Primary care migraine treatment pathway for adults

Please provide patients with a headache diary to determine frequency and pattern.

Diagnostic criteria:

- Exclude secondary headaches. See NICE for further details and a list of red flags needing immediate action.
- Recurrent headache disorder (5 or more lifetime headache attacks), manifesting in attacks lasting **4-72 hours** (untreated or unsuccessfully treated).
- Typical characteristics of the headache are (at least two or more): **unilateral** location; **pulsating** quality; moderate or severe pain intensity; aggravation by routine **physical activity** and association with (at least one): **nausea/vomiting** and **photo/phonophobia**
- **Aura:** 25% of migraineurs experience aura (for at least some of their attacks). Recurrent attacks (more than 2), lasting minutes, of unilateral fully-reversible visual, sensory or other central nervous system symptoms that usually develop gradually and followed by headache and associated migraine symptoms.
- **Chronic migraine:** Headache 15 days/month of which ≥8 are migraine days (for more than 3 months)

Acute treatment:

Offer combination therapy (See NICE and BASH (p.23-26) for further guidance):

1st: **simple analgesia** + **prokinetic antiemetic** (**do not prescribe opioids** e.g. Co-codamol).

2nd**: Triptans** + **simple analgesia** + **prokinetic antiemetic** (two different triptans should each be trialled on a minimum of two separate occasions, in line with the SEL JMF, before determining whether patient is a triptan non-responder). See further guidance on triptans and when to consider a gepant as an acute treatment in primary care (see page 2). Triptans should not be taken on ≥10 days/month and simple analgesia on ≥15 days/month to **avoid** medication overuse headache.

Preventive treatment:

Consider a preventive treatment for patients if they:

- are taking analgesics for 2 or more days per week **OR** experience migraine symptoms on more than 4-5 days per month (for more than 3 months)
- experience less than 4-5 migraine days per month, but with poor response to acute treatment
- cannot take suitable acute treatment for migraine attacks due to contraindications or intolerance

Please consider when choosing a preventative treatment from the list below: patients past medical history, co-morbidities (including depression/anxiety/suicidal ideation), and whether they have child-bearing potential. **The order in which the treatments are chosen should be individualised to the patient based on the above.**

Side-effects are common with these medications, but often improve over time, please encourage patients to **titrate** the medication as tolerated/required (see BASH (page 28-29) for further guidance) and to take at least the **target dose** for a minimum of 3 months before determining effectiveness. We suggest reviewing treatment every six months. If effective consider tapering the dose after 6-12 months and advise patient to monitor for deterioration.

	Medication:	General considerations & contraindications:
ALL SETTINGS	**Amitriptyline** ***Start:*** 10mg at night ***Target:*** 30-50mg at night ***Max:*** 100mg at night	See SmPC and safe prescribing of antidepressants and managing withdrawal – Do not exceed 1mg/kg If unable to tolerate low dose amitriptyline consider **nortriptyline** (SmPC) with the same dosing guidance.
ALL SETTINGS	**Propranolol (immediate release)** ***Start:*** 10mg twice daily ***Target:*** 40mg-80mg twice daily ***Max:*** 120mg twice daily	See SmPC – Consider switching to a long-acting formulation once a maintenance dose is achieved. Caution in co-existing depression as possible increased risk of self-harm.
ALL SETTINGS	**Candesartan** ***Start:*** 4mg at night ***Target:*** 16mg at night ***Max:*** 32mg at night	See SmPC - **Not recommended in pregnancy** and caution in breastfeeding, ensure highly effective contraception. BP and U&Es at baseline, three months and once yearly

Refer to a specialist headache service for advice and consideration of further treatment when patients have exhausted the treatment options above due to ineffectiveness, tolerability and/or contraindications. Specialist **advice** can also be obtained via Advice & Guidance (A&G).

SPECIALIST INITIATION	*Headache specialist initiation and stabilisation:* **Topiramate** ***Start:*** 25mg once daily ***Target:*** 50mg twice daily ***Max:*** 100mg twice daily	See SmPC - **Not recommended in pregnancy** (see MHRA Pregnancy Prevention Programme). Risk Awareness Form for Migraine to be completed on initiation and at annual treatment reviews. Ensure **highly effective contraception**.

Original Approval date: November 2023 **Last reviewed and approved:** October 2026 **Next review date:** October 2028 (or sooner if indicated)

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South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: SEL Integrated Care Board (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Primary care migraine treatment pathway for adults: acute treatment guidance

This guidance is **for acute treatment only**: the aim of these treatments is to stop a migraine attack, or to significantly reduce the severity of the headache and other associated symptoms.

