Centre for Sustainable Delivery

NHS SCOTLAND

Modernising Patient Pathways Programme:

Headache Prophylaxis / Treatment Advice

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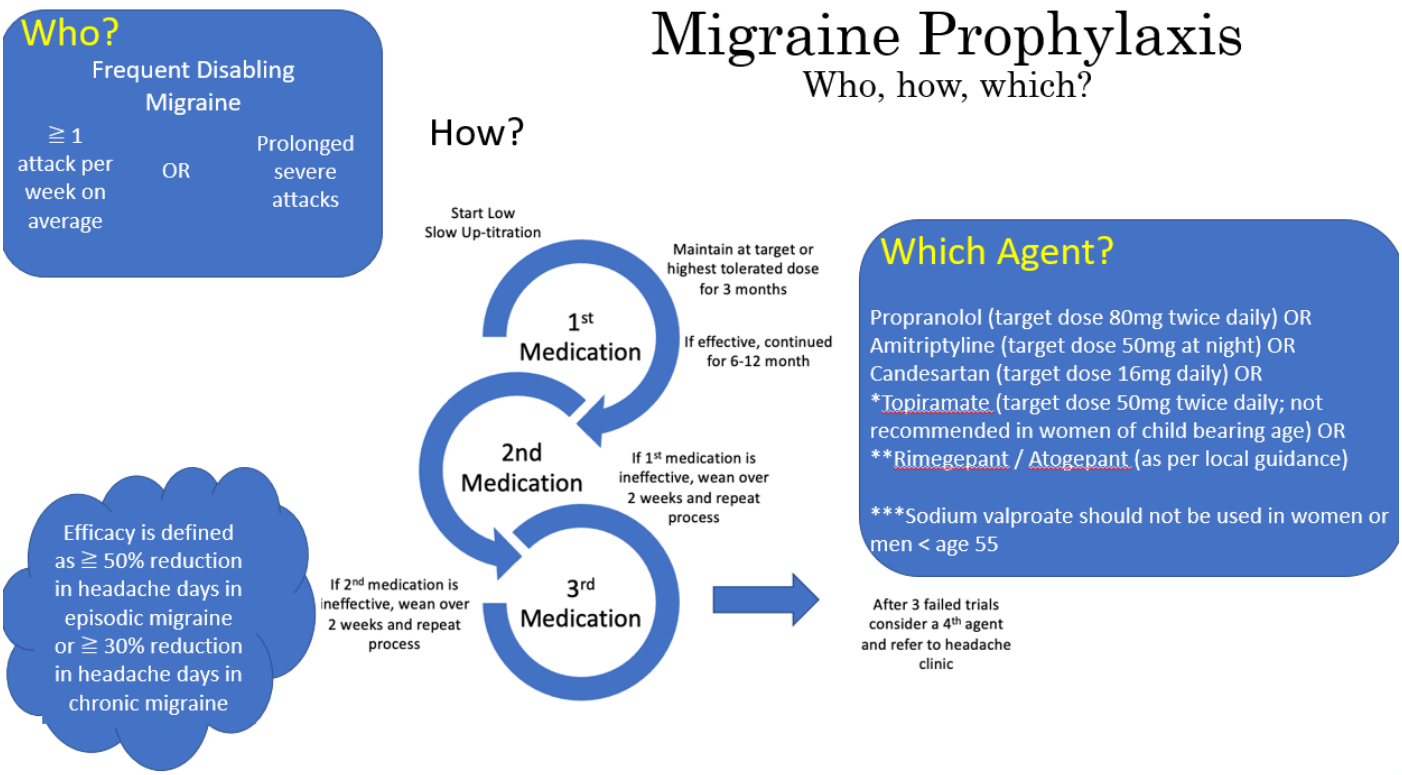
Background

- Prophylactic management of migraine in primary care should be based on SIGN guideline 155. https://www.sign.ac.uk/our-guidelines/pharmacological-management-of-migraine/
- Oral prophylactic treatments should be started at a low dose and gradually increased (every 1-2 weeks) to the minimum effective maximum tolerated dose.
- Oral prophylactic treatments should be continued for at least 8 weeks at either the target dose or the highest tolerated dose before assessing efficacy.
- The effectiveness of prophylactic treatment may be limited by Medication Overuse Headache and this should be addressed in all patients
- If an oral prophylactic medication is effective, continue the medication and review at 6-12 months, at which time a trial of withdrawal should be considered.
- Combinations of prophylactic treatments can be helpful if individual treatments are not adequately effective.
- Plans for future pregnancy and contraception advice should be discussed when prescribing prophylactic treatments

Pathway recommendations



The decision if or when to start oral prophylaxis should be tailored to the individual patient. As per SIGN 155, there is no specific number of migraine days or migraine attacks per month that indicates the need for prophylaxis. For example, patients with a few disabling migraine days per month may elect to start treatment, but patients with a larger number of mild headache days per month may not.

