

# Migraine Treatment Pathway for Adults

Norfolk and Waveney Integrated Care System

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## 2. Document Control Sheet

<b>Title</b>	Migraine treatment pathway for adults
<b>Description of policy</b>	NWICB treatment pathway for migraine
<b>Version</b>	2.1
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<b>Prepared by</b>	Medicine optimisation team With input/advice from specialists at NNUH
<b>Impact Assessment (Equalities and Environmental)</b>	
<b>Other relevant approved documents</b>	
<b>Evidence base / Legislation</b>	Level of Evidence: <del>A. based on national research based evidence and is considered best evidence</del> <b>B. mix of national and local consensus</b> <del>C. based on local good practice and consensus in the absence of national research based information.</del>
<b>Dissemination</b>	Is there any reason why any part of this document should not be available on the public web site? <b>Yes / No</b>
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### 2.1 Revision History

Revision Date	Summary of changes	Author(s)	Version Number
Aug 2025	Addition of pizofen as prophylaxis option. Information around topiramate in women of childbearing potential strengthened. Addition of information of prophylaxis withdrawal	HH	2
October 2025	Formatting of table in section 5.3. Prophylaxis changed; now clearly separated into first line options and alternative options. Addition of Pizotifen as an alternative treatment option for prophylaxis of migraines in primary care. Appendix 2 updated.	NC	2.1

### 2.2 Approvals

This document requires the following approvals either individual(s), group(s) or board.

Name	Title	Date of Issue	Version Number

### 3. Introduction

#### 3.1 Relevant NICE technology appraisals

Technology Appraisal*	Title
TA260	<a href="#">Botulinum toxin type A for the prevention of headaches in adults with chronic migraine</a>
TA659	<a href="#">Galcanezumab for preventing migraine</a>
TA682	<a href="#">Erenumab for preventing migraine</a>
TA764	<a href="#">Fremanezumab for preventing migraine</a>
TA871	<a href="#">Eptinezumab for preventing migraine</a>
TA906	<a href="#">Rimegepant for preventing migraine</a>
TA919	<a href="#">Rimegepant for treating migraine</a>
TA973	<a href="#">Atogepant for preventing migraine</a>

\*NICE recommendations **also apply to biosimilar products of the technologies** that have a marketing authorisation, allowing the use of the biosimilar for the same indication. See [Appendix 8](#) for full detail of listed TAs.

#### 3.2 Background

This pathway is to be used to guide the initiation and maintenance of high-cost drugs in the management of migraine and have been written using up to date published NICE Technology Appraisals (TAs) and evidenced based medicine.

The pathways include biologic agents:

- Anti-CGRP: Atogepant, Eptinezumab, Erenumab, Fremanezumab, Galcanezumab & Rimegepant
- Neurotoxin: Botulinum toxin type A

Drugs should be used in accordance with the relevant TA. The links are included in this document. Inclusion will be allowed for any new high-cost drugs that are approved by NICE prior to review of the pathway, provided that the relevant local “New Medicines” Policy and process has been followed. Those drugs should be used in accordance with the relevant NICE TA. The NICE recommendations also apply to biosimilar drugs, where marketing authorisations allow use of the biosimilar for the indication specified in the relevant NICE TA.

### 4. Classification

In the third edition of the International Classification of Headache Disorders (ICHD-3), migraine is classified into three main types: migraine without aura, migraine with aura, and chronic migraine<sup>1</sup>.

Migraine can be described as episodic or chronic:

- Episodic migraine is defined by the presence of headache on fewer than 15 days each month.
- Chronic migraine is defined by the presence of 15 or more headache days each month, of which at least 8 are migraine days.

Treatment of migraine involves pharmacological intervention plus lifestyle advice. Preventative treatment can be considered if the migraines are causing frequent disability, in patients at risk of medication overuse headache, when standard analgesia are not effective or contraindicated, or for uncommon types of migraine. Appropriately taken preventative treatments are likely to be effective in reducing frequency/intensity of migraine, but often do not abort all migraine attacks completely. There are several prophylactic agents for migraine available. Further information on their management in primary care can be found on clinical guideline NICE CG150.

A class of monoclonal antibodies specific for calcitonin gene-related peptide (CGRP), a neuropeptide involved in pain signalling has been developed for the prophylaxis of migraine. These drugs compete with CGRP for binding to its receptor,

and thereby interrupts the signalling pathway. This class of drug is a positive step forward in providing an alternative treatment option to patients with migraine. The drugs may be more acceptable to patients than Botulinum toxin type A since it can be self-administered as a single injection. By contrast Botulinum toxin A requires attendance at clinic every 3 months, and each treatment consists of multiple injections. Additionally, the anti-CGRP drugs are available via Homecare, allowing for virtual clinics and reduced attendance to the outpatient clinic.

#### 4.1 Common primary headache classification<sup>1,2</sup>

Tension-type headache	Migraine	Cluster headache
Episodic Bilateral	Unilateral (although often bilateral)	Unilateral (never bilateral)
Pressing, tightening, non-pulsating	Pulsating	
Mild or moderate but not disabling	Moderate or severe	Very severe
No aggravation by, or avoidance of, routine physical activity	Aggravated by, or causing avoidance of, routine physical activity	Restlessness, No aggravation by physical activity
Nausea and/or vomiting Photophobia Phonophobia	Nausea and/or vomiting Photophobia Phonophobia	<i>Ipsilateral to pain, there may be:</i> Conjunctival injection Lacrimation Nasal congestion Rhinorrhoea Eyelid swelling/drooping
Attacks last hours to days	Attacks last hours to days (usually 4-72 hours)	Attacks last from 15 mins to 3 hours
	Frequency 1-2 attacks per month	Frequency 1-3 attacks per day (up to 8) and usually occur daily for 2-3 months at a time

#### 4.2 Migraine classification<sup>1</sup>

##### 4.2.1 Migraine without aura

- A)** At least 5 attacks fulfilling criteria B-D.
- B)** Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
- C)** Headache has >2 of the following characteristics:
  - a) Unilateral location
  - b) Pulsating quality
  - c) Moderate or severe pain intensity
  - d) Aggravation by or causing avoidance of routine physical activity (e.g., walking climbing stairs)
- D)** During headache >1 of the following:
  - a) Nausea and/or vomiting.
  - b) Photophobia and phonophobia.
- E)** Not better accounted for by another ICHD-3 diagnosis

- a) 1 aura symptom spreads gradually over > 5 minutes, and/or > 2 symptoms occur in succession.
- b) each individual aura symptom lasts 5-60 minutes.
- c) 1 aura symptoms are unilateral.
- d) aura accompanied or followed in < 60 minutes by headache.
- D)** Not better accounted for by another ICHD-3 diagnosis, and TIA excluded.

##### 4.2.2 Migraine with aura

- A)** At least 2 attacks fulfilling criteria B and C
- B)** >1 of the following fully reversible aura symptoms:
  - a) Visual
  - b) Sensory
  - c) Speech and/or language
  - d) Motor Brainstem
  - e) Retinal
- C)** >2 of the following 4 characteristics:

##### 4.2.3 Chronic migraine

Headache occurring on 15 or more days/month for more than 3 months, which, on at least 8 days/month, has the feature of migraine headache.

- A)** Headache (migraine-like or tension type like) on 8 > days/month for > 3 months, and fulfilling criteria B and C
- B)** Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 Migraine with aura.
- C)** On > 8 days/month for > 3 months, fulfilling any of the following:
  - a) Criteria C and D for 1.1 Migraine without aura
  - b) Criteria B and C for 1.2 Migraine with aura
  - c) Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative.

D) Not better accounted for by another ICHD-3 diagnosis.

### 4.3 Episodic vs chronic migraine

Depending on frequency of attacks, migraine can be classified as episodic or chronic.

- Episodic migraine occurs on less than 15 days per month<sup>3</sup>.
- Chronic migraine is headache occurring on at least 15 days per month (with features of migraine headache on at least 8 days per month) for more than 3 months<sup>3</sup>.

