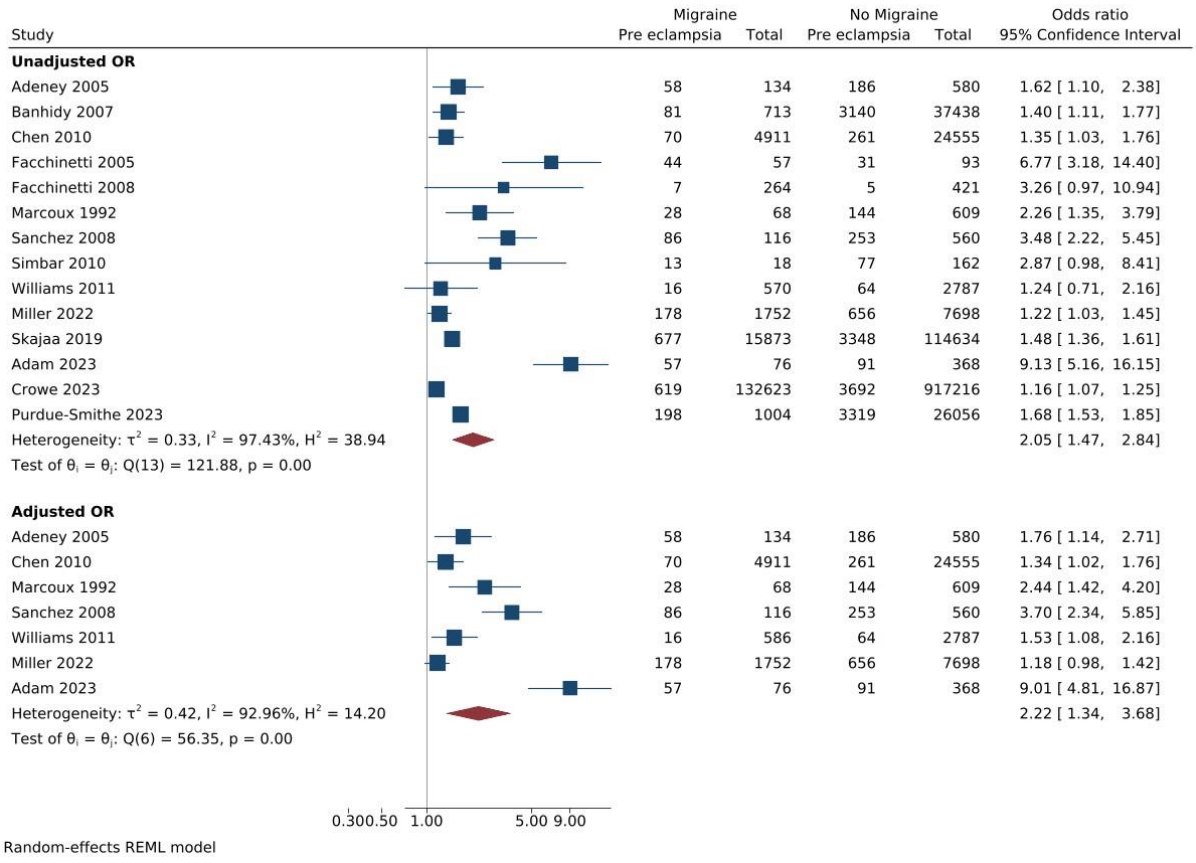
Five studies, investigating a total of 350,020 women reported on the association between migraine and low birth weight. The odds of low birth weight was 18% higher for women with migraine; pooled crude OR was 1.18 (1.11-1.24). The odds of low birth weight were higher in two studies that reported an adjusted OR, but this was not statistically significant; pooled aOR of 1.27 (0.89-1.82) (Figure 4.2d).

Small for gestational age

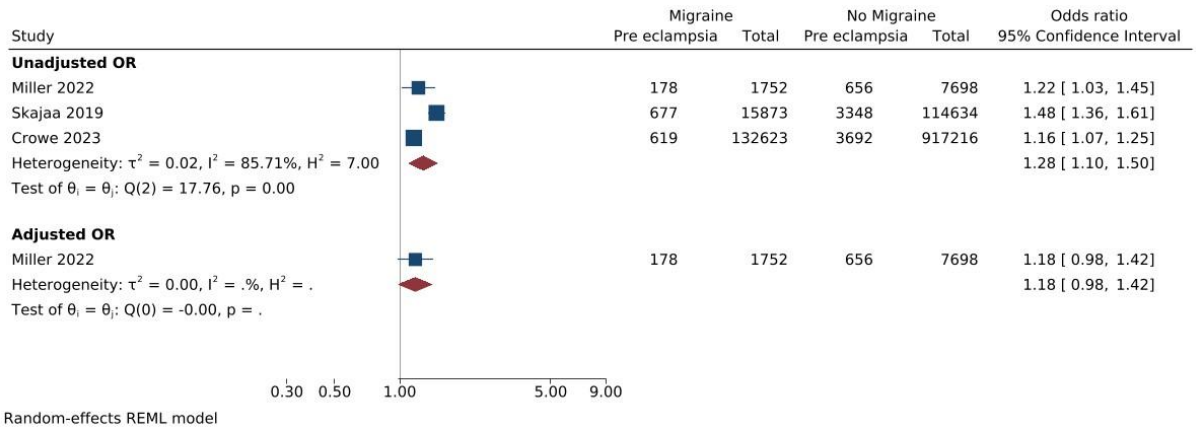
Five studies, investigating a total of 291,279 women, reported on the association between migraine and small for gestational age. There was a slightly higher risk of small for gestational age in the unadjusted analysis but this was not statistically significant; pooled crude OR of 1.08 (0.95-1.23, I^2=75%, 5 studies, n=169,770. For the studies that provided adjusted OR, the pooled aOR was 8% higher, a result that was statistically significant; 1.08 (1.01-1.15, I^2=0.01%, 3 studies, n=39,599) (Figure 4.2e).

The pooled crude ORs were not significant in sensitivity analyses of articles published in peer reviewed journals only or at low risk of bias only (Supplementary Figure 4.8).

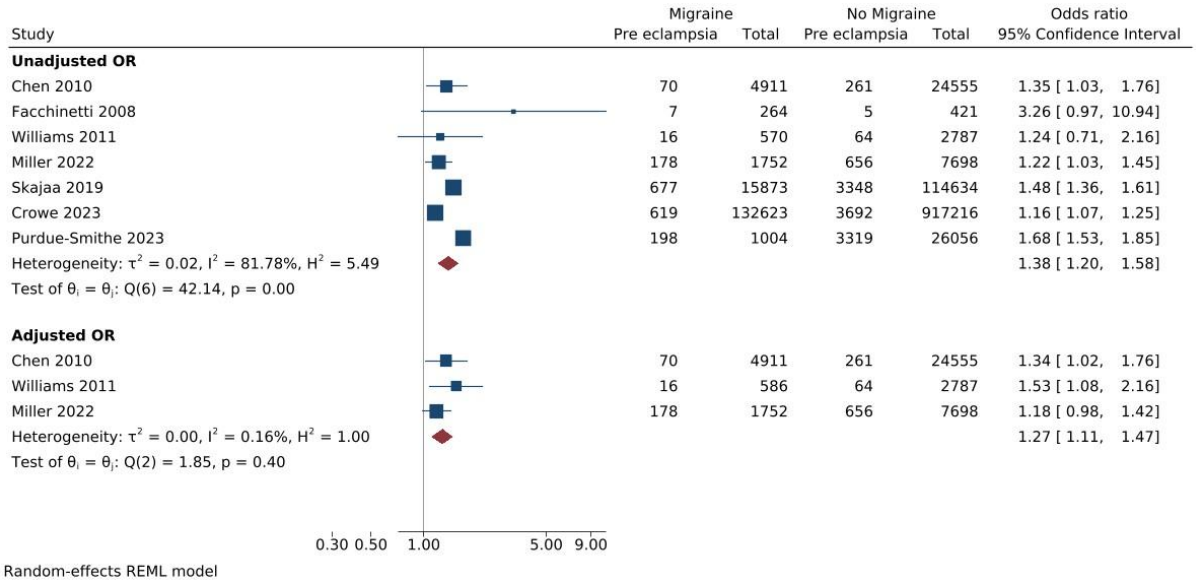
Supplementary Figure 4.3A: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preeclampsia in women with and without migraine in a sensitivity analysis including non-peer reviewed abstracts



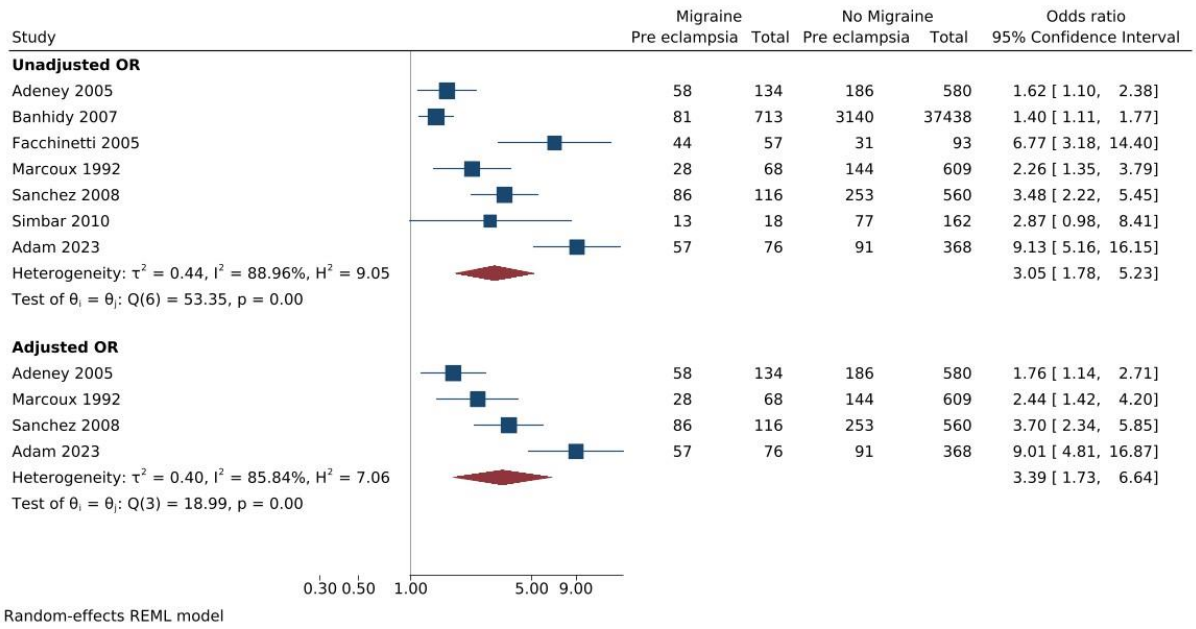
Supplementary Figure 4.3B: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preeclampsia in women with and without migraine in a sensitivity analysis including only studies at low risk of bias



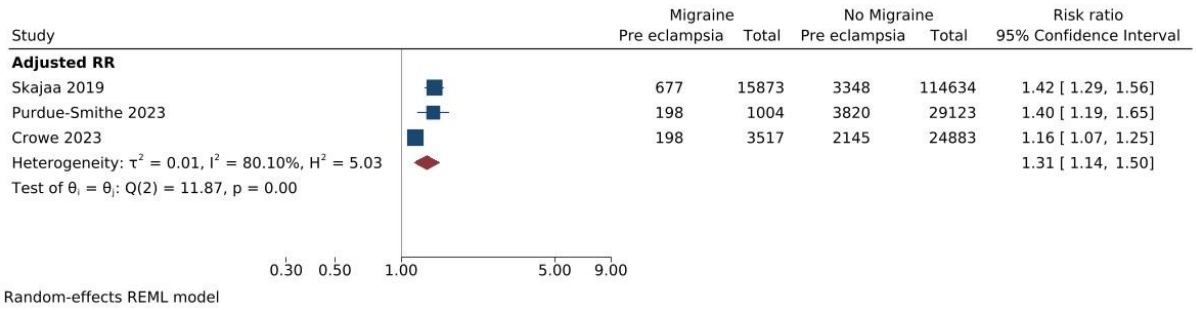
Supplementary Figure 4.3C: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preeclampsia in women with and without migraine in a sensitivity analysis of cohort studies



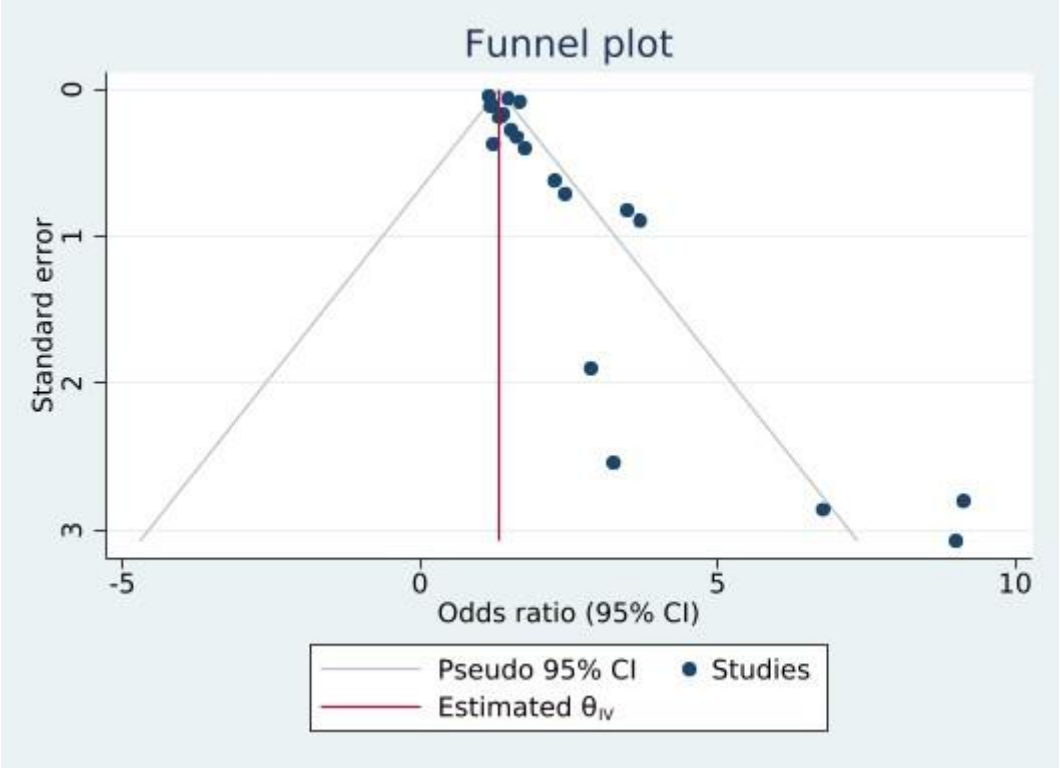
Supplementary Figure 4.3D: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preeclampsia in women with and without migraine in a sensitivity analysis of case-control studies



Supplementary Figure 4.3E: Forest plot of random effects meta-analysis of adjusted risk ratios for preeclampsia in women with and without migraine

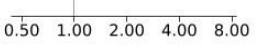


Supplementary Figure 4.4: Funnel plot of studies reporting on the association between migraine and pre-eclampsia



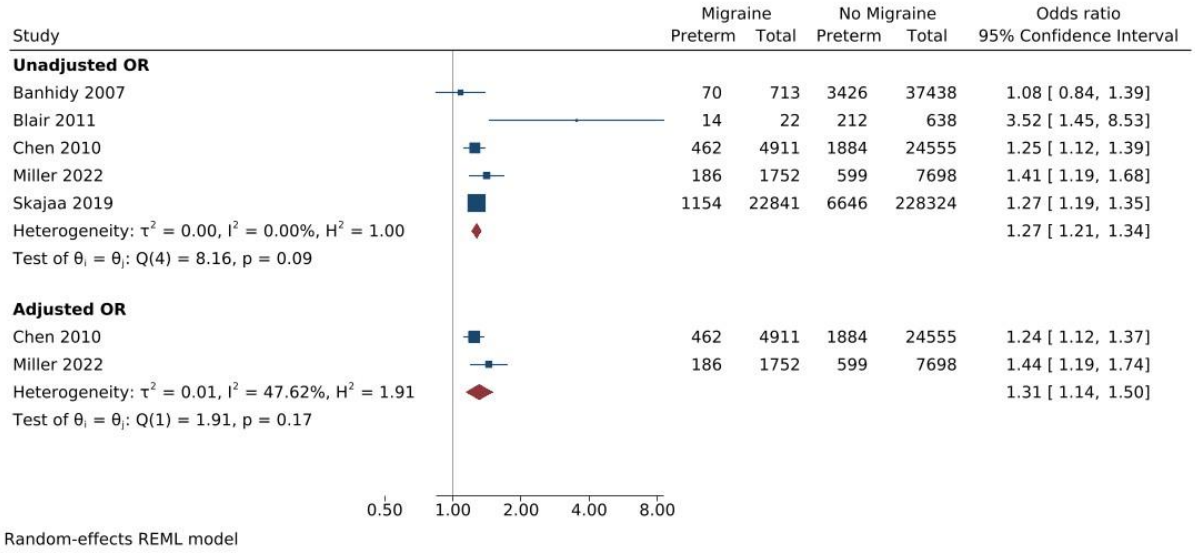
Supplementary Figure 4.5A: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preterm birth in women with and without migraine in a sensitivity analysis including non-peer reviewed abstracts