Migraine prophylactics may take many weeks to work. Judgment of efficacy should be made once on the target dose or highest tolerated dose at 8 weeks. If the migraine prophylactic is ineffective at 8 weeks, it should be weaned over 2 weeks and an alternative considered. If it is effective (i.e. reduced monthly headache days by at least 30-50%) consider weaning the drug after 6 to 12 months (it should be weaned at the approximate rate it was increased). If side effects are experienced after a dosage increase, decrease to the previous dose and then attempt a dosage increase after 2 weeks. If patients are drowsy they should be warned to refrain from driving.

Contraception

Migraine prophylaxis is usually not required in pregnancy, and certain medications are contraindicated in pregnancy (detailed in the pregnancy section). We recommend consideration of withdrawal of migraine prophylactics prior to conception. In particular, candesartan and topiramate should be avoided in pregnancy. Many forms of contraception are not suitable in patients taking topiramate (see section on Topiramate).

Medication Summary Table

Medication	Amitriptyline	Candesartan	Propranolol	Topiramate
Starting dose	10mg If side effects occur consider a switch to nortriptyline or dosulepin	2-4mg Consider baseline *U&Es	10-20mg twice a day	25mg Not recommended in women of child bearing age (MHRA guidance awaited)
Suggesting Increment	10mg every 1-2 weeks Some patients may require slower titration	2-4mg every 1-2 weeks Consider intermittent monitoring of U&Es (see text below)	10-20mg twice a day every 1-2 weeks	25mg every 1-2 weeks
Target Dose	50mg If well tolerated many patients benefit from a higher dose with further up titration up to 1mg/kg, typically a maximum of 100mg	16mg	80mg twice a day Some patients benefit from lower doses if they experience side effects at higher doses	50mg twice a day If partially effective AND well tolerated further up titration to a maximum of 100mg twice a day

*U&Es = urea and electrolyte blood testing

Migraine Prophylactic Drugs

For a full list of contraindications and cautions we recommend review of the Summary of Product Characteristics (SPC).

Amitriptyline

Start at 10mg and increase by 10mg every 1-2 weeks. The typical first target dose is 50mg. If well tolerated many patients benefit from a higher with further up titration up to 1mg/kg, typically a maximum of 100mg. If adverse effects occur, alternatives include nortriptyline, or dosulepin. Dosulepin is only available in 25mg and 75mg doses.

Contraindications include concomitant use of monoamine oxidase inhibitors, recent myocardial infarction, heart block, disorders of cardiac rhythm, and coronary artery insufficiency, and severe liver disease. We also recommend avoiding use in those patients at risk of glaucoma, and QT prolongation. Caution in those patients taking serotonergic drugs.

Patients should be warned about adverse effects which include constipation, difficulty with micturition, arrhythmias, syncope, confusion, nausea, dry mouth, drowsiness and weight gain. Patients should seek immediate medical attention if they are unable to micturate or experience visual blurring.

Candesartan

Start at 2-4mg per day, increasing by 2-4mg every 1-2 weeks to a maximum of 16mg.

Caution in patients with renal artery stenosis, hypotension and renal impairment. Candesartan is cautioned in those patients receiving lithium therapy, and in those who are taking medications which increase serum potassium such as spironolactone.

Candesartan should not be used in pregnancy, and should be discontinued before planning a pregnancy. Women of child bearing age should ensure appropriate contraception is in place. Candesartan is not recommended during breast feeding.

Consideration of alternative agents should be considered in those with renal impairment and those patients taking regular NSAIDS, since in such populations close monitoring or kidney function and potassium would be required. If using candesartan in older patients, monitoring of kidney function and potassium should be considered. Candesartan should be withheld if patients become acutely dehydrated (e.g. during a diarrhoea and vomiting illness).

Adverse effects include hypotension, renal impairment and cough.