### 4.4 Choice of therapy in primary and secondary care.

NICE advises the least costly clinically appropriate option should be selected for treatment, including patient preferences and drug and administration costs i.e., overall value proposition offered by the individual medicines (considering administration costs, dosage, price per dose and treatment frequency).

### 4.5 Defining migraine attacks, migraine days and headache days.

All preventative treatments recommended by NICE TAs, except for rimegepant (TA906), references migraine days. The exception, rimegepant, references migraine attacks.

- **Migraine attacks** are unique, migraines, which can last between a few hours and a few days.
- **Migraine days** are calendar days where the patient experiences headaches with features of migraine.
- **Headache days** are calendar days where the patient experiences headaches without features of migraine.

## 5. Primary care interventions

### 5.1 Acute treatment

There are two broad strategies:

- **Stepped approach:** Start with simple analgesics and if ineffective step-up e.g., to a triptan.
- **Stratified approach:** Target treatment based on attack severity (Associated with better patient outcomes).

**Opioids are not recommended** for the treatment of acute headache because of the significant risk of medication overuse and the most protracted withdrawal<sup>2</sup>.

See [British Association for the Study of Headache \(BASH\) guidelines](#) for more detailed information regarding treatment approach. See [Appendix 1](#) for further information regarding options which should be considered, where appropriate, before specialist referral.

Quantity of medication on patient's repeat prescribing should be limited to 2 treatments per week to support oversight of preventing [medication overuse headaches](#).

#### 5.1.1 Triptans

Triptan response is idiosyncratic, after 2 treatment failures with a particular triptan, or treatment is only effective for less than 2 of 3 migraines, consider switching to a new triptan.

Triptans taken in the preceding aura phase of the migraine are shown to be less effective. Advise patients to take early in the headache phase of the attack.

Compared to sumatriptan, some interventions provide superior outcomes<sup>4-7</sup>:

- **Lower adverse events:** Naratriptan 2.5 mg, almotriptan 12.5 mg & frovatriptan 2.5 mg.
- **Better 2-hour pain response:** Rizatriptan 10 mg, eletriptan 80 mg & almotriptan 12.5 mg.

- **Lower recurrence rate:** Frovatriptan 2.5 mg and eletriptan 40 mg.

Avoid triptans in those with ischaemic heart disease, cerebrovascular disease, previous myocardial infarction, and uncontrolled/severe hypertension.

### 5.1.2 Rimegepant (NICE TA919)

Rimegepant, an oral anti-CGRP, can be prescribed for use in acute migraine if, as per NICE TA919:

- Rimegepant is recommended as an option for the acute treatment of migraine with or without aura in adults, only if for previous migraines:
  - at least 2 triptans were tried and they did not work well enough or
  - triptans were contraindicated or not tolerated, and nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol were tried but did not work well enough.

Evidence suggests 30% of patients do not respond to any form of triptan<sup>8</sup>. Rimegepant's approval for acute use has been recommended with the intention of serving patients with repeated treatment failures to triptans, or where they are contraindicated.

As mentioned in [Acute treatment - Triptans](#), given the idiosyncratic response patients must triptans, it would be reasonable to try more than two triptans, before trialling rimegepant.

#### 5.1.2.1 Treatment efficacy

When prescribing acute treatments, it's important to ensure patients have a realistic expectation of efficacy:

- The end point of an effective treatment is a **significant response at two hours**, (the natural history for most attacks is to spontaneously improve in 4 hours<sup>2</sup>), in two out of three migraines.
- If a treatment is not effective at 2 hours, then it is unlikely to work in that attack at that dose and considering an alternative acute treatment or combination treatment would be reasonable<sup>2</sup>.

#### 5.1.2.2 Medication overuse headaches

Acute treatment on **more than 2 days per week** is associated with medication overuse, which renders preventive treatment less effective. It is important to educate patients on the risk associated with regular use of acute treatment.

Preventative treatment should be offered to those with four or more migraine days a month. Early self-referral by the patient to the GP when experiencing frequent migraines mitigates the risk of medication overuse headache.

## 5.2 Medication overuse headaches

Medication overuse headaches (MOH) can occur when ergotamine, triptans, or opioids are taken on 10 or more days per month, or 15 days for simple analgesics, for >3 months. Stopping the acute treatment is the priority to improve headaches. No difference in outcome with gradual vs abrupt withdrawal of acute treatment. For patients where opioid withdrawal may be a concern, see [local guidance related to deprescribing of opioids](#).

After stopping all acute treatments, withdrawal headaches can occur for up to 14 days. On average overuse with triptans results in a shorter withdrawal headache (~4 days). Full benefit may take up to 12 weeks to be achieved after withdrawal. Preventative treatment can be started during, or after, withdrawal of acute treatment.

If the patient does not experience any improvement within 2 months after stopping acute treatment, medication overuse headache can be excluded<sup>2</sup>. In such cases, if appropriate, [preventative treatment](#) should be considered.

## 5.3 Prophylaxis

Prophylactic treatment should be offered if the patient is experiencing 4 or more migraine days each month, or, those experience less frequent, but severe/debilitating migraines affecting quality of life.

If patient is using acute treatment  $\geq 2$  days per week consider and, if appropriate, manage medication overuse headache.

Patients should maintain a headache diary to understand the frequency, and severity of attacks. BASH have a [printable headache diary](#) available for patients to use, [Arden have their own headache diary template](#) which can be messaged to patients through. There are also several digital options available for smartphones via the app store. This includes, but is not limited to, [MigraineBuddy](#), [Migraine Monitor](#), and [N1-Headache](#).

#### Choice of prophylaxis treatment

Drug	Dose	Notes
<b>First line options</b>		
Propranolol	80-160mg daily (max 240mg daily) in divided doses	Avoid in those with Asthma.
Amitriptyline	Usual dose 25 - 75mg at night (start at 10 - 25mg then increase by 10mg - 25mg every 3-7 days if tolerated)	May help with co-morbidities such as depression/insomnia. Can be taken during pregnancy if benefits outweigh risks. Licensed in adults, off-label for young people aged 12 to 17 years. Nortriptyline may be an option for patients who experience side effects with Amitriptyline. Please note <b>Nortriptyline is unlicensed for migraine prophylaxis.</b>
<b>Alternative options</b>		
Topiramate	50–100mg daily in two divided doses (start at 25mg daily and increase in steps of 25mg each week)	<b>Contra-indicated</b> in females of childbearing potential <b>unless</b> the conditions of the Pregnancy Prevention Programme (PPP) are fulfilled which includes the use of highly effective contraception. See section “ <a href="#">5.3.2. Topiramate</a> ”. Avoid use in breastfeeding. <b>Use of topiramate in pregnancy is contra-indicated for migraine prophylaxis.</b>
Candesartan	2mg once daily, increase by 2mg every 4 weeks up to max 8mg twice daily	<b>Off-label indication.</b> Avoid in first trimester of pregnancy and contra-indicated in second and third trimesters.
Pizotifen	Initially 500 micrograms once daily at night, increased gradually to 1.5mg at night (or in divided doses). Dose to be adjusted to individual patient requirements, licensed maximum of 4.5mg daily, up to 3mg to be given as single dose.	Evidence of efficacy is limited and may be more effective in children than adults.
Acupuncture	10 sessions over 5–8 weeks	Evidence to support use in migraine & tension type headache. Not available on NHS, <b>Self-Care</b> .

See [Appendix 2: Prophylactic migraine treatment: Primary care](#) for further details on full algorithm.

### 5.3.1 Pregnancy

For patients planning to conceive, amitriptyline (1<sup>st</sup> line) or propranolol (2<sup>nd</sup> line) should be considered. Topiramate is contra-indicated in pregnancy and should only be used in women of childbearing potential if conditions of the Prevent Pregnancy Programme are met, including use of highly effective contraception.