Study	Migraine Preterm	Migraine Total	No Migraine Preterm	No Migraine Total	Odds ratio 95% Confidence Interval
Unadjusted OR					
Banhidy 2007	70	713	3426	37438	1.08 [0.84, 1.39]
Blair 2011	14	22	212	638	3.52 [1.45, 8.53]
Chen 2010	462	4911	1884	24555	1.25 [1.12, 1.39]
Cripe 2011	33	623	169	2809	0.87 [0.60, 1.27]
Facchinetti 2008	19	264	19	421	1.64 [0.85, 3.16]
Miller 2022	186	1752	599	7698	1.41 [1.19, 1.68]
Neri 2021	6	99	16	291	1.11 [0.43, 2.85]
Skajaa 2019	1154	22841	6646	228324	1.27 [1.19, 1.35]
Bandoli 2020	2937	26440	195581	2866316	1.71 [1.65, 1.78]
Wood 2021	903	7085	92448	897551	1.28 [1.19, 1.37]
Purdue-Smithe 2023	402	2547	3479	26956	1.26 [1.15, 1.38]
Heterogeneity: τ^2 = 0.02, I^2 = 88.25%, H^2 = 8.51					1.32 [1.18, 1.47]
Test of $\theta_i = \theta_j$: Q(10) = 133.04, p = 0.00					
Adjusted OR					
Chen 2010	462	4911	1884	24555	1.24 [1.12, 1.37]
Facchinetti 2008	19	264	19	421	1.57 [0.80, 3.08]
Miller 2022	186	1752	599	7698	1.44 [1.19, 1.74]
Heterogeneity: τ^2 = 0.00, I^2 = 31.49%, H^2 = 1.46					1.32 [1.15, 1.51]
Test of $\theta_i = \theta_j$: Q(2) = 2.25, p = 0.32					

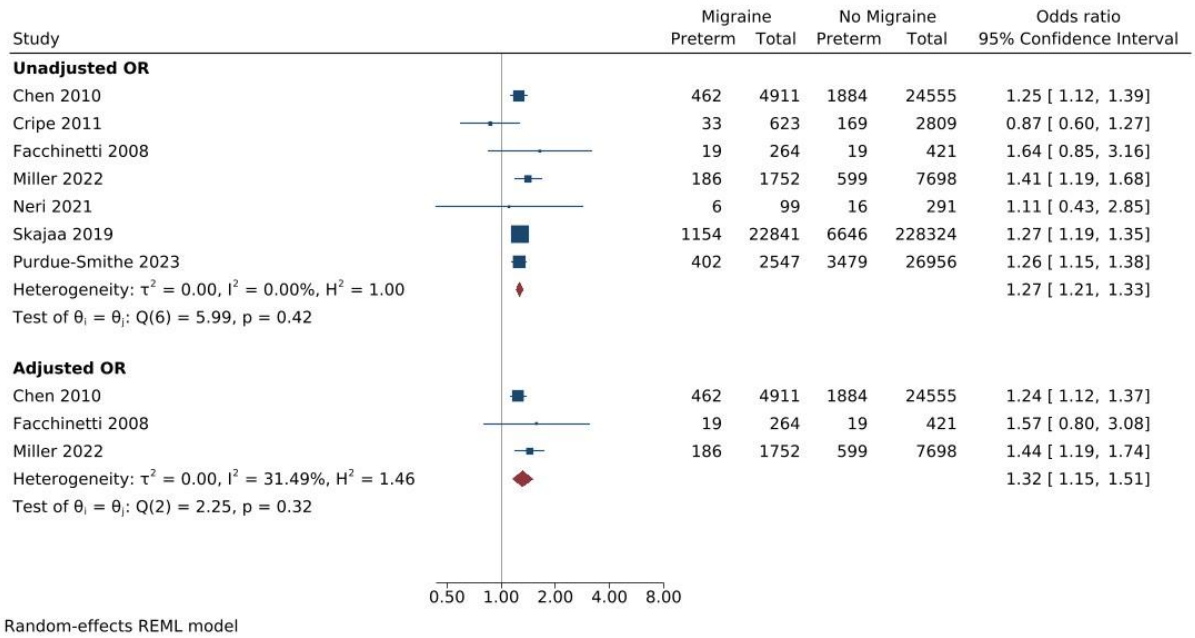


Random-effects REML model

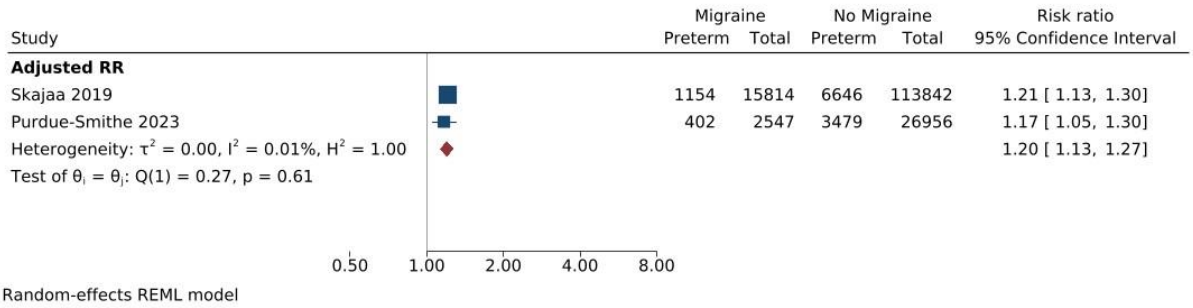
Supplementary Figure 4.5B: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preterm in women with and without migraine in a sensitivity analysis including only studies at low risk of bias



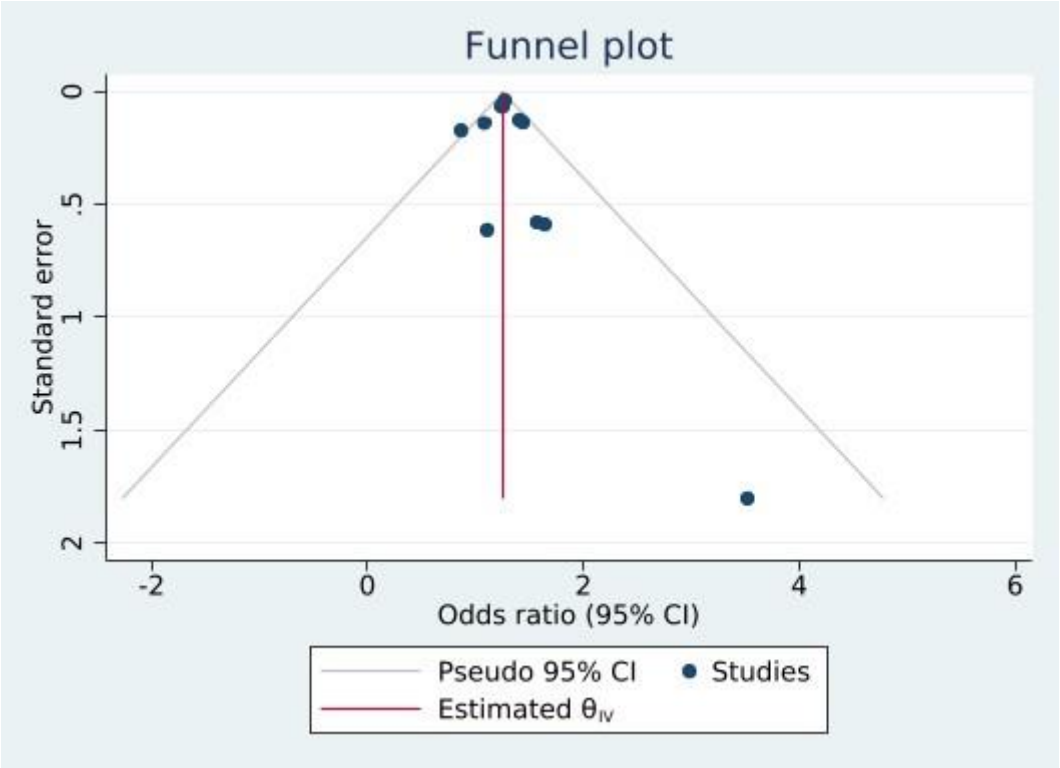
Supplementary Figure 4.5C: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for preterm birth in women with and without migraine in a sensitivity analysis of cohort studies



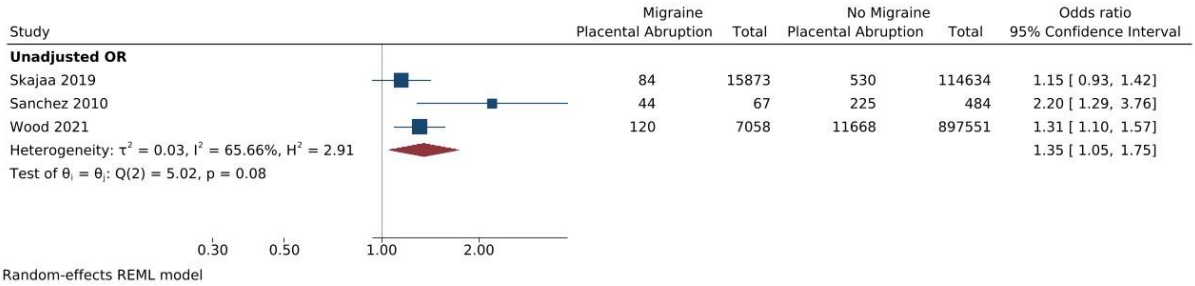
Supplementary Figure 4.5D: Forest plot of random effects meta-analysis of adjusted risk ratios for preterm birth in women with and without migraine



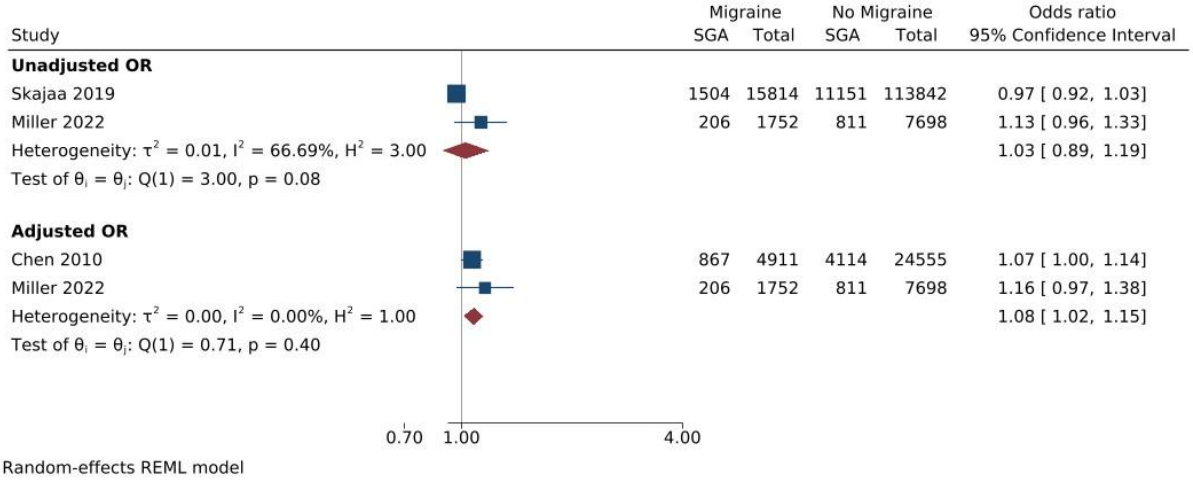
Supplementary Figure 4.6: Funnel plot of studies reporting on the association between migraine and preterm birth



Supplementary Figure 4.7: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for placental abruption in women with and without migraine in a sensitivity analysis including non-peer reviewed abstracts



Supplementary Figure 4.8: Forest plot of random effects meta-analysis of unadjusted and adjusted odds ratios for small for gestational age in women with and without migraine in a sensitivity analysis including only studies at low risk of bias



Chapter 5

Supplementary table 5.1 Codelists used for migraine and comorbidities

DESCRIPTION	READ_CODE
Migraine	F26..00
Periodic migrainous neuralgia	F262500
Common migraine	F261.00
Abdominal migraine	F262200
Classical migraine	F260.00
Hemiplegic migraine	F26y000
H/O: migraine	1474
Migraine variants	F262.00
Abdominal migraine - symptom	1967
Basilar migraine	F262300
Atypical migraine	F261000
Ophthalmic migraine	F262400
Migraine - menstrual	K584.11
Ophthalmoplegic migraine	F26y100
Migraine NOS	F26z.00
[D]Abdominal migraine	R090D00
Status migrainosus	F26y200
Migraine variant NOS	F262z00
Complicated migraine	F26y300
Other forms of migraine	F26y.00
Other forms of migraine NOS	F26yz00
Common migraine NOS	F261z00
[X]Other migraine	Fyu5300
Moebius' ophthalmoplegic migraine	F26y111
H/O migraine with aura	1474000
Migraine with aura	F260.11
Migraine without aura	F261.11
Migraine induced by oestrogen contraceptive	F262800

Drug codes for prescriptions

DESCRIPTION	BNF1
Amitriptyline 10mg tablets Amitriptyline hydrochloride 10mg Tablet Oral	04030100

Amitriptyline 25mg tablets Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg modified-release capsules Amitriptyline hydrochloride 25mg Modified-release capsule Oral	00000000
Lentizol 50mg modified-release capsules (Pfizer Ltd) Amitriptyline hydrochloride 50mg Modified-release capsule Oral	00000000
Amitriptyline 10mg tablets (Teva UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Perphenazine 2mg with Amitriptyline 25mg tablet Amitriptyline Hydrochloride/Perphenazine 2mg + 25mg Tablets Oral	04020100
Amitriptyline 25mg / Perphenazine 2mg tablets Amitriptyline hydrochloride/Perphenazine 25mg + 2mg Tablet Oral	04030100
Tryptizol mr 75mg Modified-release capsule (Merck Sharp & Dohme Ltd) Amitriptyline Hydrochloride 75mg Modified-Release Capsule Oral	04030100
Amitriptyline 10mg tablets (Almus Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml Oral solution (Rosemont Pharmaceuticals Ltd) Amitriptyline Hydrochloride 10mg/5ml Oral Solution Oral	04030100
Amitriptyline 50mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg/1ml Oral solution Oral	04030100
AMITRIPTYLINE	00000000
Amitriptyline 25mg tablets (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 75mg modified-release capsules Amitriptyline Hydrochloride 75mg Modified Release Capsules Oral	04030100
Amitriptyline 50mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg tablets (DE Pharmaceuticals) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Crescent Pharma Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg Tablet (Sussex Pharmaceutical Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
AMITRIPTYLINE 100 MG TAB	00000000

Amitriptyline 25mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Almus Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Lentizol 25mg modified-release capsules (Pfizer Ltd) Amitriptyline hydrochloride 25mg Modified-release capsule Oral	00000000
Amitriptyline 25mg tablets (Phoenix Healthcare Distribution Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Arrow Generics Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Teva UK Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Almus Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 5mg/5ml oral suspension Amitriptyline hydrochloride 1mg/1ml Oral suspension Oral	04030100
Amitriptyline 10mg Tablet (Sussex Pharmaceutical Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 100mg/5ml oral solution Amitriptyline hydrochloride 20mg/1ml Oral solution Oral	04030100
Amitriptyline 50mg/5ml oral solution sugar free Amitriptyline hydrochloride 10mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg tablets (Genesis Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Tryptizol 10mg/5ml sugar free Oral solution (Merck Sharp and Dohme Ltd) Amitriptyline Hydrochloride 10mg/5ml Oral Solution Oral	04030100
AMITRIPTYLINE S/R	00000000
Triptafen m 2mg+10mg Tablet (Goldshield Pharmaceuticals Ltd) Amitriptyline hydrochloride/Perphenazine 10mg + 2mg Tablet Oral	04020100
Amitriptyline 10mg tablets (Actavis UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Kent Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Teva UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 75mg/5ml oral solution Amitriptyline hydrochloride 15mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100

Amitriptyline 25mg tablets (IVAX Pharmaceuticals UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Wockhardt UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	00000000
Domical 25mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Domical 50mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Sigma Pharmaceuticals Plc) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
AMITRIPTYLINE S/F	00000000
Tryptizol 10mg Tablet (Merck Sharp & Dohme Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Ranbaxy (UK) Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
AMITRIPTYLINE S/F 25 MG/5ML SYR	00000000
Amitriptyline oral solution Amitriptyline Hydrochloride Oral Liquid Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg tablets (Arrow Generics Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets (DE Pharmaceuticals) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Waymade Healthcare Plc) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 12.5mg / Chlordiazepoxide 5mg capsules Amitriptyline Hydrochloride/Chlordiazepoxide 12.5mg + 5mg Capsules Oral	04030100
Domical 10mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral suspension Amitriptyline hydrochloride 2mg/1ml Oral suspension Oral	04030100
Limbitrol 10 Capsule (Roche Products Ltd) Amitriptyline Hydrochloride/Chlordiazepoxide Capsule Oral	04030100
Amitriptyline 10mg tablets (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100

