Migraine prophylaxis in adults

See also the separate Migraine and Migraine Management articles.

Migraine prophylaxis may be underused. This may be because of patient resistance in the face of unwanted side-effects, but may also be because GPs are less experienced in the use of prophylactic drugs. It may be appropriate to offer referral when control of migraine is unsatisfactory and expertise in migraine prophylaxis is needed. However, it is often appropriate to manage prophylaxis in general practice. When successful, it is very beneficial to patients' quality of life.

Aim of migraine management and prophylaxis

Migraine cannot be cured and the aim, shared with the patient, is to minimise the impact of the illness on the patient's life and lifestyle. The aim of preventative treatment is to reduce the frequency, severity, and duration of migraine attacks, and avoid medication-induced headache [1] .

Indications for prophylaxis

British Association for the Study of Headache (BASH) guidelines state that prophylaxis should be used when symptoms are inadequately controlled with acute prescriptions, or the frequency of attacks is leading to overuse of acute medicines [2] .

The National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summary (CKS) suggests prophylaxis where [1] :

- Migraine attacks are having a significant impact on quality of life and daily function - eg, they occur frequently (more than once a week on average) or are prolonged and severe despite optimal acute treatment.
- Acute treatments are either contra-indicated or ineffective.

- There is risk of medication-induced headache due to frequent use of acute drugs.

Uncommon types of migraine, such as hemiplegic migraine, or migraine with prolonged aura, should be seen by a specialist for appropriate management.

Non-pharmacological therapies for migraine prophylaxis[1] [3]

Consider non-pharmacological therapies as an adjunct or alternative to pharmacological therapy - for example:

Biofeedback, relaxation technique, and cognitive behavioural therapies have shown efficacy in the prevention of episodic migraine but data regarding efficacy in chronic migraine are limited. Cognitive behavioural therapy can be helpful as part of a combined treatment programme, and should be integrated with pharmacological interventions.

Acupuncture (up to 10 sessions over 5-8 weeks) if both topiramate and propranolol are unsuitable or ineffective. The available evidence suggests that adding acupuncture to symptomatic treatment of attacks reduces the frequency of headaches[4] .

Riboflavin 400 mg once a day - may be effective in reducing migraine frequency and intensity for some people (avoid if planning a pregnancy or pregnant).

Choice of drug for migraine prophylaxis[1] [5]

The choice of treatment depends on factors such as patient preference, drug interactions, and other comorbidities. Treatment should be started at a low dose and gradually increased to the maximum effective and tolerated dose.

Preventative treatment should be tried for at least three months at the maximum tolerated dose, before deciding whether or not it is effective. A good response to treatment is defined as a 50% reduction in the severity and frequency of migraine attacks. A review of ongoing prophylaxis should be considered after 6-12 months; treatment can be gradually withdrawn in many patients. Patients should be referred to a neurology or specialist headache clinic if trials with three or more drugs have been unsuccessful.

Propranolol (80-160 mg daily, in divided doses). Propranolol hydrochloride is recommended as first-line preventative treatment in patients with episodic or chronic migraine. If propranolol is unsuitable, other beta-blockers that can be considered are metoprolol tartrate, atenolol (unlicensed indication), nadolol, and timolol maleate. Bisoprolol fumarate (unlicensed indication) may also be considered, especially in patients already taking it for cardiac reasons under the advice of their cardiologist.

Topiramate (50-100 mg daily, in divided doses (contra-indicated in pregnancy). Topiramate can be given if a beta-blocker is unsuitable. In women of childbearing potential, advice should be given on the associated risks during pregnancy, the need to use highly effective contraception and to seek further information if pregnant or planning a pregnancy.

Amitriptyline (25-75 mg at night). Amitriptyline hydrochloride is effective for migraine prophylaxis and should be considered for patients with episodic or chronic migraine. A less sedative tricyclic antidepressant can be used if amitriptyline hydrochloride is not tolerated.

Candesartan cilexetil [unlicensed indication) can be considered in patients with episodic or chronic migraine, although there is limited evidence to support its use.

Sodium valproate (unlicensed indication) can also be considered in patients with episodic or chronic migraine. The Medicines and Healthcare products Regulatory Agency (MHRA)/Commission on Human Medicines (CHM) have released important safety information on the use of antiepileptic drugs and the risk of suicidal thoughts and behaviour. In addition, the MHRA has advised that sodium valproate must not be used in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are met and alternative treatments are ineffective or not tolerated. It must not be used during pregnancy for migraine prophylaxis.

Flunarizine (unlicensed) can also be considered in patients with episodic or chronic migraine (specialist use only). Pizotifen is used but evidence to recommend its use is limited.

Gabapentin should not be used for migraine prophylaxis. A Cochrane review found that there was evidence that gabapentin was not effective for the prophylaxis of episodic migraine in adults[6] .

Galcanezumab

NICE has issued guidance on the use of the humanised monoclonal antibody galcanezumab [7] that binds to the calcitonin gene-related peptide (CGRP) ligand, blocking its binding to the receptor. For migraine that has not responded to at least three preventative treatments, clinical trial evidence shows that galcanezumab works better than best supportive care in both episodic and chronic migraine.

NICE therefore recommends galcenezumab as an option for migraine prophylaxis for patients with at least four migraine days a month and for whom at least three preventative drug treatments have failed. It should only be considered if the company provides it according to the commercial arrangement agreed with the NHS.