Propranolol

Start propranolol 10-20mg twice a day, gradually up-titrating by 10-20mg twice a day every 1-2 weeks, to a target dose of 80mg twice a day. Propranolol 80mg MR, increasing to 160mg MR is an alternative. Some patients benefit from lower doses if they experience side effects at higher doses

Propranolol is contraindicated in a number of conditions including asthma, severe peripheral vascular disease and should not be used in patients taking verapamil.

Adverse effects include bradycardia, hypotension, fatigue, sexual dysfunction, wheezing.

Topiramate

Start topiramate at 25mg daily, increasing by 25mg every 1-2 weeks, to a target dose of 50mg twice a day. If partially effective and well tolerated further up titration to a maximum of 100mg twice a day could be considered in selected patients

We do not recommend topiramate for use in patients who have a history of glaucoma or renal stones or who have anorexia nervosa. Caution should also be exercised in patients with a history of depression. There may be interactions with digoxin, metformin, carbonic anhydrase inhibitors, and thiazide derivatives. There is a potential for serious interaction with sodium valproate.

Children exposed to topiramate in utero are at high risk of serious developmental disorders and congenital malformations. It should not be used by women who are breast feeding as it can be present in breast milk. Patients who may become pregnant should be appropriately counselled and be on highly-effective contraception before commencing topiramate. Advice on contraception is available from the Royal College of the Obstetricians and Gynaecologists Faculty of Sexual and Reproductive Healthcare, https://www.fsrh.org/standards-and-guidance/fsrh-guidelines-and-statements/. At the time of writing the MHRA are reviewing the risks of topiramate in pregnancy. For current contraceptive advice on patients prescribed topiramate check the MHRA website, www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency.

Adverse effects are common and include acute glaucoma, peripheral paraesthesias, fatigue, nausea, diarrhoea or weight loss, taste change, concentration difficulties, word finding difficulties, insomnia, anxiety, and depression.

Pizotifen

Although the evidence base is limited, pizotifen is widely used for the prevention of migraine and is another option. A suggested starting dose in 0.5mg at night, with weekly increments of 0.5mg, to a target dose of 1.5mg at night.

Sodium Valproate

Sodium Valproate should not be initiated for the prophylaxis of migraine in patients under the age of 55.

Children exposed to sodium valproate in utero are at high risk of serious developmental disorders and congenital malformations. It should therefore not be used during pregnancy. There is also a risk of transient impaired fertility in men. The Commission on Human Medicines recommends that no patients (male or female) under the age of 55 years should be initiated on valproate unless two specialists independently consider and document that there is no other effective or tolerated treatment. If prescribing sodium valproate in patients under the age of 55, the MHRA annual risk form should be completed with the patient and repeated annually.