Amitriptyline 25mg Tablet (Regent Laboratories Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Actavis UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg Tablet (Crosspharma Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free (DE Pharmaceuticals) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
TRYPTIZOL	00000000
Amitriptyline 10mg tablets (Phoenix Healthcare Distribution Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Accord Healthcare Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 50mg/5ml oral solution sugar free (Wockhardt UK Ltd) Amitriptyline hydrochloride 10mg/1ml Oral solution Oral	04030100
Amitriptyline 50mg tablets (Accord Healthcare Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg tablets (NorthStar Healthcare Unlimited Company) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
AMITRIPTYLINE 75 MG TAB	00000000
Limbitrol 5 Capsule (Roche Products Ltd) Amitriptyline Hydrochloride/Chlordiazepoxide Capsule Oral	04030100
Amitriptyline 2.5mg/5ml oral solution Amitriptyline hydrochloride 500microgram/1ml Oral solution Oral	04030100
Amitriptyline 10mg/5ml sugar free oral solution Amitriptyline Hydrochloride 10mg/5ml Oral Solution Sugar-Free Oral	04030100
Amitriptyline 25mg tablets (DE Pharmaceuticals) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Tryptizol 50mg Tablet (Merck Sharp & Dohme Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 50mg tablets (IVAX Pharmaceuticals UK Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Elavil 10mg Tablet (DDSA Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 50mg modified-release capsules Amitriptyline hydrochloride 50mg Modified-release capsule Oral	00000000

Amitriptyline 50mg tablets (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Kent Pharmaceuticals Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Sandoz Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 10mg tablets (IVAX Pharmaceuticals UK Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg tablets (Kent Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 5mg/5ml oral solution Amitriptyline hydrochloride 1mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg / Perphenazine 2mg tablets Amitriptyline hydrochloride/Perphenazine 10mg + 2mg Tablet Oral	00000000
Amitriptyline 25mg/5ml oral solution sugar free (Rosemont Pharmaceuticals Ltd) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg tablets (Mawdsley-Brooks & Company Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free (Wockhardt UK Ltd) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 25mg/5ml oral solution sugar free (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 5mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg tablets (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Wockhardt UK Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Triptafen-M tablets (Mercury Pharma Group Ltd) Amitriptyline hydrochloride/Perphenazine 10mg + 2mg Tablet Oral	00000000
Amitriptyline 25mg / Chlordiazepoxide 10mg capsules Amitriptyline Hydrochloride/Chlordiazepoxide 25mg + 10mg Capsules Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (Alliance Healthcare (Distribution) Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Amitriptyline 10mg Tablet (Berk Pharmaceuticals Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
AMITRIPTYLINE 300 MG TAB	00000000
Amitriptyline 25mg Tablet (Celltech Pharma Europe Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Accord Healthcare Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100

Amitriptyline 50mg tablets (Sigma Pharmaceuticals Plc) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Sigma Pharmaceuticals Plc) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Tryptizol 25mg Tablet (Merck Sharp & Dohme Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Wockhardt UK Ltd) Amitriptyline hydrochloride 50mg Tablet Oral	04030100
Amitriptyline 25mg tablets (A A H Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Amitriptyline 25mg tablets (Genesis Pharmaceuticals Ltd) Amitriptyline hydrochloride 25mg Tablet Oral	04030100
Perphenazine 2mg with Amitriptyline 10mg tablet Amitriptyline Hydrochloride/Perphenazine 2mg + 10mg Tablets Oral	04020100
Amitriptyline 10mg tablets (Mawdsley-Brooks & Company Ltd) Amitriptyline hydrochloride 10mg Tablet Oral	04030100
Amitriptyline 10mg/5ml oral solution sugar free (Wockhardt UK Ltd) Amitriptyline hydrochloride 2mg/1ml Oral solution Oral	04030100
Triptafen tablets (Advanz Pharma) Amitriptyline hydrochloride/Perphenazine 25mg + 2mg Tablet Oral	04030100
Amitriptyline 50mg tablets (Arrow Generics Ltd)Amitriptyline hydrochloride50mgTabletOral	04030100

DESCRIPTION	BNF1
Atenolol 50mg tablets Atenolol 50mg Tablet Oral	2040000
Atenolol 100mg tablets Atenolol 100mg Tablet Oral	2040000
Propranolol 80mg modified-release capsules Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Half Inderal LA 80mg capsules (AstraZeneca UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Propranolol 160mg modified-release capsules Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Tenormin LS 50mg tablets (AstraZeneca UK Ltd) Atenolol 50mg Tablet Oral	2040000
Tenormin 100mg tablets (AstraZeneca UK Ltd) Atenolol 100mg Tablet Oral	2040000
Propranolol 80mg tablets Propranolol hydrochloride 80mg Tablet Oral	2040000
Inderal LA 160mg capsules (AstraZeneca UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Metoprolol 100mg tablets Metoprolol tartrate 100mg Tablet Oral	2040000

Propranolol 160mg tablets Propranolol hydrochloride 160mg Tablet Oral	2040000
Betaloc-SA 200mg tablets (AstraZeneca UK Ltd) Metoprolol tartrate 200mg Modified-release tablet Oral	2040000
Inderal 80mg tablets (AstraZeneca UK Ltd) Propranolol hydrochloride 80mg Tablet Oral	2040000
Betaloc 100mg tablets (AstraZeneca UK Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Corgard 40mg tablets (Sanofi-Synthelabo Ltd) Nadolol 40mg Tablet Oral	2040000
Rapranol SR 80mg capsules (Ranbaxy (UK) Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Inderal LA 160mg capsules (Waymade Healthcare Plc) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Propranolol LA 80mg Modified-release capsule (Approved Prescription Services Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (Mylan) Atenolol 50mg Tablet Oral	2040000
Bedranol SR 160mg capsules (Sandoz Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
PROPRANOLOL S/R	0
Berkolol 160mg Tablet (Berk Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Tablet Oral	2030202
Atenolol 50mg tablets (Crescent Pharma Ltd) Atenolol 50mg Tablet Oral	2040000
Nadolol 40mg/5ml oral solution Nadolol 8mg/1ml Oral solution Oral	2040000
Bedranol 80mg tablets (Ennogen Pharma Ltd) Propranolol hydrochloride 80mg Tablet Oral	2040000
Metoprolol 100mg tablets (IVAX Pharmaceuticals UK Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Metoprolol tartrate Oral solution Metoprolol Tartrate Oral Solution Oral	2040000
Corgard 80mg tablets (Sanofi) Nadolol 80mg Tablet Oral	2040000
Beta-Prograne 160mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (Sandoz Ltd) Atenolol 50mg Tablet Oral	2040000
Betim 10mg Tablet (ICN Pharmaceuticals France S.A.) Timolol maleate 10mg Tablet Oral	2040000
Atenolol 50mg tablets (Alliance Healthcare (Distribution) Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 80mg modified-release capsules (Mawdsley-Brooks & Company Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (Actavis UK Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 80mg/5ml oral solution Propranolol Hydrochloride 80mg/5ml Oral Solution Oral	2030202
Atenamin 50mg Tablet (OPD Pharm) Atenolol 50mg Tablet Oral	2040000

Propranolol 160mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Vasaten 50mg Tablet (Shire Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Atenolol 100mg tablets (Kent Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	2040000
Atenolol 100mg tablets (A A H Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	2040000
Atenix 50 tablets (Ashbourne Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Lopresor SR 200mg tablets (Recordati Pharmaceuticals Ltd) Metoprolol tartrate 200mg Modified-release tablet Oral	2040000
Half Inderal LA 80mg capsules (Necessity Supplies Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Propranolol SR 160mg Modified-release capsule (C P Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Propanix 160mg Tablet (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Tablet Oral	2030202
Propranolol SR 160mg Modified-release capsule (Hillcross Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Propranolol 80mg tablets (Actavis UK Ltd) Propranolol hydrochloride 80mg Tablet Oral	2040000
Atenolol 50mg tablets (Teva UK Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 160mg tablets (Actavis UK Ltd) Propranolol hydrochloride 160mg Tablet Oral	2040000
Angilol 80mg Tablet (DDSA Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	2030202
Slo-Pro 160mg capsules (Mylan) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (DE Pharmaceuticals) Atenolol 50mg Tablet Oral	2040000
Atenolol 50mg tablets (Boston Healthcare Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 80mg Capsule (IVAX Pharmaceuticals UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenolol 100mg Tablet (Celltech Pharma Europe Ltd) Atenolol 100mg Tablet Oral	2040000
Metoprolol 200mg modified-release tablets Metoprolol tartrate 200mg Modified-release tablet Oral	0
Propranolol LA 160mg Capsule (Approved Prescription Services Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Nadolol 40mg tablets Nadolol 40mg Tablet Oral	2040000
Half Beta-Prograne 80mg modified-release capsules (Actavis UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000

Propranolol 80mg Modified-release capsule (Actavis UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Probeta LA 160mg Capsule (Trinity Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenix 100 tablets (Ashbourne Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	2040000
Apsolol 160mg Tablet (Approved Prescription Services Ltd) Propranolol hydrochloride 160mg Tablet Oral	2030202
Bedranol SR 80mg capsules (Sandoz Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Betadur cr 160mg Modified-release capsule (Monmouth Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Propranolol 160mg modified-release capsules (A A H Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
BEDRANOL SR 80 MG CAP	0
Lopranol la 160mg Capsule (Opus Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 100mg tablets (Almus Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	2040000
Propranolol 80mg tablets (Ranbaxy (UK) Ltd) Propranolol hydrochloride 80mg Tablet Oral	2040000
Bedranol SR 80mg capsules (Almus Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	0
Atenolol 50mg tablets (A A H Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Blocadren 10mg Tablet (Merck Sharp & Dohme Ltd) Timolol maleate 10mg Tablet Oral	2040000
Timolol 10mg tablets Timolol maleate 10mg Tablet Oral	2040000
Berkolol 80mg Tablet (Berk Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	2030202
Propranolol 80mg tablets (Mylan) Propranolol hydrochloride 80mg Tablet Oral	2040000
Propanix 160mg Modified-release capsule (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 100mg tablets (Wockhardt UK Ltd) Atenolol 100mg Tablet Oral	2040000
Nadolol 40mg/5ml oral suspension Nadolol 8mg/1ml Oral suspension Oral	2040000
Atenolol 50mg tablets (Zentiva) Atenolol 50mg Tablet Oral	2040000
Mepranix 100mg Tablet (Ashbourne Pharmaceuticals Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Propranolol 80mg Modified-release capsule (Lagap) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Half Beta-Prograne 80mg modified-release capsules (Actavis UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	0

Propranolol 160mg tablets (Mylan) Propranolol hydrochloride 160mg Tablet Oral	2040000
Atenolol 50mg tablets (Phoenix Healthcare Distribution Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 160mg Modified-release capsule (Actavis UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (Kent Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Atenolol 100mg tablets (Sandoz Ltd) Atenolol 100mg Tablet Oral	2040000
Half-betadur cr 80mg Capsule (Monmouth Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Metoprolol 100mg tablets (Waymade Healthcare Plc) Metoprolol tartrate 100mg Tablet Oral	2040000
Half Beta-Prograne 80mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Metoprolol 100mg tablets (Alliance Healthcare (Distribution) Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Propranolol 80mg tablets (Teva UK Ltd) Propranolol hydrochloride 80mg Tablet Oral	2040000
Antipressan 100mg tablets (Teva UK Ltd) Atenolol 100mg Tablet Oral	2040000
Antipressan 50mg tablets (Teva UK Ltd) Atenolol 50mg Tablet Oral	2040000
ATENOLOL	0
Atenolol 50mg tablets (Tillomed Laboratories Ltd) Atenolol 50mg Tablet Oral	2040000
Atenolol 50mg Tablet (Celltech Pharma Europe Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 160mg Modified-release capsule (Sandoz Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
HALF-INDERAL LA	0
Bedranol SR 160mg capsules (Almus Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Inderal 160mg Tablet (AstraZeneca UK Ltd) Propranolol hydrochloride 160mg Tablet Oral	2030202
Half Beta-Prograne 80mg modified-release capsules (Tillomed Laboratories Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Rapranol SR 160mg capsules (Ranbaxy (UK) Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
METOPROLOL FUMARATE 190 MG TAB	0
Atenolol 50mg tablets (Almus Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Atenolol 50mg tablets (IVAX Pharmaceuticals UK Ltd) Atenolol 50mg Tablet Oral	2040000
Beta-Prograne 160mg modified-release capsules (Tillomed Laboratories Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Nadolol Oral solution Nadolol Oral Solution	2040000
Atenolol 50mg tablets (Accord Healthcare Ltd) Atenolol 50mg Tablet Oral	2040000

Propranolol SR 80mg Modified-release capsule (C P Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Propanix 80mg Tablet (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	2030202
Beta-Prograne 160mg modified-release capsules (Actavis UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (Wockhardt UK Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 80mg modified-release capsules (Teva UK Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
ATENOLOL	0
Propranolol 80mg modified-release capsules (DE Pharmaceuticals) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Metoprolol 100mg tablets (Actavis UK Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Betim 10mg tablets (Meda Pharmaceuticals Ltd) Timolol maleate 10mg Tablet Oral	2040000
Sloprolol 160mg Capsule (C P Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Propranolol 80mg modified-release capsules (Kent Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenamin 100mg Tablet (OPD Pharm) Atenolol 100mg Tablet Oral	2040000
Metoprolol 100mg tablets (Teva UK Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Half Inderal LA 80mg capsules (DE Pharmaceuticals) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenolol 50mg Tablet (Berk Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Corgard 80mg tablets (Lexon (UK) Ltd) Nadolol 80mg Tablet Oral	2040000
Propranolol oral solution Propranolol Hydrochloride	2030202
Half propanix la 80mg Modified-release capsule (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Nadolol 80mg tablets Nadolol 80mg Tablet Oral	2040000
Lopresor 100mg tablets (Recordati Pharmaceuticals Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Atenolol 100mg tablets (Teva UK Ltd) Atenolol 100mg Tablet Oral	2040000
Bedranol SR 80mg capsules (Almus Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenolol 50mg tablets (Sigma Pharmaceuticals Plc) Atenolol 50mg Tablet Oral	2040000
Propranolol 80mg modified-release capsules (A A H Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Atenolol 100mg tablets (Mylan) Atenolol 100mg Tablet Oral	2040000

Metoprolol 100mg tablets (A A H Pharmaceuticals Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Propanix LA 160mg Modified-release capsule (Ashbourne Pharmaceuticals Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Propranolol 160mg Modified-release capsule (Lagap) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Totamol 50mg Tablet (C P Pharmaceuticals Ltd) Atenolol 50mg Tablet Oral	2040000
Bedranol sr 160mg Capsule (Lagap) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 100mg tablets (Phoenix Healthcare Distribution Ltd) Atenolol 100mg Tablet Oral	2040000
Propranolol 80mg tablets (A A H Pharmaceuticals Ltd) Propranolol hydrochloride 80mg Tablet Oral	2040000
Inderal LA 160mg capsules (Sigma Pharmaceuticals Plc) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 100mg tablets (Crescent Pharma Ltd) Atenolol 100mg Tablet Oral	2040000
Atenolol 100mg tablets (IVAX Pharmaceuticals UK Ltd) Atenolol 100mg Tablet Oral	2040000
Atenolol 50mg tablets (Strides Pharma UK Ltd) Atenolol 50mg Tablet Oral	2040000
Totamol 100mg Tablet (C P Pharmaceuticals Ltd) Atenolol 100mg Tablet Oral	2040000
Propranolol 160mg tablets (DE Pharmaceuticals) Propranolol hydrochloride 160mg Tablet Oral	2040000
Metoprolol 100mg tablets (Mylan) Metoprolol tartrate 100mg Tablet Oral	2040000
Propranolol 80mg modified-release capsules (Waymade Healthcare Plc) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Propranolol 160mg Capsule (IVAX Pharmaceuticals UK Ltd) Propranolol hydrochloride 160mg Modified-release capsule Oral	2040000
Atenolol 100mg tablets (Actavis UK Ltd) Atenolol 100mg Tablet Oral	2040000
Atenolol 50mg tablets (Waymade Healthcare Plc) Atenolol 50mg Tablet Oral	2040000
Nadolol 80mg/5ml oral suspension Nadolol 16mg/1ml Oral suspension Oral	2040000
Half propatard la 80mg Modified-release capsule (Galen Ltd) Propranolol hydrochloride 80mg Modified-release capsule Oral	2040000
Lopresor 100mg Tablet (Novartis Pharmaceuticals UK Ltd) Metoprolol tartrate 100mg Tablet Oral	2040000
Atenolol 50mg tablets (Bristol Laboratories Ltd) Atenolol 50mg Tablet Oral	2040000
Propranolol 80mg tablets (Alliance Healthcare (Distribution) Ltd)Propranolol hydrochloride80mgTabletOral	2040000
Propranolol 80mg Tablet (Celltech Pharma Europe Ltd)Propranolol hydrochloride80mgTabletOral	2030202

Inderal LA 160mg capsules (DE Pharmaceuticals)Propranolol hydrochloride160mgModified-release capsuleOral	2040000
Half Inderal LA 80mg capsules (Waymade Healthcare Plc)Propranolol hydrochloride80mgModified-release capsuleOral	2040000
Propranolol 80mg tablets (Relonchem Ltd)Propranolol hydrochloride80mgTabletOral	2040000