At conception, prophylaxis treatment should be paused as migraine symptoms tend to improve during pregnancy. However, if medication withdrawal is deemed inappropriate or unsuitable:

- Amitriptyline ([UKTIS](#), [BNF](#), [NICE CKS](#)) can be continued through pregnancy if the prescriber feels the benefits outweighs the risks.
- Propranolol ([UKTIS](#), [BNF](#), [NICE CKS](#)) could be considered if the prescriber feels the benefits outweighs the risks. Use of propranolol in pregnancy requires further monitoring due to concerns of intra-uterine growth restriction. Use should be avoided where possible in third trimester.

For more complex patients deemed higher risk, consider seeking specialist advice.

For patients experiencing headache after 12 weeks gestation consider other, pregnancy-related causes (e.g., pre-eclampsia). Check BP & Urinalysis for abnormalities.

### 5.3.2 Topiramate

In June 2024, the MHRA released a major safety review relating to [topiramate use in pregnancy](#), which resulted in the [introduction of new safety measures](#). Specifically for migraine, topiramate is contraindicated:

- in women of childbearing potential **unless** the conditions of the Pregnancy Prevention Programme are fulfilled (for all indications) which includes the use of highly effective contraception
- in pregnancy for prophylaxis of migraine

Topiramate can be prescribed in primary care, but **only** where alternatives have failed and the conditions of the PPP have been fulfilled. All women of childbearing potential prescribed topiramate should be informed of:

- the risks associated with taking topiramate during pregnancy
- the risk that potentially harmful exposure to topiramate may occur before a woman is aware she is pregnant
- the need to fulfil the conditions of the Pregnancy Prevention Programme which includes use of highly effective contraception and a completed Risk Acknowledge Form
- the need to seek urgent medical advice if taking topiramate and is pregnant or planning a pregnancy

Topiramate should be avoided in breastfeeding as it is present in breast milk. Reported adverse effects to the infant include diarrhoea, drowsiness, irritability and inadequate weight gain.

#### 5.3.2.1 Supporting materials for topiramate safety alert

All resources can be found via the [MHRA drug safety update](#). Important documents include a [patient guide](#), a guide for [healthcare professionals](#), and [annual risk assessment forms](#) (also available in [Appendix 7](#)).

### 5.3.3 Treatment failure thresholds

Preventive medications must be titrated slowly to an effective or maximum tolerable dose and continued for at least 6-8 weeks to adequately assess effect<sup>2</sup>. Patients will need an accurate headache diary to adequately assess outcomes. Treatment is considered effective in:

- **Episodic migraine:** Headache days reduces by at least 50%
- **Chronic migraine:** Headache days reduces by at least 30%

### 5.3.4 Referral to secondary care

If patients fail with three different prophylactic interventions, in more complex patients which fall outside of primary clinician competency, or unique patients which do not fit within the pathway, consider seeking specialist advice e.g. via Advice and Guidance or routine referral.

Oral rimegepant, or atogepant, may be recommended by the specialist to prescribe in primary care. This would be after initiation and 12-week review for efficacy by the specialist, see [Oral anti-CGRP provision via primary care](#) for further details.

### 5.3.5 Discontinuing prophylactic treatment

If prophylactic medication is working well, it should be continued for at least 6 months. Prophylactic treatment should be reviewed in all patients after 6-12 months and a gradual tapering of dose considered; most patients do not require ongoing prophylactic treatment so it can be gradually withdrawn. If symptoms return, the patient should be restarted.

## 6. Secondary care interventions

Patients who have tried three or more prophylactic interventions at maximum tolerated doses for at least two months (or where these are contraindicated/not tolerated), where [medication overuse headache](#) has been ruled out, and are experiencing four or more migraine days per month are eligible to receive specialist prophylactic interventions.

### 6.1 Episodic migraine

Consider anti-CGRP (oral, subcutaneous, or intravenous) for patients who are experiencing:

- Have 4 or more, but less than 15 headache days per month.
- Less than 8 of those have features of a migraine.

For treatment to be considered effective, headache days should reduce by 50% by the end of the initial review period (12 weeks).

### 6.2 Chronic migraine

Consider anti-CGRP (oral, subcutaneous, or intravenous) or botulinum toxin type A for patients who are experiencing 15 or more headache days per month.

For treatment to be considered effective, headache days should reduce by 30% by the end of the initial review period (12 weeks for anti-CGRP, 2 treatment cycles for botox).

### 6.3 Choice of therapy

For all interventions, the patient must have tried  $\geq 3$  preventative drugs which have failed, or preventative treatment is contraindicated or not tolerated. See section [choice of therapy in primary and secondary care](#) regarding choosing best value treatment option.

#### 6.3.1 Summary of available interventions

Drug	Route of administration	NICE TA	Episodic migraine	Chronic Migraine	Review period
Botox	Intramuscular	260	✗	✓	2x treatment cycles (~24 weeks)
Galcanezumab	Subcutaneous	659	✓	✓	12 weeks
Erenumab	Subcutaneous	682	✓	✓	12 weeks
Fremanezumab	Subcutaneous	764	✓	✓	12 weeks
Eptinezumab	Intravenous	871	✓	✓	12 weeks
Rimegepant	Oral	906	✓*	✗*	12 weeks
Atogepant	Oral	973	✓	✓	12 weeks

\* Note, for rimegepant eligibility migraine **attacks** must be considered, rather than migraine days.

### 6.3.1.1 Sodium Valproate

Sodium valproate is not licensed for migraine prophylaxis.

For male patients over the age of 55, or women without childbearing potential, sodium valproate may be considered when there are no other suitable treatment options.

Males initiated on Sodium Valproate under the age of 55 years where there is considered a reproductive risk must have a completed Risk Acknowledge Form (RAF) signed by two specialists that documents there is no other effective or tolerated treatment; this form does not need to be completed annually. If the reproductive risks do not apply, for example infertility, the reason must be documented on the RAF and can be signed by one specialist.

In women without childbearing potential, there would be no need for an annual review, and completing the form once would be sufficient. Risk assessments to be completed can be found in [Appendix 4 for men](#), and [Appendix 5 for women](#). See full [MHRA collection for valproate safety measures for detailed information](#).

Sodium valproate for migraine prophylaxis in all women under 55 years of childbearing potential has the formulary classification of **Black**, not commissioned no NHS prescribing in primary or secondary care. In women over the age of 55 years sodium valproate for the indication of migraine prophylaxis has the formulary classification of Amber Initiate, secondary care clinician to initiate and stabilise before transfer of prescribing to primary care.

### 6.3.2 Oral anti-CGRP provision via primary care

Rimegepant may be initiated in primary care for the treatment of Acute Migraine. Treatment with rimegepant or atogepant for use in preventing migraines should only be initiated by a specialist in the management of migraines. The specialist will initiate and provide the first 12-weeks of medication to the patient.

At the 12-week review, patients who are responsive to treatment (defined in sections regarding [episodic](#) and [chronic](#) migraine above), should be provided with a bridging prescription, and discharged to primary care for their GP to continue prescribing.

No further additional monitoring is required outside of what would normally be expected for migraine prophylactic treatment, specifically annual reviews to monitor efficacy and patient adherence.

## 7. Blueteq

Blueteq forms which comply with this pathway are available. Funding approval for the tariff excluded high-cost drugs will be required by submission of the relevant Blueteq form prior to treatment. The Blueteq forms contain a list of relevant criteria that the patient must meet to secure funding. Any patients who do not meet these criteria will require an individual funding request, further information found on [Knowledge NoW](#). All use is subject to external audit.

## 8. Pregnancy & breastfeeding

### 8.1 Pregnancy

There is limited data for safety of biologic medicines in pregnancy and breastfeeding. The decision to continue medicines throughout pregnancy must be individualised. This should consider the various therapies, severity of the mother's health prior to therapy, risk of a disease flare if therapy is discontinued, and the impact of a disease flare on the mother and unborn child. This should be discussed by a multi-disciplinary team.

#### 8.1.1 Manufacturer guidance

Animal studies for galcanezumab, erenumab, fremanezumab, eptinezumab & rimegepant do not indicate direct or indirect harmful effects with respect to reproductive toxicity<sup>9-13</sup>. The manufacture advises that it would be preferable to avoid use in pregnancy as a precautionary measure but does not explicitly contraindicate it.