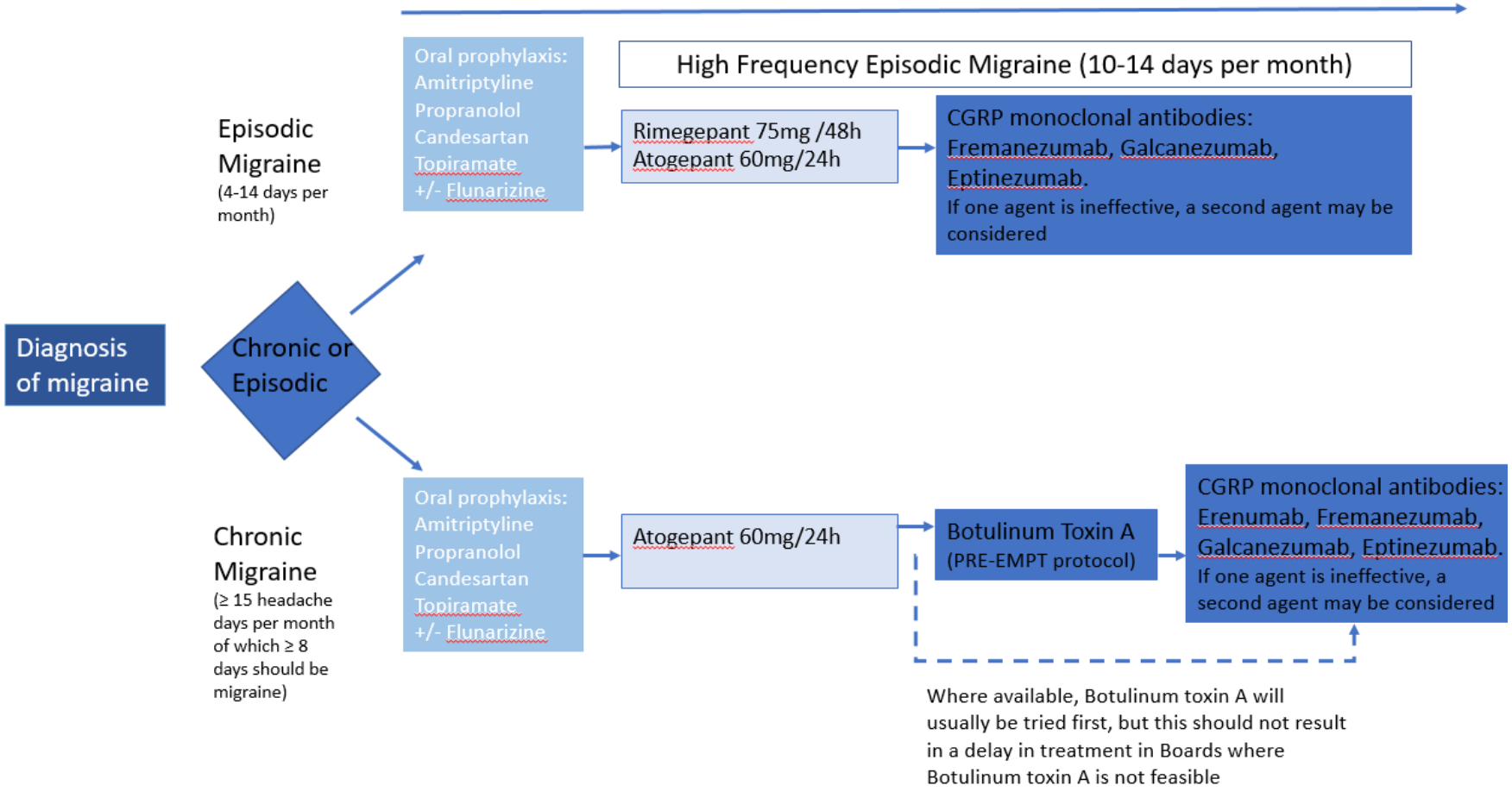
For current contraceptive advice on patients prescribed sodium valproate check the MHRA website, www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency.

Referral to secondary care following prophylaxis

Where prophylactic treatment is not successful **after three preventative medications** from different classes, consider referral to relevant secondary care services as per local arrangements.

Secondary care prophylaxis

Fig. 2 The following diagram gives an overview of the secondary care pathway



- Chronic migraine: 15 or more headache days per month, of which 8 must be migraine
- Episodic migraine: 14 or less migraine days per month (high frequency episodic migraine 10-14 days per month)

Patients should be defined as having episodic or chronic migraine using headache diaries. As per the primary care pathway, initial prophylaxis should be with oral medications, but it is expected that many agents will already have been tried in primary care. It is important to confirm that agents have been tried for an appropriate duration and at an appropriate dose.

For selected patients with both episodic and chronic migraine, Flunarizine may be a treatment option. It is an un-licenced medication and is prescribed and monitored through secondary care. Its use is often targeted to specific migraine types such as vestibular migraine.

In selected patients with disabling high frequency episodic migraine, treatment with a gepant (rimegepant or atogepant) or a monoclonal antibody to calcitonin gene related peptide (CGRP) can be considered if first line oral prophylactics are ineffective. Erenumab is only approved for chronic migraine and prescription is limited to eptinezumab, fremanezumab or galcanezumab. Botulinim toxin A is not approved for episodic migraine.

For patients with chronic migraine, atogepant, Botulinim toxin A or a monoclonal antibody to CGRP can be considered. Unless contra-indicated, Botulinum Toxin A will usually be trialled before monoclonal antibodies to CGRP. Where this is not currently feasible in a Health Board, this must not be a barrier or result in delay for a patient's treatment and the monoclonal antibody agents can be trialled without a trial of Botulinum Toxin A. If patients do not respond to Botulinum Toxin A, treatment with a monoclonal antibody to CGRP, or atogepant (if not already trialled) should be considered where appropriate. If a first monoclonal antibody is deemed to be ineffective it is reasonable to consider a trial of a second monoclonal antibody to CGRP, ideally one with a different mechanism. Rimegepant is not approved for chronic migraine.

With effective migraine prevention patients can revert to episodic migraine and remain in episodic migraine once preventative treatments are phased out / discontinued. In patients established on a preventative treatment (oral preventatives, flunarizine, gepants, Botox and CGRP monoclonal antibodies) the need for ongoing treatment should be evaluated on a yearly basis and consideration given to a treatment holiday. If headache worsens on phasing out / stopping an effective treatment this should be reinstated.