DESCRIPTION	BNF1
Aimovig 70mg/1ml solution for injection pre-filled pens (Novartis Pharmaceuticals UK Ltd) Erenumab 70mg/1ml Solution for injection Subcutaneous	04070402
Aimovig 140mg/1ml solution for injection pre-filled pens (Novartis Pharmaceuticals UK Ltd) Erenumab 140mg/1ml Solution for injection Subcutaneous	04070402
Erenumab 70mg/1ml solution for injection pre-filled disposable devicesErenumab70mg/1mlSolution for injectionSubcutaneous	04070402
Ajovy 225mg/1.5ml solution for injection pre-filled syringes (Teva UK Ltd)Fremanezumab150mg/1mlSolution for injectionSubcutaneous	04070402

DESCRIPTION	BNF1
Diclofenac sodium 50mg gastro-resistant tablets Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg Tablet (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets Diclofenac Sodium 50mg EC Tablets Oral	10010100
Voltarol 50mg gastro-resistant tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 25mg Tablet (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 25mg gastro-resistant tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Lofensaid 50mg gastro-resistant tablets (Opus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg Gastro-resistant tablet (Genus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Alliance Healthcare (Distribution) Ltd) Diclofenac potassium 50mg Tablet Oral	10010100

Diclofenac sodium 25mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Phoenix Healthcare Distribution Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Dicloflex 25mg gastro-resistant tablets (Dexcel-Pharma Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (A A H Pharmaceuticals Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Voltarol 50mg dispersible tablets (DE Pharmaceuticals) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac 50mg dispersible tablets sugar free (DE Pharmaceuticals) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Voltarol Rapid 50mg tablets (Lexon (UK) Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Waymade Healthcare Plc) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg capsules Diclofenac Sodium	10010100
Diclofenac sodium 25mg tablets Diclofenac Sodium 25mg Tablets Oral	10010100
Voltarol Pain-eze Extra Strength 25mg tablets (Novartis Consumer Health UK Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
DICLOFENAC SODIUM S/R	0
Diclofenac 10mg/5ml oral suspension Diclofenac sodium 2mg/1ml Oral suspension Oral	10010100
Dicloflex 50mg Gastro-resistant tablet (Ratiopharm UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
First Resort Double Action Pain Relief 12.5mg tablets (Actavis UK Ltd) Diclofenac potassium 12.5mg Tablet Oral	10010100
Valenac ec 50mg Gastro-resistant tablet (Shire Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Sterwin Medicines) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100

Diclofenac potassium 50mg tablets (Focus Pharmaceuticals Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Mylan) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (DE Pharmaceuticals) Diclofenac potassium 50mg Tablet Oral	10010100
Dicloflex 25mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Waymade Healthcare Plc) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Dicloflex 50mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg Tablet (C P Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Gastro-resistant tablet (Genus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Sterwin Medicines) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Medreich Plc) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets Diclofenac potassium 50mg Tablet Oral	10010100
Voltarol Rapid 25mg tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Sandoz Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Waymade Healthcare Plc) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 25mg tablets (Accord Healthcare Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac 50mg/5ml oral solution Diclofenac sodium 10mg/1ml Oral solution Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Crescent Pharma Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100

Diclofenac 50mg Tablet (Regent Laboratories Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg/5ml oral suspension Diclofenac sodium 10mg/1ml Oral suspension Oral	10010100
Diclofenac potassium 50mg tablets (DE Pharmaceuticals) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac 12.5mg/5ml oral solution Diclofenac sodium 2.5mg/1ml Oral solution Oral	10010100
Diclofenac 50mg Gastro-resistant tablet (Pharmacia Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 12.5mg tablets Diclofenac potassium 12.5mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Actavis UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Waymade Healthcare Plc) Diclofenac potassium 50mg Tablet Oral	10010100
Flamrase 50 EC tablets (Teva UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Teva UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Medreich Plc) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 25mg tablets (DE Pharmaceuticals) Diclofenac potassium 25mg Tablet Oral	10010100
Fenactol 50mg gastro-resistant tablets (Dexcel-Pharma Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 10mg dispersible tablets Diclofenac sodium 10mg Dispersible tablet Oral	10010100
Valenac ec 25mg Gastro-resistant tablet (Shire Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Teva UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Lexon (UK) Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Defanac 25mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets Diclofenac Sodium 25mg EC Tablets Oral	10010100
Diclofenac 50mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Rhumalgan 25mg Tablet (Lagap) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100

Dicloflex 50mg gastro-resistant tablets (Dexcel-Pharma Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Mawdsley-Brooks & Company Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Flamrase 25 EC tablets (Teva UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Volraman 25mg gastro-resistant tablets (LPC Medical (UK) Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Sigma Pharmaceuticals Plc) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Sigma Pharmaceuticals Plc) Diclofenac potassium 50mg Tablet Oral	10010100
Fenactol 25mg gastro-resistant tablets (Discovery Pharmaceuticals) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Mawdsley-Brooks & Company Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Defanac 50mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol Pain-eze 12.5mg tablets (Novartis Consumer Health UK Ltd) Diclofenac potassium 12.5mg Tablet Oral	10010100
Diclofenac 50mg Tablet (Approved Prescription Services Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Isclofen 50mg Gastro-resistant tablet (Isis Products Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (DE Pharmaceuticals) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Actavis UK Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclovol 50mg gastro-resistant tablets (Arun Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Dicloflex 25mg gastro-resistant tablets (Teva UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Genesis Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100

Dicloflex 25mg Gastro-resistant tablet (Ratiopharm UK Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 25mg tablets Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 50mg dispersible tablets sugar free Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac 25mg Tablet (Berk Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Lofensaid 25mg gastro-resistant tablets (Opus Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Gastro-resistant tablet (Pharmacia Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Novartis Pharmaceuticals UK Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac potassium 25mg tablets (A A H Pharmaceuticals Ltd) Diclofenac potassium 25mg Tablet Oral	10010100
Diclofenac 50mg dispersible tablets sugar free (Sigma Pharmaceuticals Plc) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Mylan) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Rhumalgan 50mg Tablet (Lagap) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 10mg/5ml oral solution Diclofenac sodium 2mg/1ml Oral solution Oral	10010100
Diclofenac sodium 50mg tablets Diclofenac Sodium 50mg Tablets Oral	10010100
Diclofenac 50mg Tablet (Berk Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac 25mg Tablet (C P Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Acoflam 50mg gastro-resistant tablets (Mercury Pharma Group Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac potassium 50mg tablets (Accord Healthcare Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclofenac 12.5mg/5ml oral suspension Diclofenac sodium 2.5mg/1ml Oral suspension Oral	10010100
Diclovol 25mg gastro-resistant tablets (Arun Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 50mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100

Diclofenac sodium 50mg gastro-resistant tablets (DE Pharmaceuticals) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets (Sandoz Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Voltarol Rapid 50mg tablets (Stephar (U.K.) Ltd) Diclofenac potassium 50mg Tablet Oral	10010100
Diclozip 25mg gastro-resistant tablets (Ashbourne Pharmaceuticals Ltd) Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Volraman 50mg gastro-resistant tablets (LPC Medical (UK) Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Sigma Pharmaceuticals Plc) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclozip 50mg gastro-resistant tablets (Ashbourne Pharmaceuticals Ltd) Diclofenac sodium 50mg Gastro-resistant tablet Oral	10010100
Voltarol 50mg dispersible tablets (Stephar (U.K.) Ltd) Diclofenac sodium 50mg Dispersible tablet Oral	10010100
Diclofenac sodium 25mg gastro-resistant tablets Diclofenac sodium 25mg Gastro-resistant tablet Oral	10010100
Diclofenac 15mg/5ml oral suspensionDiclofenac sodium3mg/1mlOral suspensionOral	10010100
Diclofenac potassium 50mg tablets (Medihealth (Northern) Ltd)Diclofenac potassium50mgTabletOral	10010100
Diclofenac sodium 25mg capsulesDiclofenac Sodium	10010100

DESCRIPTION	BNF1
Nurofen Maximum Strength Migraine Pain 684mg caplets (Reckitt Benckiser Healthcare (UK) Ltd) Ibuprofen lysine 400mg Tablet Oral	4070100
Galprofen 200mg tablets (Galpharm International Ltd) Ibuprofen 200mg Tablet Oral	10010100
Nurofen Migraine Pain 342mg tablets (Reckitt Benckiser Healthcare (UK) Ltd) Ibuprofen lysine 200mg Tablet Oral	4070100
Galprofen 100mg/5ml oral suspension (Galpharm International Ltd) Ibuprofen 20mg/1ml Oral suspension Oral	10010100
Galprofen Long Lasting 300mg capsules (Galpharm International Ltd) Ibuprofen 300mg Modified-release capsule Oral	10010100
Galprofen Long Lasting 200mg capsules (Galpharm International Ltd) Ibuprofen 200mg Modified-release capsule Oral	10010100

DESCRIPTION	BNF1
Mefenamic acid 500mg tablets Mefenamic acid 500mg Tablet Oral	10010100
Ponstan Forte 500mg tablets (Chemidex Pharma Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 500mg tablets (Alliance Healthcare (Distribution) Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Capsule (Teva UK Ltd) Mefenamic acid 250mg Capsule Oral	10010100
PONSTAN	0
Opustan 250mg Capsule (Opus Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg Capsule (Sandoz Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Zentiva) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (Essential Generics Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Actavis UK Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 500mg tablets (A A H Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Capsule (Berk Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Dysman 500 tablets (Ashbourne Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mendys 250mg Capsule (Kent Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
MEFENAMIC ACID DISPERSIBLE	0
PONSTAN FORTE	0
Mefenamic acid 250mg capsules Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Sigma Pharmaceuticals Plc) Mefenamic acid 500mg Tablet Oral	10010100
Ponstan 50mg/5ml paediatric Liquid (Chemidex Pharma Ltd) Mefenamic acid 10mg/1ml Oral suspension Oral	10010100
Meflam 500mg Tablet (Trinity Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 500mg Tablet (Berk Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Dispersible tablet Mefenamic Acid 250mg Dispersible Tablet Oral	10010100
Ponstan 250mg Dispersible tablet (Chemidex Pharma Ltd) Mefenamic Acid 250mg Dispersible Tablet Oral	10010100
Mefenamic acid 250mg/5ml oral suspension Mefenamic acid 50mg/1ml Oral suspension Oral	10010100
Opustan 500mg Tablet (Opus Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Meflam 250mg Capsule (Trinity Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg capsules (Advanz Pharma) Mefenamic acid 250mg Capsule Oral	10010100

Mefenamic acid 250mg Capsule (Actavis UK Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Dysman 250 capsules (Ashbourne Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg capsules (Mylan) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg/5ml oral suspension Mefenamic acid 100mg/1ml Oral suspension Oral	10010100
Mefenamic acid 500mg tablets (IVAX Pharmaceuticals UK Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 50mg/5ml oral suspension Mefenamic acid 10mg/1ml Oral suspension Oral	10010100
Mefenamic acid 500mg tablets (Almus Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Dysman 250mg Capsule (Ashbourne Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Contraflam 250mg Capsule (Berk Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 250mg capsules (Zentiva) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Teva UK Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (A A H Pharmaceuticals Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Waymade Healthcare Plc) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg Capsule (IVAX Pharmaceuticals UK Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Ponstan 250mg capsules (Chemidex Pharma Ltd) Mefenamic acid 250mg Capsule Oral	10010100
Contraflam 500mg Tablet (Berk Pharmaceuticals Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (Waymade Healthcare Plc) Mefenamic acid 250mg Capsule Oral	10010100
Mefenamic acid 500mg tablets (Essential Generics Ltd) Mefenamic acid 500mg Tablet Oral	10010100
Mefenamic acid 250mg capsules (Alliance Healthcare (Distribution) Ltd) Mefenamic acid 250mg Capsule Oral	10010100

DESCRIPTION	BNF1
Migraleve tablets (McNeil Products Ltd) Not applicable Route of administration not applicable	04070200
Migraleve Pink tablets (McNeil Products Ltd) Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
Paramax tablets (Sanofi) Metoclopramide hydrochloride/Paracetamol 5mg + 500mg Tablet Oral	04070401
Paramax sachets (Sanofi) Paracetamol/Metoclopramide hydrochloride 500mg + 5mg Effervescent powder Oral	04070401

Paracetamol 500mg / Metoclopramide 5mg effervescent powder sachets sugar free	
Paracetamol/Metoclopramide hydrochloride 500mg + 5mg Effervescent powder Oral	04070401
Migravess forte 5mg+450mg Effervescent tablet (Bayer Plc) Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg+450mg Effervescent Tablet Oral	04065500
Paracetamol 500mg with codeine phosphate 8mg & buclizine 6.25mg Buclizine Hydrochloride/Codeine Phosphate/Paracetamol 500mg+8mg+6.25mg Tablets Oral	03040102
Metoclopramide with aspirin 5mg + 450mg Effervescent tablet Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg + 450mg Effervescent Tablet Oral	04065500
Codeine phosphate 8mg with paracetamol 500mg with buclizine 6.25mg tablets Buclizine Hydrochloride/Codeine Phosphate/Paracetamol 8mg+500mg+6.25mg Tablets Oral	03040102
Midrid (rpr) Capsule (Rhone-Poulenc Rorer Ltd) Paracetamol/Isometheptene mucate 325mg + 65mg Capsule Oral	04070100
Generic Migraleve Pink tablets Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
MigraMax oral powder sachets (Zentiva) Metoclopramide hydrochloride/Aspirin DL-Lysine 10mg + 900mg Powder Oral	04070100
Metoclopramide with paracetamol 5mg + 500mg Tablet Metoclopramide Hydrochloride/Paracetamol 5mg + 500mg Tablet Oral	04065500
Paracetamol 500mg / Domperidone 10mg tablets Paracetamol/Domperidone maleate 500mg + 10mg Tablet Oral	00000000
Domperamol tablets (Servier Laboratories Ltd) Paracetamol/Domperidone maleate 500mg + 10mg Tablet Oral	00000000
Ergotamine tartrate with cyclizine and caffeine tablets Caffeine/Cyclizine Hydrochloride/Ergotamine Tartrate Tablets Oral	03040103
Metoclopramide with aspirin 5mg + 325mg Effervescent tablet Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg + 325mg Effervescent Tablet Oral	04065500
Metoclopramide with paracetamol 5mg + 500mg Sachets Metoclopramide Hydrochloride/Paracetamol 5mg + 500mg Sachets Oral	04065500
Paracetamol 325mg / Isometheptene 65mg capsules Paracetamol/Isometheptene mucate 325mg + 65mg Capsule Oral	04070100
Migraleve Yellow tablets (McNeil Products Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Aspirin 900mg / Metoclopramide 10mg oral powder sachets sugar free Metoclopramide hydrochloride/Aspirin DL-Lysine 10mg + 900mg Powder Oral	04070100
Migravess 5mg+325mg Effervescent tablet (Bayer Plc) Citric Acid/Metoclopramide Hydrochloride/Aspirin/Sodium Bicarbonate 5mg+325mg Effervescent Tablet Oral	04065500

Midrid 325mg/65mg capsules (DHP Healthcare Ltd) Paracetamol/Isometheptene mucate 325mg + 65mg Capsule Oral	04070100
Generic Migraleve tablets Not applicable Route of administration not applicable	04070200
Migraleve - 1 Tablet (Pfizer Consumer Healthcare Ltd) Buclizine Hydrochloride/Codeine Phosphate/Paracetamol Tablet Oral	03040102
Isometheptene mucate with paracetamol 65mg+325mg Capsule Paracetamol/Isometheptene Mucate 65mg+325mg Capsule Oral	04070100
Migril tablets (Wockhardt UK Ltd) Caffeine hydrate/Cyclizine hydrochloride/Ergotamine tartrate 100mg + 50mg + 2mg Tablet Oral	04070401
Migraleve Ultra 50mg tablets (McNeil Products Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Generic Migril tablets Caffeine hydrate/Cyclizine hydrochloride/Ergotamine tartrate 100mg + 50mg + 2mg Tablet Oral	04070401
Paracetamol 500mg / Metoclopramide 5mg tablets Metoclopramide hydrochloride/Paracetamol 5mg + 500mg Tablet Oral	04070401
Migraleve - 2 8mg+500mg Tablet (Pfizer Consumer Healthcare Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Metoclopramide with lysine acetylsalicylate 10mg + 900mg Oral solution Metoclopramide Hydrochloride/Aspirin Lysine 10mg + 900mg Oral Solution Oral	04065500
Paracetamol with codeine & buclizine tablet Buclizine Hydrochloride/Codeine Phosphate/Paracetamol Tablets Oral	03040102
Solpadeine Migraine Ibuprofen & Codeine tablets (Omega Pharma Ltd) Ibuprofen/Codeine phosphate 200mg + 12.8mg Tablet Oral	04070200
Femigraine Effervescent tablet (Nicholas Laboratories Ltd)Cyclizine Hydrochloride/AspirinEffervescent Tablet	03040103

DESCRIPTION	BNF1
Naproxen 500mg tablets Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg tablets Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Tablet (M & A Pharmachem Ltd) Naproxen 500mg Tablet Oral	10010100
Valrox 250mg Tablet (Shire Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	10010100