Animal studies for atogepant indicate reproductive toxicity and should be avoided<sup>14</sup>.

## 8.2 Breastfeeding

The decision to breastfeed or continue/discontinue therapy should consider both the benefits of breastfeeding to the infant and the benefits of therapy to the mother.

### 8.2.1 Manufacturer guidance

For galcanezumab, erenumab, fremanezumab and eptinezumab have similar recommendations within their SPC:

“There are no data on the presence of [drug] in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG is known to be excreted in breast milk during the first days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to breast-fed infants cannot be excluded during this short period. Afterwards, use of [drug] could be considered during breast-feeding only if clinically needed.”<sup>10–13</sup>

Rimegepant, has had a small study of 12 breastfeeding mothers, which shows minimal concentrations in breast milk, where “The relative percentage of a maternal dose estimated to reach the infant is less than 1%”<sup>9</sup>.

For atogepant, animal studies on lactating rats indicated “oral dosing with atogepant resulted in levels of atogepant in milk approximately 2-fold higher than those in maternal plasma”<sup>14</sup>.

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# Migraine acute treatment



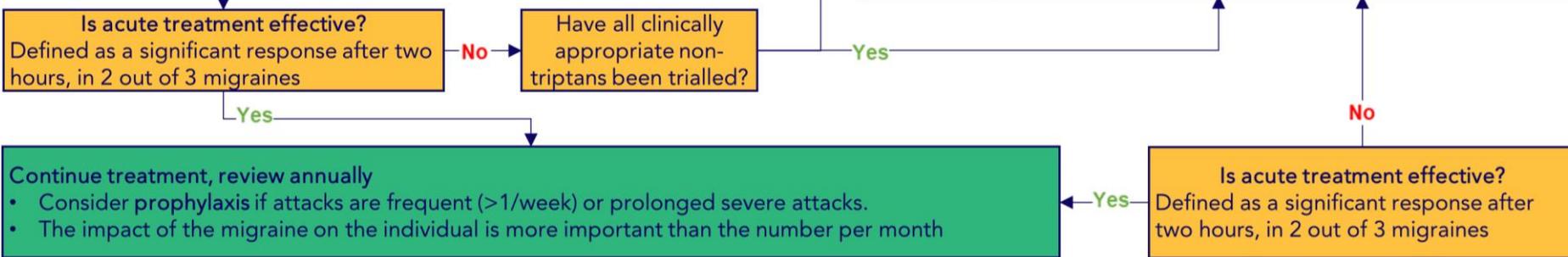
- Avoid opiates and restrict use of acute medication to 2 days/week
- Warn patients about risk of developing medication overuse headache
- Lifestyle advice <sup>[Note 1]</sup>

## Acute migraine treatment

Migraine type:	+/- aura +/- nausea /vomiting	Menstruation related	During pregnancy <sup>[Note 2]</sup>
To be taken as soon as symptoms develop			
Aspirin 900mg	Yes - 1 <sup>st</sup> line +/- triptan	No	No
Ibuprofen 400-600mg	Yes - 1 <sup>st</sup> line +/- triptan	No <sup>[Note 3]</sup>	< 28 weeks' gestation: Yes ≥ 28 weeks' gestation: No
Paracetamol 1000mg	Yes +/- triptan	Yes +/- triptan	Yes - 1 <sup>st</sup> line
Antiemetics	Prochlorperazine, Metoclopramide (risk of EPSEs) or , Domperidone		
To be taken once headache has started			
Triptans <sup>[Note 4]</sup>	Yes <sup>[4]</sup>	Yes <sup>[Note 4]</sup> 1 <sup>st</sup> line	Sumatriptan If the paracetamol & ibuprofen have failed

Drug	Formulation	Dose (mg)	£/Dose
Sumatriptan	Tablet	100	£0.20
Naratriptan	Tablet	2.5	£0.22
Rizatriptan	Tablet	10	£1.65
Rizatriptan	Orodispersible	10	£2.10
Almotriptan	Tablet	12.5	£2.81
Frovatriptan	Tablet	2.5	£3.34
Rizatriptan	Lyophilisate	10	£4.46
Zolmitriptan	Tablet	5	£4.81
Zolmitriptan	Orodispersible	5	£5.89
Zolmitriptan	Nasal Spray	5	£6.08
Sumatriptan	Nasal Spray	20	£7.08
Eletriptan	Tablet	40	£7.50
Rimegepant <sup>[5]</sup>	Tablet	75	£12.90
Sumatriptan	S.C. Injection	6	£24.10

- When prescribing a triptan start with the one that has the lowest acquisition cost (NICE CG150)
- After 2 treatment failures with a particular triptan, an alternative triptan is recommended
- Around 30% patients do not respond to any triptan
- Lack of response to one triptan does not predict response to other triptans





## Migraine prophylaxis (primary care)

Patient has frequent attacks (>1/week) or prolonged severe attacks  
 Note: The impact of the migraine on the individual is more important than the number per month

Is patient using acute treatment >2 days per week?

Yes

No

Is patient pregnant/trying to conceive?

No

Yes

**Before conception:**  
 Stop prophylaxis before/at conception – symptoms often improve during pregnancy.

**Headache after 12 weeks' gestation:**  
 Consider other pregnancy-related causes – check BP/Urinalysis. Otherwise seek specialist advice

Seek specialist advice/referral

**Consider medication overuse headaches**

- No difference in outcome with gradual vs abrupt withdrawal of acute treatment.
- After stopping all acute treatments, withdrawal headaches can occur for up to 14 days. On average overuse with triptans is shorter (~4 days)
- Can take up to 12 weeks for full benefit of withdrawal to be achieved.
- Preventative treatment can be started during, or after, withdrawal of acute treatment.

Drug	Dose	Notes
Propranolol	80-160mg daily (max 240mg) in divided doses	Avoid in those with Asthma.
Amitriptyline	Usual dose 25 - 75mg at night (start at 10 - 25mg then increase by 10mg - 25mg every 3-7 days if tolerated)	May help with co-morbidities such as depression/insomnia. Can be taken during pregnancy if benefits outweigh risks. Licensed in adults, off-label for young people aged 12 to 17 years. Nortriptyline may be an option for patients who experience side effects with Amitriptyline.
Topiramate	50-100mg daily in two divided doses (start at 25mg daily and increase in steps of 25mg each week)	<b>Contra-indicated</b> in females of childbearing potential unless the conditions of the Pregnancy Prevention Programme (PPP) are fulfilled which includes the use of highly effective contraception. See section "5.3.2. Topiramate". Avoid use in breastfeeding. <b>Use of topiramate in pregnancy is contra-indicated for migraine prophylaxis.</b>
Candesartan	2mg once daily, increase by 2mg every 4 weeks up to max 8mg twice daily	Unlicensed. Avoid in first trimester of pregnancy and contra-indicated in second and third trimesters.
Pizotifen	Initially 500 micrograms once daily at night, increased gradually to 1.5mg at night (or divided doses).	Evidence of efficacy is limited and may be more effective in children than adults. Dose to be adjusted to individual patient requirements, <i>licensed maximum of 4.5mg daily, up to 3mg to be given as single dose.</i>

Have 3 different prophylactic treatments had a lack of response to the highest tolerated dose, used for 3 months?

Yes

Loss of efficacy

**Is prophylaxis treatment effective?**  
 Failure is a lack of response<sup>6</sup> to the highest tolerated dose, used for 3 months.

No

Continue treatment, review as appropriate.