Oral prophylaxis (secondary care):

The recommendations for the prophylaxis of migraine in secondary care reflect the advice given for prophylaxis of migraine in primary care, with sequential trials (if needed) of amitriptyline, candesartan, propranolol, and topiramate being recommended (the order being tailored to the individual patient). Additional options in secondary care are flunarizine and the gepants, as discussed below.

Flunarizine

Flunarizine will be started and issued from the hospital pharmacy. The starting dose is either 5mg or 10mg taken orally at night. The maintenance dose is 10mg at night.

It is not licensed in the UK for any indication, but is recognised in SIGN 155 as a viable and effective migraine prophylactic agent. In selected patients ECG monitoring for the PR interval may be performed.

Depression is a potential side effect and patients should be warned to stop the medication if depression occurs. Severe depression occurs in a minority of people. Other potential adverse effects include sedation, weight gain, tremor and Parkinsonism, nausea, dry mouth, gingival hyperplasia, muscle aches and abdominal pain.

Concomitant use with beta blockers can cause bradycardia and impairment of cardiac conduction. We do not recommend it for use in pregnancy.

Contraindications include:

- Sick sinus syndrome
- Second and third degree heart block
- Heart failure
- Hypotension
- Severe left ventricular dysfunction
- Cardiogenic shock
- Porphyria
- Parkinsonism

Cautions include:

- History of severe depression
- Current depression
- Those taking frequent dopamine antagonist anti-emetics (increased risk of extra-pyramidal side effects)

Calcitonin Gene Related Peptide (CGRP) small molecule antagonists (gepants)

Galcitonin gene related peptide (CGRP) small molecule antagonists (gepants) are a new class of medications for the treatment of migraine. At the time of writing there are 2 such medications available in Scotland. Atogepant 60 mg daily is approved for use in episodic and chronic migraine whereas rimegepant 75mg every second day is approved for episodic migraine only. Where patients using rimegepant have a migraine attack on a non-treatment day, if there are no contraindications, then an additional dose can be used for acute treatment (refer to acute treatment section for detail).

Gepants are thought to relieve migraine by blocking CGRP-induced neurogenic vasodilation, returning dilated intracranial arteries to normal by halting the cascade of CGRP-induced neurogenic inflammation which leads to peripheral and central sensitisation and / or by inhibiting the central relay of pain signals from the trigeminal nerve to the caudal trigeminal nucleus.

Place in the migraine pathway

In selected patients with high frequency episodic migraine there is the option to treat with a gepant (atogepant and rimegepant are both licensed in this scenario) if first line oral prophylactics are ineffective. The CGRP monoclonal antibodies (as detailed below) are an alternative in patients preferring an injectable treatment. Definitions of high frequency episodic migraine vary, but patients are typically disabled by migraine and have 10 or more migraine days per month.

Atogepant can be considered for patients with chronic migraine who have not responded to first line oral prophylactics. Botulinum toxin A and the CGRP monoclonal antibodies (as detailed below) are alternatives in patients preferring an injectable treatment.

At the time of writing the Scottish Medicines Consortium have accepted the restricted use of atogepant for patients with episodic migraine and chronic migraine where at least three prophylactic treatments have failed. Rimegepant is restricted to patients with episodic migraine where three prophylactic agents have failed. In patients with a partial effect to an oral prophylactic agent, there is no requirement to stop that agent as long as the patient fulfils the criteria for starting treatment with a gepant.

Medication overuse with analgesics should be addressed prior to initiating treatment.

Adverse Effects and Cautions

The gepants are generally well tolerated. Side effects noted with atogepant in the clinical trials were constipation (7%), nausea (7%) and somnolence (5%). Atogepant should be avoided in severe hepatic impairment and dose reduction to 10mg is required in severe renal impairment. Baseline U&Es and LFTs should be considered if clinical concern. Routine monitoring is not required for patients with normal renal and liver function. Nausea is the main adverse effect with rimegepant, in 1.2% of patients. Hypersensitivity reactions have been reported but are uncommon occurring in <1%.