Naproxen 250mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (IVAX Pharmaceuticals UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg effervescent tablets sugar free Naproxen 250mg Effervescent tablet Oral	10010100
Timpron 250mg Gastro-resistant tablet (Berk Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	10010100
Rheuflex 500mg Tablet (Goldshield Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (Teva UK Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Stirlescent 250mg effervescent tablets (Stirling Anglian Pharmaceuticals Ltd) Naproxen 250mg Effervescent tablet Oral	10010100
Naprosyn 500mg tablets (Atnahs Pharma UK Ltd) Naproxen 500mg Tablet Oral	04070100
Nycopren 250mg gastro-resistant tablets (Ardern Healthcare Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (DE Pharmaceuticals) Naproxen 250mg Tablet Oral	04070100
Timpron 500mg Gastro-resistant tablet (Berk Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	10010100
Naprosyn EC 250mg tablets (Atnahs Pharma UK Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg tablets (Noumed Life Sciences Ltd) Naproxen 500mg Tablet Oral	04070100
Feminax Ultra 250mg gastro-resistant tablets (Bayer Plc) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Gastro-resistant tablet (Sterwin Medicines) Naproxen 500mg Gastro-resistant tablet Oral	10010100
Naproxen 500mg tablets (A A H Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg tablets (Waymade Healthcare Plc) Naproxen 250mg Tablet Oral	04070100
Timpron 500mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 500mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Teva UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (Teva UK Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg tablets (Sigma Pharmaceuticals Plc) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100

Naproxen 250mg tablets (Mylan) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg/5ml oral suspension Naproxen 50mg/1ml Oral suspension Oral	04070100
Naproxen 500mg tablets (Mylan) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg Tablet (Almus Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naprosyn EC 500mg tablets (Atnahs Pharma UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (DE Pharmaceuticals) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Timpron 250mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg tablets (Genesis Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Arthrosin EC 500 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Mylan) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Arthrosin EC 250 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naprosyn 250mg tablets (Atnahs Pharma UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Genesis Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Genesis Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
NAPROXEN SODIUM	00000000
NAPROXEN 250 MG CAP	00000000
Naproxen Oral solution Naproxen Oral Solution Oral	10010100
Naproxen 500mg tablets (Kent Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg tablets (Sigma Pharmaceuticals Plc) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 500mg Tablet Oral	04070100
Prosaid 250mg Tablet (BHR Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (Accord Healthcare Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Kent Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
NAPROXEN	00000000
NAPROXEN	00000000
Naproxen 500mg gastro-resistant tablets (Mylan) Naproxen 500mg Gastro-resistant tablet Oral	04070100

Naproxen 250mg tablets (Almus Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naprosyn S/R 500mg tablets (Roche Products Ltd) Naproxen sodium 500mg Modified-release tablet Oral	10010100
Arthroxen 250mg Tablet (C P Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 250mg tablets (Accord Healthcare Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Actavis UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Sovereign Medical Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Rheuflex 250mg Tablet (Goldshield Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 500mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Crescent Pharma Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (Wockhardt UK Ltd) Naproxen 500mg Tablet Oral	04070100
Boots Period Pain Relief 250mg gastro-resistant tablets (The Boots Company Plc) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Milpharm Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg tablets (Wockhardt UK Ltd) Naproxen 250mg Tablet Oral	04070100
Prosaid 500mg Tablet (BHR Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 500mg tablets (Pfizer Ltd) Naproxen 500mg Tablet Oral	04070100
Pranoxen continus 500mg Tablet (Napp Pharmaceuticals Ltd) Naproxen sodium 500mg Modified-release tablet Oral	10010100
Arthrosin 250 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (Accord Healthcare Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Teva UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 250mg Gastro-resistant tablet (Almus Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (A A H Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Gastro-resistant tablet (Galen Ltd) Naproxen 500mg Gastro-resistant tablet Oral	10010100
Naproxen 250mg tablets (Phoenix Healthcare Distribution Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg tablets (A A H Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100

Naproxen 250mg Gastro-resistant tablet (Galen Ltd) Naproxen 250mg Gastro-resistant tablet Oral	10010100
Naproxen 250mg gastro-resistant tablets (Sigma Pharmaceuticals Plc) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg tablets (Milpharm Ltd) Naproxen 500mg Tablet Oral	04070100
Nycopren 500mg gastro-resistant tablets (Ardern Healthcare Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg Tablet (Berk Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	10010100
Naproxen 500mg gastro-resistant tablets (Ranbaxy (UK) Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 250mg tablets (Kent Pharmaceuticals Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Sigma Pharmaceuticals Plc) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Waymade Healthcare Plc) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd) Naproxen 500mg Gastro-resistant tablet Oral	04070100
Valrox 500mg Tablet (Shire Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 250mg tablets (Actavis UK Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg tablets (DE Pharmaceuticals) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg Granules Naproxen 500mg Granules Oral	10010100
Arthroxen 500mg Tablet (C P Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	10010100
Naproxen 500mg tablets (Actavis UK Ltd) Naproxen 500mg Tablet Oral	04070100
Naprosyn 500mg Granules (Roche Products Ltd) Naproxen 500mg Granules Oral	10010100
Naproxen 250mg tablets (Mawdsley-Brooks & Company Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (DE Pharmaceuticals) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Arthrosin 500 tablets (Ashbourne Pharmaceuticals Ltd) Naproxen 500mg Tablet Oral	04070100
Naproxen 250mg gastro-resistant tablets (Almus Pharmaceuticals Ltd) Naproxen 250mg Gastro-resistant tablet Oral	04070100
Naproxen 500mg modified-release tablets Naproxen sodium 500mg Modified-release tablet Oral	00000000

Naproxen 250mg tablets (Alliance Healthcare (Distribution) Ltd) Naproxen 250mg Tablet Oral	04070100
Naproxen 500mg gastro-resistant tablets (Medreich Plc)Naproxen500mgGastro-resistant tabletOral	04070100
Naproxen 500mg tablets (Almus Pharmaceuticals Ltd)Naproxen500mgTabletOral	04070100
Naproxen 500mg tablets (Bristol Laboratories Ltd)Naproxen500mgTabletOral	04070100

DESCRIPTION	BNF1
Tolfenamic acid 200mg Capsule Tolfenamic Acid 200mg Capsule Oral	04070401
Clotam Rapid 200mg tablets (Galen Ltd) Tolfenamic acid 200mg Tablet Oral	04070401
Tolfenamic acid 200mg tablets (A A H Pharmaceuticals Ltd) Tolfenamic acid 200mg Tablet Oral	04070401
Tolfenamic acid 200mg tablets Tolfenamic acid 200mg Tablet Oral	04070401
Clotam 200mg Capsule (Thames Laboratories Ltd) Tolfenamic Acid 200mg Capsule Oral	04070401

DESCRIPTION	BNF1
Sumatriptan 50mg tablets Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 100mg tablets Sumatriptan succinate 100mg Tablet Oral	04070401
Migraleve tablets (McNeil Products Ltd) Not applicable Route of administration not applicable	04070200
Migraleve Pink tablets (McNeil Products Ltd) Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
Rizatriptan 10mg oral lyophilisates sugar free Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Imigran 50mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 5mg/0.1ml nasal spray unit dose Zolmitriptan 50mg/1ml Spray Nasal	04070401
Rizatriptan 10mg orodispersible tablets sugar free Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Migard 2.5mg tablets (A. Menarini Farmaceutica Internazionale SRL) Frovatriptan succinate monohydrate 2.5mg Tablet Oral	04070401
Naramig 2.5mg tablets (DE Pharmaceuticals) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Imigran 10mg nasal spray (DE Pharmaceuticals) Sumatriptan 100mg/1ml Spray Nasal	04070401
Sumatriptan 50mg tablets (Mylan) Sumatriptan succinate 50mg Tablet Oral	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Actavis UK Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Imigran Radis 50mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401

Sumatriptan 50mg tablets (Alliance Healthcare (Distribution) Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free Zolmitriptan 5mg Orodispersible tablet Oral	04070401
HealthAid 5-HTP HydroxyTryptoPhan 50mg tablets (HealthAid Ltd) Oxitriptan 50mg Modified-release tablet Oral	09040251
Zomig Rapimelt 2.5mg orodispersible tablets (Grunenthal Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (Accord Healthcare Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
MAXALT	00000000
MAXALT	00000000
Zolmitriptan 2.5mg tablets (Actavis UK Ltd) Zolmitriptan 2.5mg Tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (Merck Sharp & Dohme Ltd) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Generic Migraleve Pink tablets Buclizine hydrochloride/Paracetamol/Codeine phosphate 6.25mg + 500mg + 8mg Tablet Oral	04070200
Sumatriptan 50mg tablets (Pfizer Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Naratriptan 2.5mg tablets (A A H Pharmaceuticals Ltd) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Zolmitriptan 2.5mg tablets Zolmitriptan 2.5mg Tablet Oral	04070401
RIZATRIPTAN	00000000
RIZATRIPTAN	00000000
Imigran 100mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zolmitriptan 2.5mg orodispersible tablets sugar free (Teva UK Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (Teva UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Almotriptan 12.5mg tablets Almotriptan hydrogen malate 12.5mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Dexcel-Pharma Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 100mg tablets (A A H Pharmaceuticals Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Actavis UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Almus Pharmaceuticals Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 100mg tablets (Almus Pharmaceuticals Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zomig 5mg/0.1ml nasal spray 0.1ml unit dose (Waymade Healthcare Plc) Zolmitriptan 50mg/1ml Spray Nasal	04070401

Naramig 2.5mg tablets (GlaxoSmithKline UK Ltd) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Dr Reddy's Laboratories (UK) Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Rizatriptan 5mg tablets (A A H Pharmaceuticals Ltd) Rizatriptan benzoate 5mg Tablet Oral	04070401
Sumatriptan 100mg tablets (Arrow Generics Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free (Zentiva) Zolmitriptan 5mg Orodispersible tablet Oral	04070401
RIZATRIPTAN WAFER	00000000
Maxalt Melt 10mg oral lyophilisates (Mawdsley-Brooks & Company Ltd) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Eletriptan 20mg tablets Eletriptan hydrobromide 20mg Tablet Oral	04070401
Zolmitriptan 2.5mg tablets (Teva UK Ltd) Zolmitriptan 2.5mg Tablet Oral	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Alliance Healthcare (Distribution) Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (Sandoz Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Imigran 10mg nasal spray (Lexon (UK) Ltd) Sumatriptan 100mg/1ml Spray Nasal	04070401
Maxalt 10mg tablets (Merck Sharp & Dohme Ltd) Rizatriptan benzoate 10mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Milpharm Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 2.5mg orodispersible tablets sugar free (Alliance Healthcare (Distribution) Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Rizatriptan 10mg tablets (A A H Pharmaceuticals Ltd) Rizatriptan benzoate 10mg Tablet Oral	04070401
Imigran 50mg tablets (Lexon (UK) Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Arrow Generics Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Frovatriptan 2.5mg tablets Frovatriptan succinate monohydrate 2.5mg Tablet Oral	04070401
Relpax 20mg tablets (Upjohn UK Ltd) Eletriptan hydrobromide 20mg Tablet Oral	04070401
Zolmitriptan 5mg tablets Zolmitriptan 5mg Tablet Oral	04070401
Migraitan 50mg tablets (Bristol Laboratories Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Sumatriptan 50mg tablets (Bristol Laboratories Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Migraleve Yellow tablets (McNeil Products Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Lamberts 5-HTP 100mg tablets (Lamberts Healthcare Ltd) Oxitriptan 100mg Tablet Oral	09040251
Sumatriptan 100mg tablets (Milpharm Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Imigran Radis 50mg tablets (Waymade Healthcare Plc) Sumatriptan succinate 50mg Tablet Oral	04070401
Imigran 10mg nasal spray (GlaxoSmithKline UK Ltd) Sumatriptan 100mg/1ml Spray Nasal	04070401

Sumatriptan 100mg tablets (Dr Reddy's Laboratories (UK) Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zolmitriptan 2.5mg orodispersible tablets sugar free Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Zomig 5mg/0.1ml nasal spray 0.1ml unit dose (Grunenthal Ltd) Zolmitriptan 50mg/1ml Spray Nasal	04070401
Maxalt 10mg tablets (Waymade Healthcare Plc) Rizatriptan benzoate 10mg Tablet Oral	04070401
Zomig 2.5mg tablets (Grunenthal Ltd) Zolmitriptan 2.5mg Tablet Oral	04070401
Rizatriptan 5mg tablets Rizatriptan benzoate 5mg Tablet Oral	04070401
Imigran 50mg tablets (DE Pharmaceuticals) Sumatriptan succinate 50mg Tablet Oral	04070401
Naratriptan 2.5mg tablets Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Generic Migraleve tablets Not applicable Route of administration not applicable	04070200
Rizatriptan 10mg orodispersible tablets sugar free (A A H Pharmaceuticals Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Sumatriptan 50mg tablets (A A H Pharmaceuticals Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Migraleve - 1 Tablet (Pfizer Consumer Healthcare Ltd) Buclizine Hydrochloride/Codeine Phosphate/Paracetamol Tablet Oral	03040102
Imigran Recovery 50mg tablets (Forest Laboratories UK Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free (Teva UK Ltd) Zolmitriptan 5mg Orodispersible tablet Oral	04070401
Maxalt 10mg tablets (DE Pharmaceuticals) Rizatriptan benzoate 10mg Tablet Oral	04070401
Migraleve Ultra 50mg tablets (McNeil Products Ltd) Sumatriptan succinate 50mg Tablet Oral	04070401
Imigran Radis 100mg tablets (GlaxoSmithKline UK Ltd) Sumatriptan succinate 100mg Tablet Oral	04070401
Zomig Rapimelt 2.5mg orodispersible tablets (Mawdsley-Brooks & Company Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Rizatriptan 5mg orodispersible tablets sugar free Rizatriptan benzoate 5mg Orodispersible tablet Oral	04070401
Sumatriptan 100mg tablets (Waymade Healthcare Plc) Sumatriptan succinate 100mg Tablet Oral	04070401
Naratriptan 2.5mg tablets (Teva UK Ltd) Naratriptan hydrochloride 2.5mg Tablet Oral	04070401
Sumatriptan 20mg/0.1ml nasal spray unit dose Sumatriptan 200mg/1ml Spray Nasal	04070401
Zomig Rapimelt 5mg orodispersible tablets (Grunenthal Ltd) Zolmitriptan 5mg Orodispersible tablet Oral	04070401

Zolmitriptan 2.5mg orodispersible tablets sugar free (Actavis UK Ltd) Zolmitriptan 2.5mg Orodispersible tablet Oral	04070401
Eletriptan 40mg tablets Eletriptan hydrobromide 40mg Tablet Oral	04070401
Sumatriptan 10mg/0.1ml nasal spray unit dose Sumatriptan 100mg/1ml Spray Nasal	04070401
Relpax 40mg tablets (Upjohn UK Ltd) Eletriptan hydrobromide 40mg Tablet Oral	04070401
Migraleve - 2 8mg+500mg Tablet (Pfizer Consumer Healthcare Ltd) Paracetamol/Codeine phosphate 500mg + 8mg Tablet Oral	04070100
Maxalt 5mg tablets (Merck Sharp & Dohme Ltd) Rizatriptan benzoate 5mg Tablet Oral	04070401
Zolmitriptan 5mg tablets (Waymade Healthcare Plc) Zolmitriptan 5mg Tablet Oral	04070401
Imigran 20mg nasal spray (GlaxoSmithKline UK Ltd) Sumatriptan 200mg/1ml Spray Nasal	04070401
MAXALT MELT	00000000
Rizatriptan 10mg orodispersible tablets sugar free (Mylan) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (Lexon (UK) Ltd) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Rizatriptan 10mg orodispersible tablets sugar free (Aspire Pharma Ltd) Rizatriptan benzoate 10mg Orodispersible tablet Oral	04070401
Maxalt Melt 10mg oral lyophilisates (DE Pharmaceuticals) Rizatriptan benzoate 10mg Oral lyophilisate Oral	04070401
Almogran 12.5mg tablets (Almirall Ltd) Almotriptan hydrogen malate 12.5mg Tablet Oral	04070401
Imigran 20mg nasal spray (Lexon (UK) Ltd) Sumatriptan 200mg/1ml Spray Nasal	04070401
Rizatriptan 10mg tablets Rizatriptan benzoate 10mg Tablet Oral	04070401
Sumatriptan 100mg tablets (Mylan)Sumatriptan succinate100mgTabletOral	04070401
Sumatriptan 100mg tablets (Dexcel-Pharma Ltd)Sumatriptan succinate100mgTabletOral	04070401
Sumatriptan 50mg tablets (DE Pharmaceuticals)Sumatriptan succinate50mgTabletOral	04070401
Zolmitriptan 5mg orodispersible tablets sugar free (A A H Pharmaceuticals Ltd)Zolmitriptan5mgOrodispersible tabletOral	04070401
Maxalt 5mg tablets (Mawdsley-Brooks & Company Ltd)Rizatriptan benzoate5mgTabletOral	04070401
Sumatriptan 100mg tablets (Pfizer Ltd)Sumatriptan succinate100mgTabletOral	04070401
Imigran 20mg nasal spray (Dowelhurst Ltd)Sumatriptan200mg/1mlSprayNasal	04070401

Codelists for covariate conditions can be found at: https://github.com/mumpredict

Codelists for miscarriage outcome can be found in the supporting information for Minassian C, Williams R, Meeraus WH, Smeeth L, Campbell OMR, Thomas SL. Methods to generate and validate a Pregnancy Register in the UK Clinical Practice Research Datalink primary care

database. Pharmacoepidemiology and Drug Safety [Internet] 2019;28(7):923–33. Available from: https://dx.doi.org/10.1002/pds.4811

Supplementary table 5.2 results of logistic regression for association between medications and early miscarriage