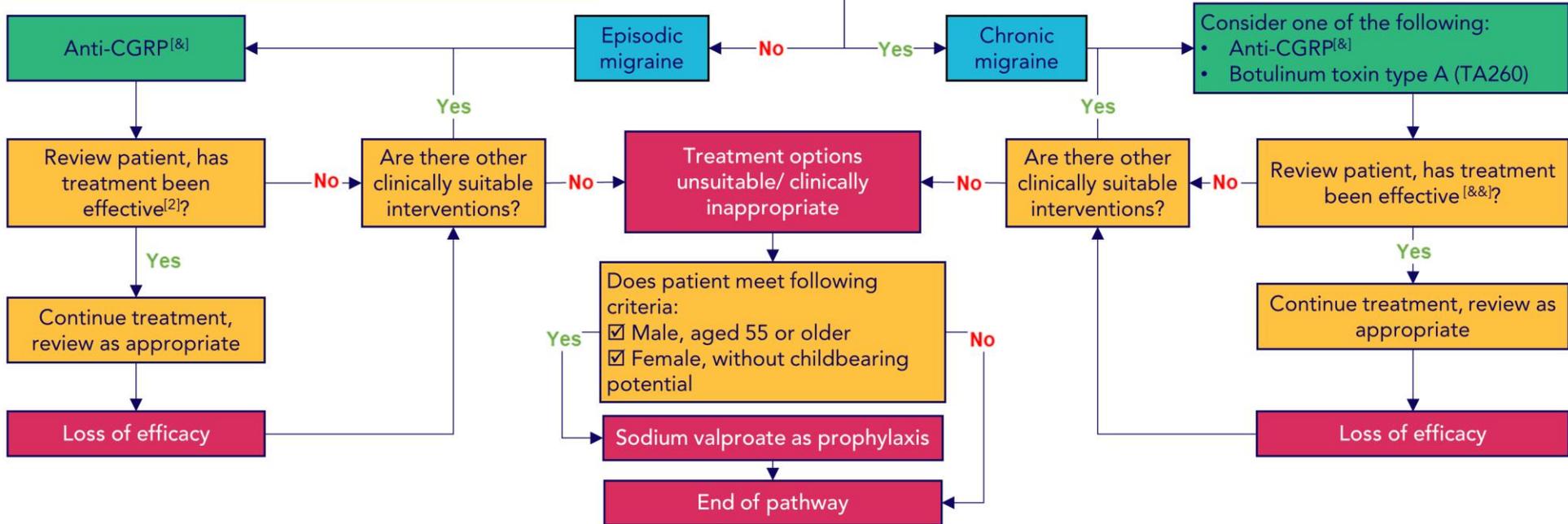
# Migraine prophylaxis (secondary care)



**Patient must:**  
 Have four or more migraine days per month  
 Medication overuse headache has been addressed

**Plus meet one of the following criteria:**  
 The patient has tried  $\geq 3$  preventative drugs and failed  
 Preventative treatment is contraindicated or not tolerated

Does patient meet following criteria:  
  $\geq 15$  headache days/month  
  $\geq 8$  of those are migraine days/have features of migraine



**[1]: Anti-CGRP**

Subcutaneous Anti-CGRP: Galcanezumab TA659  
 Intravenous Anti-CGRP: Eptinezumab TA871  
 Oral Anti-CGRP: Rimegepant<sup>[i]</sup> TA906  
 Erenumab TA682  
 Fremanezumab TA764  
 Atogepant TA973

**[i] Rimegepant is only available if:**

- Have a maximum of 14 migraine attacks per month
- Have a maximum of 14 headache days per month

**[2]: NICE review thresholds:**  
 Adequate response defined as:

Episodic migraine: Headache days reduces by at least 50%  
 Chronic migraine: Headache days reduces by at least 30%

**Within:**

- Anti-CGRP: 12-weeks
- Botox: 2 treatment cycles

## Additional notes



### [1]: Lifestyle advice

- Appropriate water intake, regular meals, adequate sleep and exercise
- Avoid known triggers
- Restrict caffeine intake
- Relaxation activities (mindfulness, yoga, meditation)

### [2] Pregnancy

Only if lifestyle advice<sup>[Note 1]</sup> is ineffective, exclude pre-eclampsia/CVT if > 12 weeks' gestation.

### [3] Ibuprofen/NSAIDs in menstruation related migraine

There is a small amount of evidence that mefenamic acid is effective for acute treatment of patients with menstrual migraine

### [4] Triptans

Migraine +/- aura: 1<sup>st</sup> line: Sumatriptan

Migraine + aura & nausea/vomiting: Nasal zolmitriptan or subcutaneous sumatriptan

Menstrual-related migraine: For menstrual-related migraine that does not respond to standard acute treatment, consider for the expected migraine days:

- Frovatriptan 2.5 mg twice a day or
- Zolmitriptan 2.5 mg twice - three times a day

### [5] Rimegepant - NICE TA919 for treatment of migraine

Rimegepant only recommended if: 2 triptans have been ineffective. If triptans are contraindicated, NSAIDs/paracetamol were ineffective.

### [6] Expected response from prophylactic intervention

Episodic migraine: Headache days reduces by at least 50%

Chronic migraine: Headache days reduces by at least 30%

### [7] Topiramate- Pregnancy Prevention Programme

In June 2024, the MHRA released a major safety review relating to [topiramate use in pregnancy](#). For further detail see [guidance on introduction of new safety measures](#). For migraine, topiramate is contraindicated:

- in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled (for all indications).
- in pregnancy for prophylaxis of migraine.

## 14. Appendix 5: Male risk assessment form for sodium valproate

# Risk Acknowledgement Form FOR MALE PATIENTS STARTING VALPROATE

This form is used for new male patients starting a medicine containing valproate.

Valproate should not be started in male patients aged under 55 years unless two specialists consider and document that there is no other effective or tolerated treatment or the risk of infertility or potential risk of testicular toxicity do not apply.

This form applies to male patients aged under 55 years because this is the age group most likely to be affected by the risk of infertility and the potential risk of testicular toxicity. However, if these risks do not apply (e.g., the patient is permanently infertile), the countersigning specialist is not required, and the specialist prescriber should use this form to document the reason and record in the patients notes.

- This form is to support and record the discussion of risks with male patients aged under 55 years starting treatment with valproate or their responsible person or parents/care givers (if applicable).
- The specialist prescriber must provide this form to male patients aged under 55 years being started on valproate (Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil) – or to their “responsible person”.
- In this instance, a responsible person is a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision, or a person acknowledging that the treatment is in the best interests of the patient.
- The countersigning specialist must document their decision.

Once completed, a copy of this form should be given to the patient or their responsible person and stored in their medical notes, it should also be shared with all healthcare professionals listed in the table below.

Name of patient:

---

Patient's date of birth:

---

Patient's NHS number:

---

Patient's hospital number:

---

Name and contact details of specialist prescriber:

---

Role and unique identifier:

---

Signature of specialist prescriber:

---

Date of signature:

---

Name of countersigning specialist:

---

Role and unique identifier:

---

Signature of countersigning specialist (if needed specialist prescriber can sign here to confirm that discussion with countersigning specialist has occurred):

---

Date of signature:

---

Name and address of patient's GP:

---

Date form completed:

---

### Step 1: Specialist prescriber and countersigning specialist: Document the prescribing decision

Actions to be completed by the specialist prescriber to confirm the prescribing decision	Initial to confirm all that apply
<ul style="list-style-type: none"> <li>The patient's condition does not respond adequately to other treatments or other treatments are not tolerated.</li> </ul>	
<ul style="list-style-type: none"> <li>I have discussed the risks with the patient, and I consider the balance of benefits and risks to be favourable.</li> </ul>	
<ul style="list-style-type: none"> <li>I have offered the patient a copy of the Patient Guide and they know where to get further information.</li> </ul>	
<ul style="list-style-type: none"> <li>The risk of infertility or potential risk of testicular toxicity do not apply for the following reason(s):</li> </ul>	

To be completed by the countersigning specialist prescriber (can be completed by specialist prescriber following discussion with countersigning specialist, if needed)	Initial to confirm all that apply
<ul style="list-style-type: none"> <li>Their condition does not respond to other treatments or other treatments are not tolerated.</li> </ul>	
<ul style="list-style-type: none"> <li>They have been informed of the risks and I consider the balance of benefits and risks to be favourable.</li> </ul>	