If atogepant is prescribed along with a strong CYP3A4 inhibitor (e.g., clarithromycin, itraconazole) or a strong OATP inhibitor (e.g., rifampicin, atazanavir, ritonavir, tipranavir, ciclosporin, telmisartan) then the dose should be reduced to 10mg. Candesartan is a moderate OATP inhibitor and concurrent use does not require dose reduction. For those where the strong CYP3A4 inhibitor or OATP inhibitor is prescribed for a short course of treatment then it is acceptable to temporarily stop atogepant and re-start it when the treatment course has completed.

Atogepant should be avoided in severe hepatic impairment and dose reduction to 10mg is required in severe renal impairment. Baseline U&Es and LFTs should be considered if clinical concern. Routine monitoring is not required for patients with normal renal and liver function.

Concurrent administration of rimegepant along with a strong CYP3A4 inhibitor (e.g., clarithromycin, itraconazole) is not recommended. If it is prescribed a with a moderate CYP3A4 inhibitor (erythromycin, fluconazole), a second dose should be delayed for 48 hours i.e. patients should not be allowed to use concurrent acute treatment whilst on a moderate CYP3A4 inhibitor.

It is important to note that CGRP mediates vascular effects such as potentially mediating vasodilatation, and having other potential effects on the vascular endothelium and vascular smooth muscle. Whilst no cardiovascular adverse effects were noted in the trials and there is no restriction to using gepants in patients with cardiovascular risk factors, we recommend a pre-treatment BP and counselling regarding Reynaud's. BP should be repeated at 3 months and regularly thereafter (see CGRP monoclonal antibodies section).

Pregnancy and Lactation

Gepants should not be used in pregnancy. They have a short half-life and these agents should be stopped 1 month prior to trying for a pregnancy. Due to insufficient safety data, routine use of these agents in lactating women is not recommended.

Assessment of Response

Headache diaries should be used to assess the response. Response to treatment should be assessed after 3 months using headache diaries.

If there is a good response to treatment, the agent may be continued for a pre-defined period as determined locally (e.g. 12-24 months), before consideration of a treatment holiday. If there is recurrence of headache during a treatment holiday, treatment may be re-initiated. Alternatively, if there is a sustained positive response after a treatment holiday, the agent should not be re-initiated. In patients continuing treatment beyond 12-24 months, the need for ongoing treatment should be evaluated on a yearly basis.

In HFEM if one agent is ineffective after 3 months a second agent can be trialled.

Criteria for continuing and stopping may take into account a number of indices:

1. Episodic migraine: reduction of at least 50% in frequency or severity of migraine.
2. Chronic migraine: reduction of at least 30% in frequency or severity of headache / migraine.

Dosing

Dosing should be performed as per the product license.

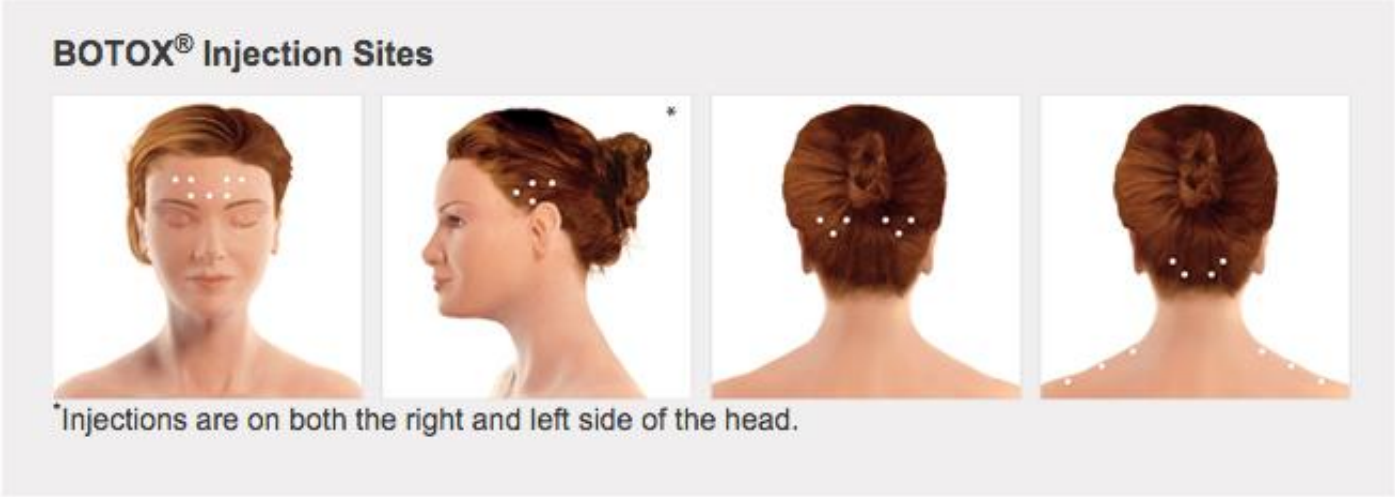
Atogepant 60mg daily is prescribed in primary care, either directly or on secondary care recommendation depending on local arrangements. If the patient is on strong CYP3A4 inhibitor or a strong OATP inhibitor (as detailed above) the dose is reduced to 10mg. If a short course of a strong CYP3A4 inhibitor or a strong OATP inhibitor is planned (e.g. of an antibiotic) then it is acceptable to temporarily stop atogepant and re-start it when the treatment course has completed.