Preventative guidance can be found on page 1.

Triptan prescribing guidance:

- This guidance should be used in patients naïve or not responding to triptans and **should be read in conjunction** with the medications SmPC and the SEL Joint Medicines Formulary (SEL JMF). Consider interactions.
- Triptans should be prescribed with caution in patients older than 65 years.
- Contraindications include ischaemic heart disease, cerebrovascular disease, previous myocardial infarction and uncontrolled hypertension. Specialist input may be obtained via Advice & Guidance (A&G) or referral to secondary care.
- Triptans are most effective if taken early in the headache phase (not aura phase) of an attack (see BASH for further info).
- If symptoms recur, a second dose can be given with a minimal 2 hour interval (not exceeding maximum dose in 24 hours). If migraine consistently recurs, consider combining a triptan with naproxen 500mg (if not contraindicated).

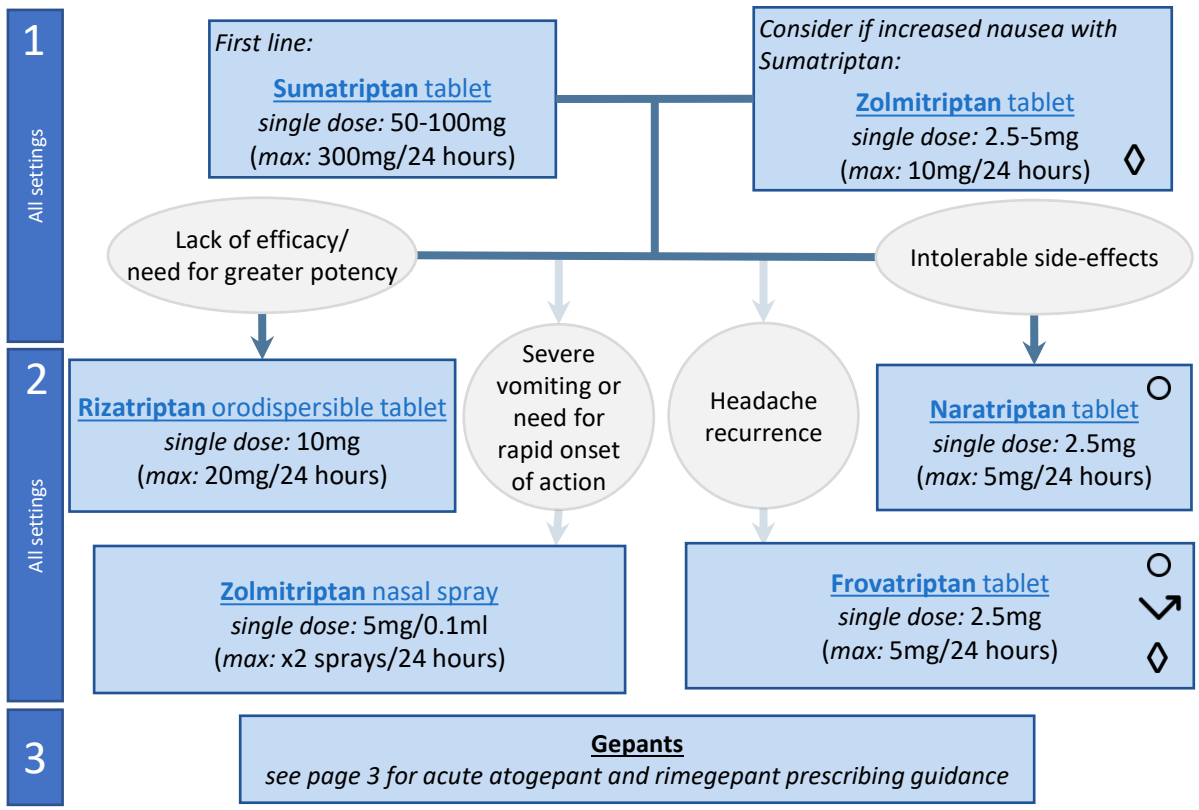
Response to triptans:

- Effective triptan treatment is defined as the improvement of headache to mild or absent and/or absence or minimal non-pain symptoms with no drug related adverse events for at least 24 hours.
- Each triptan should be tried on a minimum of 2 separate migraine attacks, if well tolerated, before response is assessed. As effectiveness may vary between individual attacks, treatment should not be considered ineffective based on one unsuccessful treatment episode.