### Step 2: Specialist prescriber: Explain the risks to the patient or responsible person

Information to be discussed with the patient or responsible person	Initial to confirm you have discussed
<b>Fertility while on valproate</b> <ul style="list-style-type: none"> <li>Valproate may cause infertility in some male patients. This can make it difficult to have a baby.</li> <li>Male infertility may be reversible after valproate is stopped or after a dose reduction in some patients.</li> </ul>	
<b>Effects on male reproductive system</b> <ul style="list-style-type: none"> <li>Some studies in male animals have shown valproate to have an adverse effect on parts of the male reproductive system. These include toxic effects on the testes (testicles).</li> <li>The weight of the developing testes (testicles) was lower in young animals given valproate and it is unclear what this means for humans.</li> </ul>	
<b>Risks of stopping valproate without medical advice</b> <ul style="list-style-type: none"> <li>Patients on valproate should not stop taking their medicine or change their dose unless they are told to do so by a specialist.</li> <li>This is because their condition may become worse, including an increase in seizures in patients treated for epilepsy and an increased risk of relapse in patients treated for bipolar disorder.</li> </ul>	

### Step 3: To be completed by the patient or responsible person

Completing this section of the form confirms that you, the patient (or your responsible person), have discussed and acknowledge the risk of male infertility, and the toxic effect of valproate on the testes of animals using valproate. It is recommended that you keep a copy of this form which will also be added to your medical notes.

I have discussed the benefits and risks of valproate compared to other treatments with my specialist prescriber and I acknowledge that:	Initial to confirm you acknowledge each item
<ul style="list-style-type: none"> <li>Valproate may cause infertility in some male patients and that this infertility may be reversible after valproate is stopped or after the dose is reduced for some patients.</li> </ul>	
<ul style="list-style-type: none"> <li>There are animal studies showing that valproate may have an effect on testes (testicles) and it is unclear what this means for humans.</li> </ul>	
<ul style="list-style-type: none"> <li>I should not stop valproate or change the dose unless told to do so by my specialist as my condition may become worse, including an increase in seizures in patients treated for epilepsy and an increased risk of relapse in patients treated for bipolar disorder.</li> <li>If my condition becomes worse, I should contact my specialist straight away.</li> </ul>	
<ul style="list-style-type: none"> <li>I have been offered the Patient Guide and know where I can access this information online using the QR code on the leaflet in the pack.</li> </ul>	
<b>Name of patient:</b>	
<b>Name of responsible person (if applicable):</b>	
<b>Signature of patient (or responsible person):</b>	<b>Date:</b>

15. Appendix 6: Female risk assessment form for sodium valproate

## Annual Risk Acknowledgement Form for Female Patients VALPROATE HAS RISKS IN PREGNANCY

Children exposed to valproate during pregnancy have a high risk for congenital malformations and neurodevelopmental disorders which may lead to permanent disability.

Valproate should not be used in female patients aged under 55 years unless two specialists (specialist prescriber and countersigning specialist) independently consider and document, in this form, that there is no other effective or tolerated treatment. This form outlines the conditions of **prevent** - the valproate Pregnancy Prevention Programme and when these must be fulfilled.

Female patients who have a permanent reason that they do not have the potential to get pregnant (e.g., post-menopausal patients or those after hysterectomy) do not need to complete this form beyond step 1. This form can be used to support documentation in the medical notes that **prevent** does not apply to this patient.

- This form is used to support and record the prescribing decision and, where applicable, discussion with the patient or their responsible person of the risks associated with the use of valproate during pregnancy and the measures needed to minimise the risks in female patients.
- The specialist prescriber must provide this form to female patients treated with valproate (Epilim, Depakote, Convulex, Episenta, Epival, Sodium Valproate, Syonell, Belvo & Dyzantil) – or to their “responsible person” i.e., a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision, or a person acknowledging that the treatment is in the best interests of the patient.
- The decision of the countersigning specialist must be documented in step 2. A countersigning specialist is only required for patients newly starting valproate and for existing female patients at one annual review. Subsequent annual reviews do not require the countersigning specialist unless the patient’s circumstances have changed.

Once completed, a copy of this form should be given to the patient or their responsible person and stored in their medical notes, it should also be shared with all healthcare professionals listed in the table below.

Name of patient:	_____	Patient’s date of birth:	_____
Patient’s NHS number:	_____	Patient’s hospital number:	_____
Name and contact details of specialist prescriber:	_____	Role and unique identifier:	_____
Signature of specialist prescriber:	_____	Date of signature:	_____
Name of countersigning specialist:	_____	Role and unique identifier:	_____
Signature of countersigning specialist (if needed specialist prescriber can sign here to confirm that discussion with countersigning specialist has occurred):	_____	Date of signature:	_____
Name and address of patient’s General Practitioner (GP):	_____		
Date form completed:	_____		

**WARNING:** Prescribing valproate to a woman of childbearing potential without the conditions of **prevent - the Pregnancy Prevention Programme** being fulfilled is contraindicated and represents an unlicensed use of the drug. Use of valproate during pregnancy for bipolar disorder, and during pregnancy for epilepsy (unless there is no other effective or tolerated treatment), are both unlicensed. This is the case even when treatment is based on an informed choice made by the patient.

More information can also be found online at [www.medicines.org.uk](http://www.medicines.org.uk) by entering “valproate” in the search box and then clicking on “Risk Materials” next to any of the medicines listed.

# Annual Risk Acknowledgement Form for Female Patients VALPROATE HAS RISKS IN PREGNANCY

## Step 1 – Specialist prescriber: Establish whether the patient is at risk of the reproductive harms of valproate

The following issues should be considered when evaluating the risks associated with the use of valproate during pregnancy:

- Women of childbearing potential (from menarche to menopause) who are taking any medicine containing valproate, regardless of the indication, should fulfil all the conditions of **prevent** unless there are compelling reasons that there is no risk of pregnancy which should be documented below.
- If the potential for not becoming pregnant is permanent, the reason should be documented below and the conditions of **prevent DO NOT** need to be fulfilled.
- Female children who have not yet reached menarche (not started her periods) **DO NOT** need to fulfil the conditions of **prevent**, but they and their responsible person need to be aware of the risks for the future. You should provide a copy of the Patient Guide and remind the responsible person to contact their GP once the female child using valproate experiences menarche. Their GP will refer the patient back to the specialist prescriber.
- If the compelling reason(s) suggesting no risk of pregnancy may be subject to change, the risks should be discussed at subsequent annual reviews or sooner if their circumstances change.

If you consider there is a reason that indicates **prevent** does not apply, *tick* which reason applies and record here. If the reason is permanent, steps 2, 3 and 4 do not need to be completed.

To be completed by the specialist prescriber if they consider <b>prevent</b> - the valproate Pregnancy Prevention Programme (PPP) - is not needed	
<input type="checkbox"/>	The patient has not yet reached menarche at the time of this appointment. I have asked the patient and their family to inform their GP to refer the patient back to the specialist prescriber if this changes before their next annual review.
<input type="checkbox"/>	The absence of pregnancy risk is considered to be permanent for the following reason ( <i>insert reason</i> ):
<input type="checkbox"/>	There are other reasons that conditions of <b>prevent</b> are not applicable ( <i>insert reason</i> ):

More information can also be found online at [www.medicines.org.uk](http://www.medicines.org.uk) by entering “valproate” in the search box and then clicking on “Risk Materials” next to any of the medicines listed.

# Annual Risk Acknowledgement Form for Female Patients VALPROATE HAS RISKS IN PREGNANCY

## Step 2: Specialist prescriber and countersigning specialist: Document the prescribing decision.

Actions to be completed by the specialist prescriber to confirm the prescribing decision	Initial to confirm all that apply
• The patient's condition does not respond to other treatments or other treatments are not tolerated.	
• I have discussed the risks with the patient, and I consider the balance of benefits and risks to be favourable.	
• I have offered the patient a copy of the Patient Guide and they know where to get further information.	
• The patient is in the process of changing treatment away from valproate.	