Rimegepant 75 mg alternate days is prescribed in primary care, either directly or on secondary care recommendation depending on local arrangements. Where patients have a migraine attack on a non-treatment day, if there are no contraindications, then an additional dose can be used for acute treatment, except where the patient is on a moderate CYP3A4 inhibitor.

Because of the small risk of somnolence, patients should be counselled regarding driving before initiating treatment.

Botulinum Toxin A Therapy (chronic migraine only)

For chronic migraine, if patients are either ineligible for, or do not respond to the oral prophylactics, they should be considered for Botulinum toxin A. Botulinum toxin A therapy is licensed for chronic migraine only (defined as at least 15 headache days per month, at least 8 of which are migraine). Medication overuse should be addressed prior to initiation. Botulinum toxin A should be administered by appropriately trained clinicians using the PRE-EMPT protocol



An adequate trial consists of two cycles of treatment, three months apart. Headache diaries should be completed by patients before and during therapy. Patients should be evaluated 3 months after the second cycle, against pre-defined criteria (NICE Technology Appraisal Guidance TA260), to determine whether the treatment should be stopped or continued. Treatment should be continued where there is a good response to treatment but the patient continues to suffer a significant headache burden (e.g remains in a chronic migraine pattern). Treatment should be stopped if there is an insufficient response to treatment, or alternatively if there is an excellent response to treatment (e.g. patient has well controlled episodic migraine). If treatment is continued, headache diaries should be reviewed at each injection visit to confirm the ongoing indication for treatment. A treatment holiday should be considered at 2 years. In patients continuing treatment beyond 2 years, the need for ongoing treatment should be evaluated on a yearly basis.

Criteria for continuing and stopping may take into account a number of indices, for example

- Headache days (reduction of 30% or more is typically considered a good response)
- Migraine days or severe headache days (reduction of 30% or more is typically considered a good response)
- Disability (reduction of 50% or more is typically considered a good response)

There is limited evidence for the safety of Botulinum Toxin A in pregnant or lactating women. Whilst the risk is likely to be low, treatment using Botox is not recommended in pregnant and lactating women. Practice varies between headache centres and some centres do use Botulinum Toxin A in selected patients who are pregnant or lactating. Before considering Botox in pregnancy or lactation the clinician should fully discuss the uncertainty and the potential risks with the patient, written consent should be obtained and the patient should be entered on a pregnancy registry.

Monoclonal antibodies to Calcitonin Gene Related Peptide (CGRP)

Background

Monoclonal antibodies to calcitonin gene related peptide (CGRP) are a new class of medications for the treatment of migraine. At the time of writing there are 4 such medications available in Scotland. Erenumab, fremanezumab and galcanezumab are provided by monthly subcutaneous injections. Fremanezumab can also be given quarterly. Eptinezumab is only available as a quarterly intravenous infusion. All medications target CGRP, a key neuropeptide involved in the pathogenesis of migraine. Erenumab is a monoclonal antibody directed toward the canonical CGRP receptor. Fremanezumab, galcanezumab and Eptinezumab are monoclonal antibodies directed toward the CGRP ligand.

Place in the migraine pathway

In selected patients with high frequency episodic migraine there is the option to treat with a monoclonal antibody to CGRP (fremanezumab, galcanezumab and eptinezumab are licensed in this scenario) if oral prophylactics are ineffective. Atogepant and rimegepant (as detailed above), if not already trialled, are alternatives in patients preferring an oral medication. Definitions of high frequency episodic migraine vary, but patients are typically disabled by migraine and have 10 or more migraine days per month.