Medication overuse:

- Triptans should not be taken on ≥10 days/month and simple analgesia on ≥15 days/month to avoid medication overuse headache.
- Rimegepant and atogepant are unlikely to cause medication overuse headache.

Firstly, ensure that simple analgesia +/- prokinetic antiemetic has been appropriately trialled (e.g. aspirin 600-900mg or naproxen 500mg +/- metoclopramide 10mg). See NICE and BASH (p.23-26) for further guidance.



Key: ◊ Consider as a preventative treatment in **menstrual migraine**. See NICE and BASH for further guidance.

↘ Consider in cases of **headache recurrence**: significant response to a triptan, but headache consistently rebounds or recurs within 24 hours.

○ Consider in cases of **intolerable side-effects** - generally better tolerated

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Primary care migraine treatment pathway for adults: acute treatment guidance

3

All settings

Gepant prescribing guidance:

- Gepants are recommended for acute treatment of migraine attacks in adults **who have tried at least two triptans** that did not work well enough or are contraindicated or not tolerated (in addition to simple analgesia being tried and ineffective). The triptan guidance on page 2 should be followed before prescribing rimegepant or atogepant.
- For acute treatment, atogepant and rimegepant are clinically similar CGRP receptor antagonists used after failure, intolerance or contraindication to at least two triptans. In line with NICE guidance to use the least costly option.
- Each gepant should be tried on a minimum of 3-4 separate migraine attacks, if well tolerated, before response is assessed. As effectiveness may vary between individual attacks, treatment should not be considered ineffective based on one unsuccessful treatment episode.

Atogepant tablet

single dose: 60mg (see dose modification guidance for 10mg below)
(*max:* 60mg/24 hours)

Atogepant prescribing guidance:

- See NICE and SmPC for full list of interactions and further prescribing guidance (these include some commonly prescribed medications)
- Prescribe four 60mg tablets (2 x 2 tablet pack) initially, whilst determining effectiveness (note that 10mg minimum pack size is 7 tablets).
- **A reduced dose of atogepant 10mg once daily is recommended when it is concomitantly administered with:**
  - Strong CYP3A4 inhibitors
  - Strong OATP inhibitors
- **Contraindications and precautions for use include (but not limited to):**
  - **Severe hepatic impairment:** use of atogepant should be avoided.
  - **Severe renal impairment and end-stage renal disease**: recommended dose is 10mg once daily (see SmPC for dosing with dialysis).
  - **Recent history (within the last 6 months) of acute coronary syndrome, stroke and transient ischaemic attack:** use of atogepant should be avoided
- If effective (significant pain or most bothersome symptom relief at 2 hours post dose) prescribe sufficient supply for one tablet to be taken for the patients expected number of migraine days per month.

Rimegepant oral lyophilisate

single dose: 75mg
(*max:* 75mg/24 hours)

Rimegepant prescribing guidance:

- See NICE and SmPC for full list of interactions and further prescribing guidance (these include some commonly prescribed medications)
- Prescribe four 75mg tablets (2 x 2 oral lyophilisate pack) initially, whilst determining effectiveness.
- **Concomitant use should be avoided with:**
  - Strong CYP3A4 inhibitors
  - Moderate and strong CYP3A4 inducers
- **Another dose of rimegepant within 48 hours should be avoided when it is concomitantly administered with:**
  - Moderate CYP3A4 inhibitors:
  - Strong P-gp inhibitors
- **Contraindications and precautions for use include (but not limited to):**
  - **Severe hepatic impairment:** use of rimegepant should be avoided
  - **End-stage renal disease:** use of rimegepant should be avoided
  - **Recent history (within the last 6 months) of acute coronary syndrome, stroke and transient ischaemic attack:** use of rimegepant should be avoided
- If effective (significant pain or most bothersome symptom relief at 2 hours post dose) prescribe sufficient supply for one tablet to be taken for the patients expected number of migraine days per month.

If migraine attacks remain poorly controlled despite appropriate trials of acute treatments, consider preventive treatment as outlined in the guidance on page 1.
Refer to a specialist headache service (or seek Advice & Guidance) if migraine remains disabling despite appropriate acute and preventive treatments, or where treatment options are limited by contraindications or intolerance.

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A&G: Advice and Guidance

BASH: British Association for the Study of Headache

SEL JMF: South East London Joint Medicines Formulary

SmPC: Summary of Product Characteristics

NICE: National Institute of Health and Care Excellence

MHRA: Medicines and Healthcare products Regulatory Agency

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