To be completed by the countersigning specialist (can be completed by specialist prescriber following discussion with countersigning specialist if needed)	Initial to confirm all that apply
• I confirm that this patient should be treated with valproate.	
• The patient's condition does not respond to other treatments or other treatments are not tolerated.	
• The patient has been informed of the risks and I consider the balance of benefits and risks to be favourable.	
• The patient is in the process of changing treatment away from valproate.	

## Step 3: Specialist prescriber: Explain the risks to the patient or responsible person.

The risks must be discussed with the patient or their responsible person (if applicable), and the patient (or responsible person) must sign the subsequent section of this form to confirm they have discussed and acknowledge the risks of taking valproate during pregnancy.

Information to be discussed with the patient or their responsible person	Initial to confirm you have discussed
That their medication should be reviewed regularly (at least once a year) and their medication may need to be changed if their circumstances change, increasing the risks.	
That valproate can cause serious harm to an unborn baby if taken by a mother during pregnancy, which may lead to permanent disability. The overall risks in children exposed to valproate during pregnancy are: • an approximately 11% chance of physical birth defects • up to a 30% to 40% chance of neurodevelopmental disorders	
Explain the conditions of <b>prevent - the Pregnancy Prevention Programme</b> and why these must be fulfilled.	
The need for a negative (ideally serum) pregnancy test result before starting treatment with valproate and, if needed, further pregnancy tests at appointments thereafter.	
The need to use effective birth control (contraception), without interruption, throughout treatment with valproate.	
The need to consult their general practitioner (GP) for referral to the specialist as soon as they are planning pregnancy to ensure timely discussion and switching to another treatment before the child is conceived and before birth control (contraception) is discontinued.	
The need for the patient to contact their GP immediately, to be urgently referred to their specialist prescriber for an urgent review of their treatment in case of suspected or unplanned pregnancy.	
Explain the risks of stopping valproate without medical advice. Patients on valproate should not stop taking their medicine or change their dose unless they are told to do so by a specialist. This is because their condition may become worse, including an increase in seizures in patients treated for epilepsy and an increased risk of relapse in patients treated for bipolar disorder.	

More information can also be found online at [www.medicines.org.uk](http://www.medicines.org.uk) by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines listed.

# Annual Risk Acknowledgement Form for Female Patients

## VALPROATE HAS RISKS IN PREGNANCY

### Step 4: To be completed by the patient or responsible person

Completing this section of the form confirms that you, the patient (or your responsible person), have discussed and acknowledge the risks of using valproate during pregnancy and the measures needed to reduce the risk with your specialist prescriber.

It is recommended that you keep a copy of this form which will also be added to your medical notes.

I have discussed the benefits and risks of valproate compared to other treatments with my specialist prescriber and I acknowledge that:	Initial to confirm you acknowledge each item
My medication should be reviewed regularly (at least once a year) and may need to be changed depending on my circumstances.	
Valproate can cause serious harm to an unborn baby if taken by a mother during pregnancy and may lead to permanent disability. The risks in children whose mothers took valproate during pregnancy are: <ul style="list-style-type: none"> <li>• An approximately 11% chance of physical birth defects</li> <li>• Up to 30% to 40% of children may have problems with early childhood development. Children affected can be slow to walk and talk, intellectually less able than other children, and have difficulty with language and memory, or problems with development (behaviour and learning disorders) which can be seriously debilitating and/or permanent.</li> </ul>	
I am aware of the need to have a negative pregnancy test before starting treatment with valproate and if needed, further pregnancy tests at subsequent appointments.	
I am aware of the need to use an effective method of birth control (contraception), without stopping or interruption, while taking valproate.	
The options for effective long-term methods of birth control (contraception) have been discussed (or a consultation has been planned with a professional who can give me advice).	
I need to consult my GP to be referred to my specialist prescriber as soon as I start thinking about becoming pregnant. This is to make sure I have time to switch to another treatment before I come off birth control (contraception).	
I should request an urgent appointment with my GP, to be urgently referred to my specialist prescriber, if I think I am pregnant.	
I have been offered a copy of the valproate Patient Guide and know where to find more information online using the QR code on the leaflet in the pack.	
I should not stop valproate or change the dose unless told to do so by my specialist as my condition may become worse, including an increase in seizures in patients treated for epilepsy and an increased risk of relapse in patients treated for bipolar disorder.	
<b>Name of patient:</b>	
<b>Name of responsible person (if applicable):</b>	
<b>Signature of patient (or responsible person):</b>	<b>Date:</b>

More information can also be found online at [www.medicines.org.uk](http://www.medicines.org.uk) by entering “valproate” in the search box and then clicking on “Risk Materials” next to any of the medicines listed.

## 16. Appendix 7: Female risk assessment form for topiramate

### Information for Patients

Topiramate is one of a range of effective medicines for the prevention of migraine. As with all medicines it has risks as well as benefits.

#### **If you take topiramate when pregnant it can seriously harm the baby.**

Children whose mothers take topiramate during pregnancy have a higher risk of:

- Being born with birth defects
- Mental development and learning problems, such as autism spectrum disorder and attention deficit hyperactivity disorder
- Being smaller and weighing less than expected at birth (small for gestational age)

Due to these risks, patients who can get pregnant must use effective birth control (contraception) at all times while taking topiramate. They must also follow the requirements of the Pregnancy Prevention Programme.

This Annual Risk Awareness Form is to make sure you know about the risks of taking topiramate during pregnancy. Your healthcare professional will go through this form with you. You will receive a copy of the completed form – please keep the copy safe.

### Information for the healthcare professional

Topiramate should not be used in patients of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled. This form outlines the conditions of the topiramate Pregnancy Prevention Programme and when these must be fulfilled. The form should be used to support and record the prescribing decision.

You must complete this form for **all patients of childbearing potential**. Step 1 is completed by you in discussion with the patient. Step 2 is completed by you and the patient – this part records the discussions about the risks associated with the use of topiramate during pregnancy and the measures needed to minimise those risks. Once completed, give a copy of the form to the patient and store it in their medical notes.

**WARNING:** Prescribing topiramate to a patient of childbearing potential without the Pregnancy Prevention Programme conditions being fulfilled is contraindicated and represents an unlicensed use of topiramate. This is the case even when treatment is based on an informed choice made by the patient.

<b>Name of patient:</b>	<b>Patient's date of birth:</b>
<b>Patient's NHS/CHI number:</b>	<b>Patient's hospital number*:</b>
<b>Name and contact details of healthcare professional:</b>	<b>Role and unique identifier:</b>
<b>Signature of healthcare professional:</b>	<b>Date of signature:</b>
<b>Name and address of patient's GP*:</b>	
<b>Date form completed:</b>	

\* If applicable

## Step 1: Establish whether the patient is at risk of the reproductive harms of topiramate

- The risks apply to all patients who can get pregnant (from when first period occurs to menopause) and are taking any medicine containing topiramate
- If there is a possibility of pregnancy, patients will need to follow the conditions of the Pregnancy Prevention Programme

If you consider there is a compelling reason that indicates there is no potential for pregnancy, tick which reason applies and record here. In this event, step 2 does not need to be completed.

To be completed by the healthcare professional when they consider the topiramate Pregnancy Prevention Programme (PPP) is not needed	
<input type="checkbox"/>	The absence of pregnancy risk is permanent for the following reason (insert reason):
<input type="checkbox"/>	There are other reasons that conditions of the topiramate Pregnancy Prevention Programme are not applicable (insert reason):
<b>Signature of patient to confirm that PPP is not needed at this time</b>	<b>Date</b>

## Step 2: Explain the risks and document awareness

Healthcare professionals and patients must both complete this section of the form. This records that you have discussed the risks of taking topiramate during pregnancy and the measures needed to reduce the risks. The patient must also sign the form to confirm they are aware of these risks.