	Migraine patients whose pregnancies ended in early miscarriage N= 18,943	**Migraine patients whose pregnancies did not end in early miscarriage N= 36,603**
Exposure to triptans		
Pregnancies exposed to triptan N (%)	662 (3.49)	1,014 (2.77)
Unadjusted OR (95% CI)	1.27 (1.15-1.41)	
Adjusted* OR (95% CI)	1.23 (1.10-1.38)	
Exposure to Amitriptyline		
Pregnancies exposed to amitriptyline N (%)	342 (1.81)	486 (1.33)
Unadjusted OR (95% CI)	1.37 (1.19-1.57)	
Adjusted* OR (95% CI)	1.26 (1.08-1.47)	
Exposure to Beta Blockers		
Pregnancies exposed to beta blockers N (%)	156 (0.82)	272 (0.74)
Unadjusted OR (95% CI)	1.11 (0.91-1.36)	
Adjusted* OR (95% CI)	0.99 (0.79-1.24)	
Exposure to NSAIDs		
Pregnancies exposed to NSAIDs N (%)	674 (3.56)	724 (1.98)
Unadjusted OR (95% CI)	1.83 (1.64-2.03)	
Adjusted* OR (95% CI)	1.73 (1.55-1.93)	

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of pregnancy, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism,

hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

Supplementary table 5.3 results of logistic regression of association between medication and miscarriage (risk set sample)

	Migraine patients whose pregnancies ended in miscarriage N= 20,778	**Migraine patients whose pregnancies did not end in miscarriage N= 40,423**
Exposure to triptans		
Pregnancies exposed to triptan N (%)	722 (3.47)	1,165 (2.88)
Unadjusted OR (95% CI)	1.21 (1.10-1.33)	
Adjusted* OR (95% CI)	1.20 (1.08-1.32)	
Exposure to Amitriptyline		
Pregnancies exposed to amitriptyline N (%)	380 (1.83)	567 (1.40)
Unadjusted OR (95% CI)	1.31 (1.15-1.49)	
Adjusted* OR (95% CI)	1.21 (1.05-1.39)	
Exposure to Beta Blockers		
Pregnancies exposed to beta blockers N (%)	173 (0.83)	292 (0.72)
Unadjusted OR (95% CI)	1.15 (0.96-1.39)	

Adjusted* OR (95% CI)	1.09 (0.88-1.35)	
Exposure to NSAIDs		
Pregnancies exposed to NSAIDs N (%)	733 (3.53)	810 (2.00)
Unadjusted OR (95% CI)	1.79 (1.62-1.97)	
Adjusted* OR (95% CI)	1.71 (1.55-1.89)	

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of pregnancy, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

Supplementary table 5.4 results of logistic regression of association between medication and miscarriage (sensitivity analysis excluding unknown outcomes)

	Migraine patients whose pregnancies ended in miscarriage N= 20,777	**Migraine patients whose pregnancies did not end in miscarriage N= 40,301**
Exposure to triptans		
Pregnancies exposed to triptan N (%)	722 (3.47)	1,131 (2.81)
Unadjusted OR (95% CI)	1.25 (1.13-1.37)	
Adjusted* OR (95% CI)	1.24 (1.12-1.37)	
Exposure to Amitriptyline		

Pregnancies exposed to amitriptyline N (%)	380 (1.83)	556 (1.38)
Unadjusted OR (95% CI)	1.33 (1.17-1.52)	
Adjusted* OR (95% CI)	1.22 (1.05-1.41)	
Exposure to Beta Blockers		
Pregnancies exposed to beta blockers N (%)	173 (0.83)	286 (0.71)
Unadjusted OR (95% CI)	1.17 (0.97-1.42)	
Adjusted* OR (95% CI)	1.10 (0.90-1.36)	
Exposure to NSAIDs		
Pregnancies exposed to NSAIDs N (%)	733 (3.53)	840 (2.08)
Unadjusted OR (95% CI)	1.72 (1.56-1.90)	
Adjusted* OR (95% CI)	1.62 (1.46-1.79)	

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of pregnancy, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

Supplementary table 5.5 results of logistic regression for association between medication combinations and early miscarriage

	Exposed patients whose pregnancies ended in miscarriage, n (%)	Exposed patients whose pregnancies did not end in miscarriage, n (%)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Not exposed to triptans, amitriptyline or NSAIDs	17,409 (91.9)	34,522 (94.31)	ref	ref
Exposure to Triptan only	557 (2.94)	909 (2.48)	1.22 (1.09-1.36)	1.19 (1.06-1.34)
Exposure to Amitriptyline only	258 (1.38)	384 (1.05)	1.33 (1.14-1.56)	1.25 (1.05-1.48)
Exposure to NSAIDs only	578 (3.05)	649 (1.77)	1.77 (1.58-1.98)	1.68 (1.50-1.89)
Exposure to Triptan and amitriptyline	45 (0.24)	64 (0.17)	1.39 (0.92-2.12)	1.32 (0.86-2.03)
Exposure to Triptan and NSAIDs	57 (0.30)	37 (0.10)	3.05 (2.02-4.63)	2.88 (1.88-4.40)
Exposure to Amitriptyline and NSAIDs	36 (0.19)	34 (0.09)	2.10 (1.32-3.33)	1.92 (1.20-3.08)
Exposure to Triptans, Amitriptyline and NSAIDs	3 (0.02)	4 (0.01)	1.49 (0.33-6.65)	1.37 (0.31-6.17)

***** Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of pregnancy, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism,

hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

Supplementary table 5.6 results of logistic regression of association between combinations of medications and miscarriage (risk set sample)

	Exposed patients whose pregnancies ended in miscarriage, n (%)	**Exposed patients whose pregnancies did not end in miscarriage, n (%)**	**Unadjusted OR (95% CI)**	**Adjusted* OR (95% CI)**
Not exposed to triptans, amitriptyline or NSAIDs	19,101 (91.93)	38,065 (94.17)	ref	ref
Exposure to Triptan only	608 (2.93)	1.021 (2.53)	1.19 (1.07-1.31)	1.18 (1.06-1.32)
Exposure to Amitriptyline only	286 (1.38)	449 (1.11)	1.27 (1.10-1.47)	1.18 (1.01-1.38)
Exposure to NSAIDs only	630 (3.03)	711 (1.76)	1.77 (1.59-1.96)	1.70 (1.53-1.89)
Exposure to Triptan and amitriptyline	50 (0.24)	78 (0.19)	1.28 (0.87-1.87)	1.22 (0.83-1.80)

Exposure to Triptan and NSAIDs	59 (0.28)	59 (0.15)	1.99 (1.40-2.84)	1.92 (1.33-2.75)
Exposure to Amitriptyline and NSAIDs	39 (0.19)	33 (0.08)	2.36 (1.52-3.64)	2.15 (1.38-3.36)
Exposure to Triptans, Amitriptyline and NSAIDs	5 (0.02)	7 (0.02)	1.42 (0.45-4.49)	1.39 (0.44-4.38)

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of birth, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

Supplementary table 5.7 results of logistic regression of association between combinations of medications and miscarriage (sensitivity analysis excluding unknown outcomes)

	Exposed patients whose pregnancies ended in miscarriage, n (%)	**Exposed patients whose pregnancies did not end in miscarriage, n (%)**	**Unadjusted OR (95% CI)**	**Adjusted* OR (95% CI)**

Not exposed to triptans, amitriptyline or NSAIDs	19,100 (91.93)	37,991 (94.27)	ref	ref
Exposure to Triptan only	608 (2.93)	971 (2.41)	1.25 (1.12-1.38)	1.25 (1.12-1.39)
Exposure to Amitriptyline only	286 (1.38)	411 (1.02)	1.38 (1.19-1.61)	1.28 (1.09-1.39)
Exposure to NSAIDs only	630 (3.03)	721 (1.79)	1.74 (1.56-1.93)	1.65 (1.48-1.84)
Exposure to Triptan and amitriptyline	50 (0.24)	88 (0.22)	1.13 (0.77-1.66)	1.08 (0.73-1.60)
Exposure to Triptan and NSAIDs	59 (0.28)	62 (0.15)	1.89 (1.34-2.67)	1.84 (1.30-2.61)
Exposure to Amitriptyline and NSAIDs	39 (0.19)	47 (0.12)	1.65 (1.07-2.54)	1.49 (0.96-2.30)
Exposure to Triptans, Amitriptyline and NSAIDs	5 (0.02)	10 (0.02)	0.99 (0.34-2.91)	0.92 (0.31-2.75)

* Adjusted for age, ethnicity, deprivation, BMI, smoking status, year of birth, asthma, depression, type 1 diabetes type 2 diabetes, hypertension, hypothyroidism, hyperthyroidism, inflammatory bowel disease, endometriosis, SLE, CKD, PCOS and drugs (triptan, amitriptyline, B blocker and NSAIDs).

References

1. The National Institute for Health and Care Excellence. Headaches in over 12s: diagnosis and management. Clinical Guideline 150. London: NICE 2021.
2. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629-808.
3. Rasmussen BK, Olesen J. Migraine with aura and migraine without aura: an epidemiological study. Cephalalgia. 1992;12(4):221-8; discussion 186.
4. Russell MB, Ulrich V, Gervil M, Olesen J. Migraine Without Aura and Migraine With Aura Are Distinct Disorders. A Population-Based Twin Survey. Headache: The Journal of Head and Face Pain. 2002;42(5):332-6.
5. NICE Clinical Knowledge Summaries (2022). Migraine. Retrieved from: https://cks.nice.org.uk/topics/migraine/.
6. NICE Clinical Knowledge Summaries. Migraine: How common is it?2021.
7. Ashina M, Katsarava Z, Do TP, Buse DC, Pozo-Rosich P, Özge A, et al. Migraine: epidemiology and systems of care. The Lancet. 2021;397(10283):1485-95.
8. Buse DC, Fanning KM, Reed ML, Murray S, Dumas PK, Adams AM, et al. Life With Migraine: Effects on Relationships, Career, and Finances From the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study. Headache: The Journal of Head and Face Pain. 2019;59(8):1286-99.
9. Linde M, Gustavsson A, Stovner LJ, Steiner TJ, Barré J, Katsarava Z, et al. The cost of headache disorders in Europe: the Eurolight project. European Journal of Neurology. 2012;19(5):703-11.
10. NHS England. Improved NHS migraine care to save thousands of hospital stays 2020 [Available from: https://www.england.nhs.uk/2020/01/improved-nhs-migraine-care/.
11. The Work Foundation. Society's Headache: The Socioeconomic Impact of Migraine. Lancaster: Lancaster University; 2018.
12. Pescador Ruschel MA, De Jesus O. Migraine Headache. StatPearls. Treasure Island (FL) with ineligible companies. Disclosure: Orlando De Jesus declares no relevant financial relationships with ineligible companies.: StatPearls Publishing

13. Grangeon L, Lange KS, Waliszewska-Prosół M, Onan D, Marschollek K, Wiels W, et al. Genetics of migraine: where are we now? J Headache Pain. 2023;24(1):12.
14. Borsook D, Maleki N, Burstein R. Chapter 42 - Migraine. In: Zigmond MJ, Rowland LP, Coyle JT, editors. Neurobiology of Brain Disorders. San Diego: Academic Press; 2015. p. 693-708.
15. Durham PL. Calcitonin gene-related peptide (CGRP) and migraine. Headache. 2006;46 Suppl 1(Suppl 1):S3-8.
16. Hu X, Zhou Y, Zhao H, Peng C. Migraine and the risk of stroke: an updated meta-analysis of prospective cohort studies. Neurological Sciences. 2017;38(1):33-40.
17. Schürks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and cardiovascular disease: systematic review and meta-analysis. BMJ. 2009;339:b3914.
18. Øie LR, Kurth T, Gulati S, Dodick DW. Migraine and risk of stroke. Journal of Neurology, Neurosurgery & Psychiatry. 2020;91(6):593-604.

19. Sacco S, Ornello R, Ripa P, Tiseo C, Degan D, Pistoia F, et al. Migraine and risk of ischaemic heart disease: a systematic review and meta-analysis of observational studies. European Journal of Neurology. 2015;22(6):1001-11.
20. Sacco S, Ripa P, Grassi D, Pistoia F, Ornello R, Carolei A, et al. Peripheral vascular dysfunction in migraine: a review. The Journal of Headache and Pain. 2013;14(1):80.
21. Murinova N, Krashin DL, Lucas S. Vascular Risk in Migraineurs: Interaction of Endothelial and Cortical Excitability Factors. Headache: The Journal of Head and Face Pain. 2014;54(3):583-90.
22. Scher AI, Terwindt GM, Picavet HS, Verschuren WM, Ferrari MD, Launer LJ. Cardiovascular risk factors and migraine: the GEM population-based study. Neurology. 2005;64(4):614-20.
23. Stovner LJ, Hagen K, Linde M, Steiner TJ. The global prevalence of headache: an update, with analysis of the influences of methodological factors on prevalence estimates. The Journal of Headache and Pain. 2022;23(1).
24. Steiner T, Scher A, Stewart W, Kolodner K, Liberman J, Lipton R. The Prevalence and Disability Burden of Adult Migraine in England and their Relationships to Age, Gender and Ethnicity. Cephalalgia. 2003;23(7):519-27.
25. MacGregor EA. Migraine in pregnancy and lactation: a clinical review. J Fam Plann Reprod Health Care. 2007;33(2):83-93.
26. Allais G, Chiarle G, Sinigaglia S, Mana O, Benedetto C. Migraine during pregnancy and in the puerperium. Neurological Sciences. 2019.
27. Kvisvik EV, Stovner LJ, Helde G, Bovim G, Linde M. Headache and migraine during pregnancy and puerperium: the MIGRA-study. The Journal of Headache and Pain. 2011;12(4):443-51.
28. Ives CW, Sinkey R, Rajapreyar I, Tita ATN, Oparil S. Preeclampsia—Pathophysiology and Clinical Presentations: JACC State-of-the-Art Review. Journal of the American College of Cardiology. 2020;76(14):1690-702.
29. Aukes AM, Yurtsever FN, Boutin A, Visser MC, de Groot CJM. Associations Between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis. Obstetrical & Gynecological Survey. 2019;74(12).
30. Facchinetti F, Sacco A. Preeclampsia and migraine: a prediction perspective. Neurol Sci. 2018;39(Suppl 1):79-80.
31. Qiu C, Luthy DA, Zhang C, Walsh SW, Leisenring WM, Williams MA. A prospective study of maternal serum C-reactive protein concentrations and risk of preeclampsia. Am J Hypertens. 2004;17(2):154-60.
32. Chambers JC, Fusi L, Malik IS, Haskard DO, De Swiet M, Kooner JS. Association of maternal endothelial dysfunction with preeclampsia. Jama. 2001;285(12):1607-12.
33. Lewis DF, Canzoneri BJ, Gu Y, Zhao S, Wang Y. Maternal levels of prostacyclin, thromboxane, ICAM, and VCAM in normal and preeclamptic pregnancies. Am J Reprod Immunol. 2010;64(6):376-83.
34. Perini F, D'Andrea G, Galloni E, Pignatelli F, Billo G, Alba S, et al. Plasma cytokine levels in migraineurs and controls. Headache. 2005;45(7):926-31.
35. Wadhwa PD, Culhane JF, Rauh V, Barve SS. Stress and preterm birth: neuroendocrine, immune/inflammatory, and vascular mechanisms. Matern Child Health J. 2001;5(2):119-25.

36. Germain AM, Romanik MC, Guerra I, Solari S, Reyes MS, Johnson RJ, et al. Endothelial dysfunction: a link among preeclampsia, recurrent pregnancy loss, and future cardiovascular events? Hypertension. 2007;49(1):90-5.
37. Aukes AM, Yurtsever FN, Boutin A, Visser MC, De Groot CJM. Associations between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis. Obstetrical and Gynecological Survey. 2019;74(12):738-48.
38. Quenby S, Gallos ID, Dhillon-Smith RK, Podesek M, Stephenson MD, Fisher J, et al. Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. The Lancet. 2021;397(10285):1658-67.
39. WHO Manual of the international statistical classification of diseases, injuries, and causes of death : based on the recommendations of the ninth revision conference, 1975, and adopted by the Twenty-ninth World Health Assembly, 1975 revision https://apps.who.int/iris/handle/10665/40492, Accessed 10th April 2024.
40. Petrou S, Trinder J, Brocklehurst P, Smith L. Economic evaluation of alternative management methods of first-trimester miscarriage based on results from the MIST trial. Bjog. 2006;113(8):879-89.
41. Petrou S, McIntosh E. Women's preferences for attributes of first-trimester miscarriage management: a stated preference discrete-choice experiment. Value Health. 2009;12(4):551-9.
42. Vogel JP, Chawanpaiboon S, Moller A-B, Watananirun K, Bonet M, Lumbiganon P. The global epidemiology of preterm birth. Best Practice & Research Clinical Obstetrics & Gynaecology. 2018;52:3-12.
43. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The Lancet. 2008;371(9606):75-84.
44. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes; Behrman RE BA, editors. Preterm Birth: Causes, Consequences, and Prevention Washington (DC): National Academies Press (US)2007.
45. Souza RT, Cecatti JG, Passini R, Jr., Tedesco RP, Lajos GJ, Nomura ML, et al. The Burden of Provider-Initiated Preterm Birth and Associated Factors: Evidence from the Brazilian Multicenter Study on Preterm Birth (EMIP). PLoS One. 2016;11(2):e0148244.
46. WHO International Classification of Diseases 10th revision (ICD-10). 2010 [Available from: http://wwwwhoint/classifications/icd/ICD10Volume2_en_2010pdf?ua=1.
47. Blencowe H, Krasevec J, De Onis M, Black RE, An X, Stevens GA, et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. The Lancet Global Health. 2019;7(7):e849-e60.
48. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. Clin Med Insights Pediatr. 2016;10:67-83.
49. Cutland CL, Lackritz EM, Mallett-Moore T, Bardají A, Chandrasekaran R, Lahariya C, et al. Low birth weight: Case definition & guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine. 2017;35(48 Pt A):6492-500.
50. Scaffidi J, Mol BW, Keelan JA. The pregnant women as a drug orphan: a global survey of registered clinical trials of pharmacological interventions in pregnancy. Bjog. 2017;124(1):132-40.