Erenumab

Erenumab is another human monoclonal antibody that binds to the CGRP receptor, inhibiting the function of CGRP, and thereby preventing migraine attacks.

Erenumab is recommended by NICE as an option for preventing migraine in adults, only if [8] :

- They have four or more migraine days a month.
- At least three preventative drug treatments have failed.
- The 140 mg dose of erenumab is used.

NICE recommends stopping erenumab after 12 weeks of treatment if:

- In episodic migraine (fewer than 15 headache days a month) the frequency does not reduce by at least 50%.
- In chronic migraine (15 headache days a month or more with at least eight of those having features of migraine) the frequency does not reduce by at least 30%.

Editor's note

Dr Sarah Jarvis, 7th February 2022

Fremanezumab for preventing migraine

NICE has issued new guidance on the use of fremanezumab - another human monoclonal antibody that binds to the CGRP receptor - for prevention of migraine. It recommends that fremanezumab is considered as an option for patients fulfilling the same criteria as for erenumab, and that the same criteria for discontinuation should be used [9].

Editor's Note Dr Krishna Vakharia**, 4th May 2023**

Eptinezumab for preventing migraine [10]

NICE has recommended eptinezumab be recommended as an option for preventing migraine in adults. It is given as an infusion unlike erenumab, fremanezumab and galcanezumab, which are injections.

To be considered as an option, they must fulfil the same criteria as those for the other monoclonal antibody options and they also have the same criteria for discontinuation.

Editor's Note Dr Krishna Vakharia, 28th July 2023

Rimegepant for preventing migraine [11]

NICE have recommended the use of the oral medication rimegepant as an option for preventing episodic migraine in adults who have at least 4 and fewer than 15 migraine attacks per month. It is only indicated for those that have tried at least 3 preventative treatments and they have not worked.

It has been advised that rimegepant should be stopped after 12 weeks of treatment if the frequency of migraine attacks has not reduced by at least 50%.

Clinical trial evidence shows that rimegepant reduces monthly migraine days more than placebo. It has been suggested that it is similar to or less effective than the injectable options - erenumab, fremanezumab or galcanezumab.

Botulinum toxin type A

Botulinum toxin type A (specialist use only) is recommended for prophylaxis of chronic migraine where medication overuse has been addressed and where three or more oral prophylactic treatments have failed.

Botulinum toxin type A is recommended by NICE as an option for the prophylaxis of headaches in adults with chronic migraine [12] :

- That has not responded to at least three prior pharmacological prophylaxis therapies; **and**

- Whose condition is appropriately managed for medication overuse.

Treatment with botulinum toxin type A that is initially recommended should be stopped in people whose condition [12] :

- Is not adequately responding to treatment (defined as less than a 30% reduction in headache days per month after two treatment cycles); **or**
- Has changed to episodic migraine (defined as fewer than 15 headache days per month) for three consecutive months.

Menstrual migraine [1] [5]

Accurate diagnosis to treat this successfully is essential. This should be confirmed with diary evidence to show migraine without aura occurring regularly within up to two days of onset of menstruation and at no other time over three months.

- Mefenamic acid 500 mg qds as first-line if menorrhagia and/or dysmenorrhoea co-exist, taken at the onset of menstruation and continued prophylactically until the last day of bleeding.
- Progestogen-only methods (that inhibit the ovarian cycle) may also be used if contraception is also required. Cerazette®, Nexplanon® or depot medroxyprogesterone acetate are all suggested.

For women with predictable menstrual-related migraine that does not respond adequately to lifestyle measures and standard acute treatment and where there are no contra-indications, consider treatment (off-label) with:

- Frovatriptan (unlicensed indication) can be given instead of, or in addition to, standard prophylactic treatment in women with perimenstrual migraine. It is given from two days before until three days after menstruation starts.
- Both zolmitriptan (unlicensed indication) and naratriptan (unlicensed indication) are suitable alternatives to frovatriptan.

In order for treatment to be effective, the patient's menstrual cycle must be regular.

Migraine in pregnancy and lactation

Often migraine improves during pregnancy and prophylaxis is not required. Propranolol and amitriptyline have the best evidence for safety and efficacy but drugs should be avoided if possible.

Follow-up[1]

Arrange follow-up to monitor effectiveness, titrate dose and assess for adverse effects.
Review regularly during titration (for example every 2-3 weeks). Advise the person:

- To keep a headache diary.
- To seek review sooner if adverse effects/new features develop.
- That improvement may take 4-8 weeks from initiation of treatment to become apparent.

Consider the need for referral to neurology if prophylactic treatment in primary care fails, is not appropriate or any red flags or atypical clinical features develop.

Treatment is considered to have failed if there is a lack of response to the highest tolerated dose after three months of treatment.

After 6-12 months of successful therapy:

- Review the need for continuing migraine prophylaxis.
- Consider gradual drug withdrawal.

Referral[1]

Consider admission or urgent referral if:

- A serious cause of headache is suspected.
- There is severe, uncontrolled status migrainosus (migraine lasting for more than 72 hours).

Seek advice/refer to neurology (with urgency depending on the clinical situation) if:

- A complication of migraine has developed.
- Atypical symptoms (such as motor weakness or poor balance) are present.
- The diagnosis is uncertain.
- Optimal treatment in primary care does not adequately control the symptoms (consider medication overuse headache).

Authored by:	Peer Reviewed by: Dr Laurence Knott	
Originally Published: 20/11/2023	Next review date: 21/04/2021	Document ID: doc_239