Information to be discussed with the patient	Healthcare professional to initial to confirm you have discussed	Patient to initial to confirm you are aware
Their medication should be reviewed regularly (at least once a year). At this review your healthcare professional will decide with you whether topiramate continues to be the best treatment for you. This will take into account any change in your circumstances.		
Topiramate can cause serious harm to an unborn baby if taken by a mother during pregnancy. For babies of mothers who take topiramate while pregnant the risks are: <ul style="list-style-type: none"> <li>• Around 4 to 9 babies in every 100 will have birth defects compared with 1 to 3 babies in 100 of mothers in the general population.</li> <li>• A 2-3 times higher risk of autism spectrum disorder, attention deficit hyperactivity disorder and intellectual disabilities compared with babies born to women without epilepsy not taking epilepsy medicines.</li> <li>• Around 18 babies in every 100 will be born small for gestational age compared with around 5 in every 100 babies of mothers in the general population.</li> </ul>		
Need for a pregnancy test to exclude pregnancy before starting topiramate. Further pregnancy tests may be needed during treatment.		
Need to use effective birth control (contraception) at all times during treatment with topiramate and for four weeks after stopping topiramate.		
The importance of discussing any plans for a pregnancy with their healthcare professional as soon as they are planning pregnancy to ensure timely discussion.		
In case of suspected or unplanned pregnancy, and patient is only taking topiramate to prevent migraine, they need to: <ul style="list-style-type: none"> <li>• stop taking topiramate straight away.</li> <li>• contact their healthcare professional.</li> </ul>		
A copy of the Patient Guide has been offered		
<b>Signature of healthcare professional:</b>	<b>Date</b>	
<b>Signature of Patient:</b>	<b>Date</b>	

## 17. Appendix 8: NICE technology appraisal detail

TA260	<p>Botulinum toxin type A for the prevention of headaches in adults with chronic migraine</p> <ol style="list-style-type: none"> <li>1. Botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with chronic migraine (defined as headaches on at least 15 days per month of which at least 8 days are with migraine):             <ol style="list-style-type: none"> <li>1.1. that has not responded to at least three prior pharmacological prophylaxis therapies and</li> <li>1.2. those condition is appropriately managed for medication overuse.</li> </ol> </li> <li>2. Treatment with botulinum toxin type A that is recommended according to 1.1 should be stopped in people whose condition:             <ol style="list-style-type: none"> <li>2.1. is not adequately responding to treatment (defined as less than a 30% reduction in headache days per month after two treatment cycles) or</li> <li>2.2. has changed to episodic migraine (defined as fewer than 15 headache days per month) for three consecutive months.</li> </ol> </li> <li>3. People currently receiving botulinum toxin type A that is not recommended according to 1 and 2 should have the option to continue treatment until they and their clinician consider it appropriate to stop.</li> </ol>
TA659	<p>Galcanezumab for preventing migraine</p> <ol style="list-style-type: none"> <li>1. Galcanezumab is recommended as an option for preventing migraine in adults, only if:             <ol style="list-style-type: none"> <li>1.1. they have 4 or more migraine days a month</li> <li>1.2. at least 3 preventive drug treatments have failed and</li> <li>1.3. the company provides it according to the commercial arrangement.</li> </ol> </li> <li>2. Stop Galcanezumab after 12 weeks of treatment if:             <ol style="list-style-type: none"> <li>2.1. in episodic migraine (less than 15 headache days a month) the frequency does not reduce by at least 50%</li> <li>2.2. in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine) the frequency does not reduce by at least 30%.</li> </ol> </li> <li>3. This recommendation is not intended to affect treatment with Galcanezumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.</li> </ol>
TA682	<p>Erenumab for preventing migraine</p> <ol style="list-style-type: none"> <li>1. Erenumab is recommended as an option for preventing migraine in adults, only if:             <ol style="list-style-type: none"> <li>1.1. they have 4 or more migraine days a month</li> <li>1.2. at least 3 preventive drug treatments have failed</li> <li>1.3. the 140 mg dose of erenumab is used and</li> <li>1.4. the company provides it according to the commercial arrangement.</li> </ol> </li> <li>2. Stop erenumab after 12 weeks of treatment if:             <ol style="list-style-type: none"> <li>2.1. in episodic migraine (less than 15 headache days a month) the frequency does not reduce by at least 50%</li> <li>2.2. in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine) the frequency does not reduce by at least 30%.</li> </ol> </li> <li>3. These recommendations are not intended to affect treatment with erenumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.</li> </ol>

TA764	<p>Fremanezumab for preventing migraine</p> <ol style="list-style-type: none"> <li>1. Fremanezumab is recommended as an option for preventing migraine in adults, only if: <ol style="list-style-type: none"> <li>1.1. they have 4 or more migraine days a month</li> <li>1.2. at least 3 preventive drug treatments have failed and</li> <li>1.3. the company provides it according to the commercial arrangement.</li> </ol> </li> <li>2. Stop fremanezumab after 12 weeks of treatment if: <ol style="list-style-type: none"> <li>2.1. in episodic migraine (fewer than 15 headache days a month), the frequency does not reduce by at least 50%</li> <li>2.2. in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine), the frequency does not reduce by at least 30%.</li> </ol> </li> <li>3. These recommendations are not intended to affect treatment with fremanezumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.</li> </ol>
TA871	<p>Eptinezumab for preventing migraine</p> <ol style="list-style-type: none"> <li>1. Eptinezumab is recommended as an option for preventing migraine in adults, only if: <ol style="list-style-type: none"> <li>1.1. they have 4 or more migraine days a month</li> <li>1.2. at least 3 preventive drug treatments have failed and</li> <li>1.3. the company provides it according to the commercial arrangement.</li> </ol> </li> <li>2. Stop eptinezumab after 12 weeks of treatment if: <ol style="list-style-type: none"> <li>2.1. in episodic migraine (fewer than 15 headache days a month), the frequency does not reduce by at least 50%</li> <li>2.2. in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine), the frequency does not reduce by at least 30%.</li> </ol> </li> <li>3. If people with the condition and their clinicians consider eptinezumab to be 1 of a range of suitable treatments (including erenumab, fremanezumab and galcanezumab), discuss the advantages and disadvantages of the available treatments. After that discussion, if more than 1 treatment is suitable, choose the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.</li> <li>4. These recommendations are not intended to affect treatment with eptinezumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.</li> </ol>
TA906	<p>Rimegepant for preventing migraine</p> <ol style="list-style-type: none"> <li>1. Rimegepant is recommended as an option for preventing episodic migraine in adults who have at least 4 and fewer than 15 migraine attacks per month, only if at least 3 preventative treatments have not worked.</li> <li>2. Stop rimegepant after 12 weeks of treatment if the frequency of migraine attacks does not reduce by at least 50%.</li> <li>3. If people with the condition and their clinicians consider rimegepant to be 1 of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.</li> <li>4. These recommendations are not intended to affect treatment with rimegepant that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.</li> </ol>
TA919	<p>Rimegepant for treating migraine.</p>

	<ol style="list-style-type: none"> <li>1. Rimegepant is recommended as an option for the acute treatment of migraine with or without aura in adults, only if for previous migraines: <ol style="list-style-type: none"> <li>1.1. at least 2 triptans were tried and they did not work well enough or</li> <li>1.2. triptans were contraindicated or not tolerated, and nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol were tried but did not work well enough.</li> </ol> </li> <li>2. This recommendation is not intended to affect treatment with rimegepant that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.</li> </ol>
TA973	<p>Atogepant for preventing migraine</p> <ol style="list-style-type: none"> <li>1. Atogepant is recommended as an option for preventing migraine in adults who have at least 4 migraine days per month, only if at least 3 preventive medicines have failed.</li> <li>2. Stop atogepant after 12 weeks if the frequency of migraines does not reduce by: <ol style="list-style-type: none"> <li>a. at least 50% in episodic migraine (defined as fewer than 15 headache days per month)</li> <li>b. at least 30% in chronic migraine (defined as 15 or more headache days per month, with at least 8 of those having features of migraine).</li> </ol> </li> <li>3. If people with the condition and their healthcare professional consider atogepant to be 1 of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.</li> <li>4. This recommendation is not intended to affect treatment with atogepant that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.</li> </ol>