51. Illamola SM, Bucci-Rechtweg C, Costantine MM, Tsilou E, Sherwin CM, Zajicek A. Inclusion of pregnant and breastfeeding women in research - efforts and initiatives. Br J Clin Pharmacol. 2018;84(2):215-22.
52. Kim JH, Scialli AR. Thalidomide: The Tragedy of Birth Defects and the Effective Treatment of Disease. Toxicological Sciences. 2011;122(1):1-6.
53. Knight M, Bunch K, Felker A, Patel R, Kotnis R, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care Core Report - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2019-21. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2023.
54. Scottish Intercollegiate Guideline Network (SIGN). Pharmacological management of migraine. Edinburgh: SIGN; 2023 (SIGN publication no. 155). {March 2023}. Available from URL: http://www.sign.ac.uk.
55. Wood M, Hernandez-Diaz S. Migraine in a cohort of commercially insured women in the United States: Natural history and association with preeclampsia, placental abruption, and preterm birth. Paediatric and Perinatal Epidemiology. 2021;35(SUPPL 1):50.
56. Wyszynski DF, Nambisan M, Surve T, Alsdorf RM, Smith CR, Holmes LB. Increased rate of major malformations in offspring exposed to valproate during pregnancy. Neurology. 2005;64(6):961-5.
57. Jentink J, Loane MA, Dolk H, Barisic I, Garne E, Morris JK, et al. Valproic acid monotherapy in pregnancy and major congenital malformations. N Engl J Med. 2010;362(23):2185-93.
58. Margulis AV, Mitchell AA, Gilboa SM, Werler MM, Mittleman MA, Glynn RJ, et al. Use of topiramate in pregnancy and risk of oral clefts. American Journal of Obstetrics and Gynecology. 2012;207(5):405.e1-.e7.
59. Yallampalli C, Chauhan M, Thota CS, Kondapaka S, Wimalawansa SJ. Calcitonin gene-related peptide in pregnancy and its emerging receptor heterogeneity. Trends in Endocrinology & Metabolism. 2002;13(6):263-9.
60. Gangula PR, Dong YL, Wimalawansa SJ, Yallampalli C. Infusion of pregnant rats with calcitonin gene-related peptide (CGRP)(8-37), a CGRP receptor antagonist, increases blood pressure and fetal mortality and decreases fetal growth. Biol Reprod. 2002;67(2):624-9.
61. Noseda R, Bedussi F, Gobbi C, Ceschi A, Zecca C. Safety profile of monoclonal antibodies targeting the calcitonin gene-related peptide system in pregnancy: Updated analysis in VigiBase®. Cephalalgia. 2023;43(4):03331024231158083.
62. Noseda R, Bedussi F, Gobbi C, Ceschi A, Zecca C. Calcitonin gene-related peptide antagonists in pregnancy: a disproportionality analysis in VigiBase®. The Journal of Headache and Pain. 2024;25(1):10.
63. Nicolas S, Nicolas D. Triptans. [Updated 2023 Mar 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554507/.
64. Marchenko A, Etwel F, Olutunfese O, Nickel C, Koren G, Nulman I. Pregnancy outcome following prenatal exposure to Triptan medications: A meta-analysis. Headache. 2015;55(4):490-501.
65. Dudman DC, Tauqeer F, Kaur M, Ritchey ME, Li H, Lopez-Leon S. A systematic review and meta-analyses on the prevalence of pregnancy outcomes in migraine

treated patients: a contribution from the IMI2 ConcePTION project. Journal of Neurology. 2022;269(2):742-9.
66. Castro CT, Gama RS, Pereira M, Oliveira MG, Dal-Pizzol TS, Barreto ML, et al. Effect of Acetaminophen use during pregnancy on adverse pregnancy outcomes: a systematic review and meta-analysis. Expert Opinion on Drug Safety. 2022;21(2):241-51.
67. Dean A, van den Driesche S, Wang Y, McKinnell C, Macpherson S, Eddie SL, et al. Analgesic exposure in pregnant rats affects fetal germ cell development with inter-generational reproductive consequences. Scientific Reports. 2016;6(1):19789.
68. Ying XH, Bao DN, Jiang HY, Shi YD. Maternal non-steroidal anti-inflammatory drug exposure during pregnancy and risk of miscarriage: a systematic review and meta-analysis. Eur J Clin Pharmacol. 2022;78(2):171-80.
69. Koren G, Florescu A, Costei AM, Boskovic R, Moretti ME. Nonsteroidal Antiinflammatory Drugs During Third Trimester and the Risk of Premature Closure of the Ductus Arteriosus: A Meta-Analysis. Annals of Pharmacotherapy. 2006;40(5):824-9.
70. Schreiber K, Frishman M, Russell MD, Dey M, Flint J, Allen A, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: comorbidity medications used in rheumatology practice. Rheumatology. 2022;62(4):e89-e104.
71. Flint J, Panchal S, Hurrell A, van de Venne M, Gayed M, Schreiber K, et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part II: analgesics and other drugs used in rheumatology practice. Rheumatology. 2016;55(9):1698-702.
72. Østensen M, Khamashta M, Lockshin M, Parke A, Brucato A, Carp H, et al. Arthritis Research & Therapy. 2006;8(3):209.
73. Propanolol in pregnancy. United Kingdom Teratology Information Service. [Cited 2024 April 11]. Available from: http://www.toxbase.org/.
74. Amitriptyline in pregnancy. United Kingdom Teratology Information Service. [Cited 2024 April 11]. Available from: http://www.toxbase.org/.
75. Smith B, Chu LK, Smith TC, Amoroso PJ, Boyko EJ, Hooper TI, et al. Challenges of self-reported medical conditions and electronic medical records among members of a large military cohort. BMC Medical Research Methodology. 2008;8(1):37.
76. Hafferty JD, Campbell AI, Navrady LB, Adams MJ, MacIntyre D, Lawrie SM, et al. Self-reported medication use validated through record linkage to national prescribing data. Journal of Clinical Epidemiology. 2018;94:132-42.
77. United Kingdom Research and Innovation. Cohort directory [cited 2023 7th January]. Available from: https://www.ukri.org/councils/mrc/facilities-and-resources/find-an-mrc-facility-or-resource/cohort-directory/. .
78. Crowe HM, Wesselink AK, Wise LA, Jick SS, Rothman KJ, Mikkelsen EM, et al. Pre-pregnancy migraine diagnosis, medication use, and spontaneous abortion: a prospective cohort study. The Journal of Headache and Pain. 2022;23(1).
79. Oulman E, Kim THM, Yunis K, Tamim H. Prevalence and predictors of unintended pregnancy among women: an analysis of the Canadian Maternity Experiences Survey. BMC Pregnancy and Childbirth. 2015;15(1).
80. Public Health England. Health matters: reproductive health and pregnancy planning. 2018.

81. Welk B. Routinely collected data for population-based outcomes research. Canadian Urological Association Journal. 2019;14(2).
82. Kontopantelis E, Buchan I, Reeves D, Checkland K, Doran T. Relationship between quality of care and choice of clinical computing system: retrospective analysis of family practice performance under the UK's quality and outcomes framework. BMJ Open. 2013;3(8):e003190.
83. Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). International Journal of Epidemiology. 2015;44(3):827-36.
84. Jick S, Vasilakis-Scaramozza C, Persson R, Neasham D, Kafatos G, Hagberg KW. Use of the CPRD Aurum Database: Insights Gained from New Data Quality Assessments. Clin Epidemiol. 2023;15:1219-22.
85. Booth N. What are the Read Codes? Health Libr Rev. 1994;11(3):177-82.
86. Minassian C, Williams R, Meeraus WH, Smeeth L, Campbell OMR, Thomas SL. Methods to generate and validate a Pregnancy Register in the UK Clinical Practice Research Datalink primary care database. Pharmacoepidemiology and Drug Safety. 2019;28(7):923-33.
87. Ammon Avalos L, Galindo C, Li DK. A systematic review to calculate background miscarriage rates using life table analysis. Birth Defects Res A Clin Mol Teratol. 2012;94(6):417-23.
88. Campbell J, Bhaskaran K, Thomas S, Williams R, McDonald HI, Minassian C. Investigating the optimal handling of uncertain pregnancy episodes in the CPRD GOLD Pregnancy Register: a methodological study using UK primary care data. BMJ Open. 2022;12(2):e055773.
89. 2018 survey of women's experiences of maternity care, 2020. Available: https://www.cqc.org.uk/sites/default/files/20200128_mat19_statisticalrelease.pdf.
90. Herbert A, Wijlaars L, Zylbersztejn A, Cromwell D, Hardelid P. Data Resource Profile: Hospital Episode Statistics Admitted Patient Care (HES APC). International Journal of Epidemiology. 2017;46(4):1093-i.
91. Office of National Statistics (ONS) (2019) *Birth characteristics in England and Wales: 2019,* ONS website. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthcharacteristicsinenglandandwales/2019#place-of-birth.
92. Murray J, Saxena S, Modi N, Majeed A, Aylin P, Bottle A, et al. Quality of routine hospital birth records and the feasibility of their use for creating birth cohorts. Journal of Public Health. 2012;35(2):298-307.
93. Padmanabhan S, Carty L, Cameron E, Ghosh RE, Williams R, Strongman H. Approach to record linkage of primary care data from Clinical Practice Research Datalink to other health-related patient data: overview and implications. European Journal of Epidemiology. 2019;34(1):91-9.
94. Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc. 2015;13(3):132-40.
95. Okoth K, Chandan JS, Marshall T, Thangaratinam S, Thomas GN, Nirantharakumar K, et al. Association between the reproductive health of young women and cardiovascular disease in later life: umbrella review. BMJ. 2020:m3502.

96. Garner P, Hopewell S, Chandler J, Maclehose H, Schünemann HJ, Akl EA, et al. When and how to update systematic reviews: consensus and checklist. BMJ. 2016:i3507.
97. Suissa S, Dell'aniello S, Vahey S, Renoux C. Time-window bias in case-control studies: statins and lung cancer. Epidemiology. 2011;22(2):228-31.
98. Hu L, Du J, Lv H, Zhao J, Chen M, Wang Y, et al. Influencing factors of pregnancy loss and survival probability of clinical pregnancies conceived through assisted reproductive technology. Reprod Biol Endocrinol. 2018;16(1):74.
99. Nakhai-Pour HR, Broy P, Berard A. Use of antidepressants during pregnancy and the risk of spontaneous abortion. Canadian Medical Association Journal. 2010;182(10):1031-7.
100. Einarson A, Choi J, Einarson TR, Koren G. Rates of spontaneous and therapeutic abortions following use of antidepressants in pregnancy: results from a large prospective database. J Obstet Gynaecol Can. 2009;31(5):452-6.
101. Gokhale KM, Chandan JS, Toulis K, Gkoutos G, Tino P, Nirantharakumar K. Data extraction for epidemiological research (DExtER): a novel tool for automated clinical epidemiology studies. Eur J Epidemiol. 2021;36(2):165-78.
102. Fan L, Wu Y, Wei J, Xia F, Cai Y, Zhang S, et al. Global, regional, and national time trends in incidence for migraine, from 1990 to 2019: an age-period-cohort analysis for the GBD 2019. The Journal of Headache and Pain. 2023;24(1):79.
103. Burch R, Rizzoli P, Loder E. The prevalence and impact of migraine and severe headache in the United States: Updated age, sex, and socioeconomic-specific estimates from government health surveys. Headache. 2021;61(1):60-8.
104. Statistics OfN. Birth characteristics in England and Wales: 2021 ons.gov.uk: Office for National Statistics; 2021 [Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthcharacteristicsinenglandandwales/2021#:~:text=In%202021%2C%20the%20average%20age,fathers%20remained%20at%2033.7%20years.
105. Aukes AM, Yurtsever FN, Boutin A, Visser MC, De Groot CJM. Associations between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis. Obstetrical and Gynecological Survey. 2019;74(12):738-48.
106. Skajaa N, Szépligeti SK, Xue F, Sørensen HT, Ehrenstein V, Eisele O, et al. Pregnancy, Birth, Neonatal, and Postnatal Neurological Outcomes After Pregnancy With Migraine. Headache: The Journal of Head and Face Pain. 2019;59(6):869-79.
107. Pace M, Lanzieri G, Glickman M, Zupanič T. Revision of the European Standard Population: report of Eurostat's task force: Publications Office of the European Union; 2013.
108. Tauqeer F, Wood M, Hjorth S, Lupattelli A, Nordeng H. Perinatal use of triptans and other drugs for migraine—A nationwide drug utilization study. PLOS ONE. 2021;16(8):e0256214.
109. Wood ME, Burch RC, Hernandez-Diaz S. Polypharmacy and comorbidities during pregnancy in a cohort of women with migraine. Cephalalgia. 2021;41(3):392-403.
110. Molenaar NM, Bais B, Lambregtse-Van Den Berg MP, Mulder CL, Howell EA, Fox NS, et al. The international prevalence of antidepressant use before, during, and after pregnancy: A systematic review and meta-analysis of timing, type of prescriptions and geographical variability. Journal of Affective Disorders. 2020;264:82-9.

111. Xie R-h, Guo Y, Krewski D, Mattison D, Nerenberg K, Walker MC, et al. Trends in using beta-blockers and methyldopa for hypertensive disorders during pregnancy in a Canadian population. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2013;171(2):281-5.
112. Subramanian A, Azcoaga-Lorenzo A, Anand A, Phillips K, Lee SI, Cockburn N, et al. Polypharmacy during pregnancy and associated risk factors: a retrospective analysis of 577 medication exposures among 1.5 million pregnancies in the UK, 2000-2019. BMC Medicine. 2023;21(1).
113. IHS Classification ICHD-3 Evoluation of IHS-Classification 1-4 alpha. Available from: https://ichd-3.org/evolution-of-ihs-classification-1-3/.
114. Tepper SJ. History and Review of anti-Calcitonin Gene-Related Peptide (CGRP) Therapies: From Translational Research to Treatment. Headache. 2018;58 Suppl 3:238-75.
115. Excellence NIfHaC. Headaches. Diagnosis and Management of Headaches in Young People and Adults. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3722827/: NICE; 2012 [
116. Adams J, Waal Zvd, Rushton S, Rankin J. Associations between introduction and withdrawal of a financial incentive and timing of attendance for antenatal care and incidence of small for gestational age: natural experimental evaluation using interrupted time series methods. BMJ Open. 2018;8(1):e017697.
117. National Collaborating Centre for Women's and Children's Health. Antenatal care: routine care for the healthy pregnant woman. London: National Institute for Health and Clinical Excellence, 2008.
118. Lean SC, Derricott H, Jones RL, Heazell AEP. Advanced maternal age and adverse pregnancy outcomes: A systematic review and meta-analysis. PLOS ONE. 2017;12(10):e0186287.
119. Jardine J, Walker K, Gurol-Urganci I, Webster K, Muller P, Hawdon J, et al. Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study. The Lancet. 2021;398(10314):1905-12.
120. Marchi J, Berg M, Dencker A, Olander EK, Begley C. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. Obes Rev. 2015;16(8):621-38.
121. Brown HK, McKnight A, Aker A. Association between pre-pregnancy multimorbidity and adverse maternal outcomes: A systematic review. Journal of Multimorbidity and Comorbidity. 2022;12:26335565221096584.
122. Birmingham Health Partners. Healthy Mum, Healthy Baby, Healthy Future 2022 [Available from: https://www.birminghamhealthpartners.co.uk/wp-content/uploads/2022/05/Final-Healthy-Mum-Healthy-Baby-Healthy-Future-Report-AW_Accessible-PDF-REDUCED-FILE-SIZE.pdf
123. Benjamin RW. Medication-overuse headache. Practical Neurology. 2019;19(5):399.
124. Aukes AM, Yurtsever FN, Boutin A, Visser MC, de Groot CJM. Associations Between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis. Obstet Gynecol Surv. 2019;74(12):738-48.
125. Skajaa N, Szépligeti SK, Xue F, Sørensen HT, Ehrenstein V, Eisele O, et al. Pregnancy, Birth, Neonatal, and Postnatal Neurological Outcomes After Pregnancy With Migraine. Headache. 2019;59(6):869-79.

126. Jarvis S, Dassan P, Piercy CN. Managing migraine in pregnancy. Bmj. 2018;360:k80.
127. Phillips K, Davison J, Wakerley B. Headache in pregnancy: a brief practical guide. British Journal of General Practice. 2022;72(725):593-4.
128. Barus J, Sudharta H, Adriani D. Study of the Mechanisms and Therapeutic Approaches of Migraine in Women and Pregnancy: A Literature Review. Cureus. 2023.
129. Dudman DC, Tauqeer F, Kaur M, Ritchey ME, Li H, Lopez-Leon S. A systematic review and meta-analyses on the prevalence of pregnancy outcomes in migraine treated patients: a contribution from the IMI2 ConcePTION project. J Neurol. 2022;269(2):742-9.
130. Macclellan LR, Giles W, Cole J, Wozniak M, Stern B, Mitchell BD, et al. Probable Migraine With Visual Aura and Risk of Ischemic Stroke. Stroke. 2007;38(9):2438-45.
131. Lee SI, Hope H, O'Reilly D, Kent L, Santorelli G, Subramanian A, et al. Maternal and child outcomes for pregnant women with pre-existing multiple long-term conditions: protocol for an observational study in the UK. BMJ Open. 2023;13(2):e068718.
132. Haddaway NR, Land M, Macura B. "A little learning is a dangerous thing": A call for better understanding of the term 'systematic review'. Environment International. 2017;99:356-60.
133. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic Reviews. 2016;5(1):210.
134. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017:j4008.
135. Perry R, Whitmarsh A, Leach V, Davies P. A comparison of two assessment tools used in overviews of systematic reviews: ROBIS versus AMSTAR-2. Systematic Reviews. 2021;10(1):273.
136. Pieper D, Antoine SL, Mathes T, Neugebauer EA, Eikermann M. Systematic review finds overlapping reviews were not mentioned in every other overview. J Clin Epidemiol. 2014;67(4):368-75.
137. Brown HK, Qazilbash A, Rahim N, Dennis CL, Vigod SN. Chronic Medical Conditions and Peripartum Mental Illness: A Systematic Review and Meta-Analysis. Am J Epidemiol. 2018;187(9):2060-8.
138. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2013;170(1):1-7.
139. Ohuma EO, Moller A-B, Bradley E, Chakwera S, Hussain-Alkhateeb L, Lewin A, et al. National, regional, and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis. The Lancet. 2023;402(10409):1261-71.
140. Amundsen S, Nordeng H, Nezvalová-Henriksen K, Stovner LJ, Spigset O. Pharmacological treatment of migraine during pregnancy and breastfeeding. Nat Rev Neurol. 2015;11(4):209-19.
141. Facchinetti F, Allais G, Nappi RE, D'Amico R, Marozio L, Bertozzi L, et al. Migraine is a risk factor for hypertensive disorders in pregnancy: a prospective cohort study. Cephalalgia. 2009;29(3):286-92.

142. Sheikh HU, Pavlovic J, Loder E, Burch R. Risk of Stroke Associated With Use of Estrogen Containing Contraceptives in Women With Migraine: A Systematic Review. Headache. 2018;58(1):5-21.
143. Welch KM, Brandes AW, Salerno L, Brandes JL. C-reactive protein may be increased in migraine patients who present with complex clinical features. Headache. 2006;46(2):197-9.
144. Viard D, Gérard A, Tahiri J, Tieulié N, Van Obberghen E, Drici MD. Triptan overuse during pregnancy: a possible cause of placental hypoperfusion. Eur J Clin Pharmacol. 2021;77(2):269-70.
145. Li DK, Liu L, Odouli R. Exposure to non-steroidal anti-inflammatory drugs during pregnancy and risk of miscarriage: population based cohort study. Bmj. 2003;327(7411):368.
146. Nielsen GL. Danish group reanalyses miscarriage in NSAID users. BMJ. 2004;328(7431):109-.
147. Edwards DR, Aldridge T, Baird DD, Funk MJ, Savitz DA, Hartmann KE. Periconceptional over-the-counter nonsteroidal anti-inflammatory drug exposure and risk for spontaneous abortion. Obstet Gynecol. 2012;120(1):113-22.
148. Nezvalová-Henriksen K, Spigset O, Nordeng H. Triptan safety during pregnancy: a Norwegian population registry study. European Journal of Epidemiology. 2013;28(9):759-69.
149. Olesen C, Steffensen FH, Sorensen HT, Nielsen GL, Olsen J. Pregnancy outcome following prescription for sumatriptan. Headache. 2000;40(1):20-4.
150. Allais G, Chiarle G, Sinigaglia S, Mana O, Benedetto C. Migraine during pregnancy and in the puerperium. Neurol Sci. 2019;40(Suppl 1):81-91.
151. Magnus MC, Morken N-H, Wensaas K-A, Wilcox AJ, Håberg SE. Risk of miscarriage in women with chronic diseases in Norway: A registry linkage study. PLOS Medicine. 2021;18(5):e1003603.
152. Jarvis S, Dassan P, Piercy CN. Managing migraine in pregnancy. BMJ. 2018:k80.
153. Bérard A, Strom S, Zhao J-P, Kori S, Albrecht D. Dihydroergotamine and triptan use to treat migraine during pregnancy and the risk of adverse pregnancy outcomes. Scientific Reports. 2021;11(1).
154. Ying X-H, Bao D-N, Jiang H-Y, Shi Y-D. Maternal non-steroidal anti-inflammatory drug exposure during pregnancy and risk of miscarriage: a systematic review and meta-analysis. European Journal of Clinical Pharmacology. 2022;78(2):171-80.
155. Ban L, Tata LJ, West J, Fiaschi L, Gibson JE. Live and Non-Live Pregnancy Outcomes among Women with Depression and Anxiety: A Population-Based Study. PLoS ONE. 2012;7(8):e43462.
156. Kjaersgaard MIS, Parner ET, Vestergaard M, Sørensen MJ, Olsen J, Christensen J, et al. Prenatal Antidepressant Exposure and Risk of Spontaneous Abortion – A Population-Based Study. PLoS ONE. 2013;8(8):e72095.
157. Li Y, Zhang J, Zhang K, Wang E, Shu J. Significance of dynamically monitoring serum estrogen and β-human chorionic gonadotropin in early pregnancy assessment. Journal of Clinical Laboratory Analysis. 2021;35(1).
158. Reddy N, Desai MN, Schoenbrunner A, Schneeberger S, Janis JE. The complex relationship between estrogen and migraines: a scoping review. Systematic Reviews. 2021;10(1).

159. Marchenko A, Etwel F, Olutunfese O, Nickel C, Koren G, Nulman I. Pregnancy Outcome Following Prenatal Exposure to Triptan Medications: A Meta-Analysis. Headache: The Journal of Head and Face Pain. 2015;55(4):490-501.
160. Germain AM, Romanik MC, Guerra I, Solari S, Reyes MAS, Johnson RJ, et al. Endothelial Dysfunction. Hypertension. 2007;49(1):90-5.
161. Bassiouni BA, Rafei AA. 5-Hydroxytryptamine (serotonin), copper and ceruloplasmin plasma concentrations in spontaneous abortion. European Journal of Obstetrics & Gynecology and Reproductive Biology. 1979;9(2):81-8.
162. Russell MD, Dey M, Flint J, Davie P, Allen A, Crossley A, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). 2023;62(4):e48-e88.
163. Quantin C, Yamdjieu Ngadeu C, Cottenet J, Escolano S, Bechraoui-Quantin S, Rozenberg P, et al. Early exposure of pregnant women to non-steroidal anti-inflammatory drugs delivered outside hospitals and preterm birth risk: nationwide cohort study. BJOG: An International Journal of Obstetrics & Gynaecology. 2021;128(10):1575-84.
164. Li DK. Exposure to non-steroidal anti-inflammatory drugs during pregnancy and risk of miscarriage: population based cohort study. BMJ. 2003;327(7411):368-0.
165. Edwards DRV, Aldridge T, Baird DD, Funk MJ, Savitz DA, Hartmann KE. Periconceptional Over-the-Counter Nonsteroidal Anti-inflammatory Drug Exposure and Risk for Spontaneous Abortion. Obstetrics & Gynecology. 2012;120(1).
166. Blaylock R, Trickey H, Sanders J, Murphy C. WRISK voices: A mixed-methods study of women's experiences of pregnancy-related public health advice and risk messages in the UK. Midwifery. 2022;113:103433.
167. Murray S, Augustyniak M, Murase JE, Fischer-Betz R, Nelson-Piercy C, Peniuta M, et al. Barriers to shared decision-making with women of reproductive age affected by a chronic inflammatory disease: a mixed-methods needs assessment of dermatologists and rheumatologists. BMJ Open. 2021;11(6):e043960.
168. Whybrow R, Webster LM, Seed PT, Sandall J, Chappell LC. The effectiveness of decision aids for pregnancy related decision-making in women with pre-pregnancy morbidity; systematic review and meta-analysis. BMC Pregnancy and Childbirth. 2022;22(1).
169. Chen HM, Chen SF, Chen YH, Lin HC. Increased risk of adverse pregnancy outcomes for women with migraines: A nationwide population-based study. Cephalalgia. 2010;30(4):433-8.
170. Purdue-Smithe AC, Stuart JJ, Farland LV, Kang JH, Harriott AM, Rich-Edwards JW, et al. Prepregnancy Migraine, Migraine Phenotype, and Risk of Adverse Pregnancy Outcomes. Neurology. 2023;100(14):e1464-e73.
171. Miller EC, Chau K, Mammadli G, Levine LD, Grobman WA, Wapner R, et al. Migraine and adverse pregnancy outcomes: the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be. Am J Obstet Gynecol. 2022;227(3):535-6.
172. Cripe SM, Frederick IO, Qiu C, Williams MA. Risk of preterm delivery and hypertensive disorders of pregnancy in relation to maternal co-morbid mood and migraine disorders during pregnancy. Paediatric and Perinatal Epidemiology. 2011;25(2):116-23.

173. Phillips K, Clerkin-Oliver C, Nirantharakumar K, Crowe FL, Wakerley BR. How migraine and its associated treatment impact on pregnancy outcomes: Umbrella review with updated systematic review and meta-analysis. Cephalalgia. 2024;44(2):03331024241229410.
174. Grossman TB, Dayal AK, Robbins MS. Delivery outcomes after acute migraine treatment in pregnancy: A retrospective study. Cephalalgia. 2015;35(6 SUPPL. 1):25.
175. The National Institute for Health and Care Excellence. Caesarean birth. Clinical Guideline 192. London: NICE 2021.
176. Darnal N, Dangal G. Maternal and Fetal Outcome in Emergency versus Elective Caesarean Section. J Nepal Health Res Counc. 2020;18(2):186-9.
177. Banhidy F, Acs N, Horvath-Puho E, Czeizel AE. Pregnancy complications and delivery outcomes in pregnant women with severe migraine. Obstetrical and Gynecological Survey. 2008;63(2):79-81.
178. Wainscott G, Sullivan FM, Volans GN, Wilkinson M. The outcome of pregnancy in women suffering from migraine. Postgrad Med J. 1978;54(628):98-102.
179. ONS. Birth characteristics in England and Wales: 2019. 2019.
180. Fox NS, Rebarber A, Klauser CK, Roman AS, Saltzman DH. Intrauterine growth restriction in twin pregnancies: incidence and associated risk factors. Am J Perinatol. 2011;28(4):267-72.
181. Steiner TJ, Scher AI, Stewart WF, Kolodner K, Liberman J, Lipton RB. The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. Cephalalgia. 2003;23(7):519-27.
182. Kiarashi J, VanderPluym J, Szperka CL, Turner S, Minen MT, Broner S, et al. Factors Associated With, and Mitigation Strategies for, Health Care Disparities Faced by Patients With Headache Disorders. Neurology. 2021;97(6):280-9.
183. Burch R, Rizzoli P, Loder E. The Prevalence and Impact of Migraine and Severe Headache in the United States: Figures and Trends From Government Health Studies. Headache. 2018;58(4):496-505.
184. Broere-Brown ZA, Schalekamp-Timmermans S, Jaddoe VWV, Steegers EAP. Deceleration of fetal growth rate as alternative predictor for childhood outcomes: a birth cohort study. BMC Pregnancy and Childbirth. 2019;19(1):216.
185. Osuchukwu OO, Reed DJ. Small for Gestational Age. [Updated 2022 Nov 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563247/.
186. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller A-B, et al. Born Too Soon: The global epidemiology of 15 million preterm births. Reproductive Health. 2013;10(1):S2.
187. Feise RJ. Do multiple outcome measures require p-value adjustment? BMC Med Res Methodol. 2002;2:8.
188. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, et al. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. JAMA. 2016;316(4):410-9.
189. Ness A, Mayo JA, El-Sayed YY, Druzin ML, Stevenson DK, Shaw GM. Trends in Spontaneous and Medically Indicated Preterm Birth in Twins versus Singletons: A California Cohort 2007 to 2011. Am J Perinatol. 2023;40(1):62-7.

190. **The National Institute for Health and Care Excellence.** Hypertension in pregnancy: diagnosis and management. Clinical Guideline 133. London: NICE 2019.
191. Tikkanen M. Placental abruption: epidemiology, risk factors and consequences. Acta Obstet Gynecol Scand. 2011;90(2):140-9.
192. Sławek-Szmyt S, Kawka-Paciorkowska K, Ciepłucha A, Lesiak M, Ropacka-Lesiak M. Preeclampsia and Fetal Growth Restriction as Risk Factors of Future Maternal Cardiovascular Disease-A Review. J Clin Med. 2022;11(20).
193. ONS. Births in England and Wales 2021. 2022.
194. Wardinger JE, Ambati S. Placental Insufficiency. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563171/.
195. Pinney SE. Chapter 14 - Metabolic Disorders and Developmental Origins of Health and Disease. In: Rosenfeld CS, editor. The Epigenome and Developmental Origins of Health and Disease. Boston: Academic Press; 2016. p. 267-89.
196. Gardosi J, Francis A, Turner S, Williams M. Customized growth charts: rationale, validation and clinical benefits. Am J Obstet Gynecol. 2018;218(2s):S609-s18.
197. White IR, Thompson SG. Adjusting for partially missing baseline measurements in randomized trials. Statistics in Medicine. 2005;24(7):993-1007.
198. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. BMC Medical Research Methodology. 2017;17(1):162.
199. Zhang G, Rose CE, Zhang Y, Li R, Lee FC, Massetti G, et al. Multiple Imputation of Missing Race and Ethnicity in CDC COVID-19 Case-Level Surveillance Data. International Journal of Statistics in Medical Research. 2022;11:1-11.
200. Du Fossé NA, Van Der Hoorn M-LP, Van Lith JMM, Le Cessie S, Lashley EELO. Advanced paternal age is associated with an increased risk of spontaneous miscarriage: a systematic review and meta-analysis. Human Reproduction Update. 2020;26(5):650-69.
201. Acton EK, Willis AW, Hennessy S. Core concepts in pharmacoepidemiology: Key biases arising in pharmacoepidemiologic studies. Pharmacoepidemiology and Drug Safety. 2023;32(1):9-18.
202. Gormley P, Anttila V, Winsvold BS, Palta P, Esko T, Pers TH, et al. Meta-analysis of 375,000 individuals identifies 38 susceptibility loci for migraine. Nat Genet. 2016;48(8):856-66.
203. Kogelman LJA, Esserlind AL, Francke Christensen A, Awasthi S, Ripke S, Ingason A, et al. Migraine polygenic risk score associates with efficacy of migraine-specific drugs. Neurol Genet. 2019;5(6):e364.
204. Crowe HM, Wesselink AK, Hatch EE, Wise LA, Jick SS. Migraine and risk of hypertensive disorders of pregnancy: A population-based cohort study. Cephalalgia. 2023;43(4):03331024231161746.
205. Nezvalova-Henriksen K, Spigset O, Nordeng H. Triptan safety during pregnancy: A Norwegian population registry study. European Journal of Epidemiology. 2013;28(9):759-69.
206. Olesen C, Steffensen FH, Sorensen HT, Nielsen GL, Olsen J. Pregnancy outcome following prescription for sumatriptan. Headache. 2000;40(1):20-4.

207. Weng S-C, Wu C-L, Kor C-T, Chiu P-F, Wu M-J, Chang C-C, et al. Migraine and subsequent chronic kidney disease risk: a nationwide population-based cohort study. BMJ Open. 2017;7(12):e018483.
208. Rose KM, Wong TY, Carson AP, Couper DJ, Klein R, Sharrett AR. Migraine and retinal microvascular abnormalities: the Atherosclerosis Risk in Communities Study. Neurology. 2007;68(20):1694-700.
209. Tietjen G. Migraine as a Systemic Vasculopathy. Cephalalgia. 2009;29(9):989-96.
210. Bandoli G, Baer RJ, Gano D, Pawlowski LJ, Chambers C. Migraines During Pregnancy and the Risk of Maternal Stroke. JAMA Neurol. 2020;77(9):1177-9.
211. Crowe HM, Wesselink AK, Hatch EE, Wise LA, Jick SS. Migraine and risk of hypertensive disorders of pregnancy: A population-based cohort study. Cephalalgia : an international journal of headache. 2023;43(4):3331024231161746.
212. Neri I, Menichini D, Monari F, Bascio LS, Banchelli F, Facchinetti F. Perinatal outcomes in women affected by different types of headache disorders: A prospective cohort study. Cephalalgia. 2021;41(14):1492-8.
213. Shoaib M, Tareen MS, Saifullah S, Umar F. Effect of Maternal Migraine during Gestation and Delivery Outcomes. Pakistan Journal of Medical and Health Sciences. 2021;15(12):3310-1.
214. Adam I, Elmugabil A, AlHabardi N. History of maternal migraine and its association with preeclampsia: A case-control study in a low-resource setting in Sudan, Africa. Cephalalgia : an international journal of headache. 2023;43(8):3000605231193823.