CGRP monoclonal antibodies can be considered for patients with chronic migraine who have not responded to first line oral prophylactics. Botulinum toxin A will usually have been trialled before considering the CGRP monoclonal antibodies, however, if treatment with Botulinum toxin A is not feasable, this should not be a barrier to treatment. Atogepant (as detailed above), if not already trialled, is an alternative in patients preferring an oral medication.

Medication overuse with analgesics should be addressed prior to initiating treatment.

At the time of writing the Scottish Medicines Consortium have accepted the restricted use of erenumab for patients with chronic migraine where at least three prophylactic treatments have failed. The SMC have accepted fremanezumab, galcanezumab and eptinezumab for patients with chronic and episodic migraine where three prophylactic agents have failed. In patients with a partial effect to an oral prophylactic agent, there is no requirement to stop that agent as long as the patient fulfils the criteria for starting the monoclonal antibody treatment.

The specific choice of agent should be decided locally. Centres may benefit from developing dedicated clinics to pre-assess patients, provide training regarding injection technique, and to assess response. Injections are typically delivered to patients by a homecare service, and are self-administered by patients at home. Patients will require a hospital admission (or a suitable alternative) to receive intravenous eptinezumab.

Adverse Effects and Cautions

The cap of the erenumab pre-filled syringe / pen contains latex and should not be given to patients with a latex allergy.

Although the monoclonal antibodies have a favourable side effect profile, a number of adverse effects should be noted. Patients should be warned about side effects including the risk of constipation (mainly with erenumab, but only occasionally severe enough to warrant treatment cessation), injection site reactions, itch, rash, and hair loss. There have been reports of anaphylaxis and angioedema.

It is important to note that CGRP mediates vascular effects such as potentially mediating vasodilatation, and having other potential effects on the vascular endothelium and vascular smooth muscle. Patients with certain cardiovascular diseases were excluded from clinical trials and long-term effects of these agents in such patients is unknown. There have been early reports in the post-marketing setting of increases in blood pressure after initiation of erenumab. We do not recommend the use of such agents in patients with uncontrolled hypertension, and use in patients with cerebrovascular and cardiovascular disorders is not advised until further safety data becomes available. CGRP monoclonal antibodies can raise both systolic and diastolic BP, and regular BP checks are recommended for patients on CGRP monoclonal antibodies to ensure hypertension does not develop.

Recommended BP monitoring:

1. Before starting CGRP monoclonal antibody a pre-treatment BP should be obtained. This can either be at the headache clinic or using a home monitor. If > 140/90 this should be repeated and, if sustained, treated as per NICE guidelines. A CGRP monoclonal antibody should not be initiated until BP has normalised.

2. A repeat BP should be obtained at the 3 months CGRP treatment review and regularly thereafter for patients remaining on treatment. If > 140/90 this should be repeated and, if sustained, treated as per NICE guidelines.

There is a small risk of hypersensitivity reactions during the infusion with eptinezumab.

Pregnancy and Lactation

Monoclonal antibodies to CGRP should not be used in pregnancy. Due to the long half-life, these agents should be stopped at least 6 months prior to pregnancy. Due to insufficient safety data, routine use of these agents in lactating women is not recommended.

Due to their short half-life the gepants may be more appropriate to use in women considering a pregnancy due to the shorter time interval required between stopping treatment and trying for a pregnancy.

Assessment of Response

Headache diaries should be used to assess the response. Response to treatment should be assessed after 3 months using headache diaries.

If there is a good response to treatment, the agent may be continued for a pre-defined period as determined locally (e.g. 12-24 months), before consideration of a treatment holiday. If there is recurrence of headache during a treatment holiday, treatment may be re-initiated. Alternatively, if there is a sustained positive response after a treatment holiday, the agent should not be re-initiated. In patients continuing treatment beyond 12-24 months, the need for ongoing treatment should be evaluated on a yearly basis.

If one agent is ineffective after 3 months a second agent can be trialled. It is preferable for the second agent to be of a different class than the first. For example, if erenumab is ineffective, consider a trial of either fremanezumab, galcanezumab or eptinezumab; if either fremanezumab, galcanezumab or eptinezumab are ineffective, consider a trial of erenumab. The Scottish Medicines Consortium permits the use of fremanezumab, galcanezumab and eptinezumab for patients with high frequency episodic migraine. Where one of these agents is ineffective, another may be tried.

Criteria for continuing and stopping may take into account a number of indices:

1. Episodic migraine: reduction of at least 50% in frequency or severity of migraine.
2. Chronic migraine: reduction of at least 30% in frequency or severity of headache / migraine.

Dosing

Dosing should be performed as per the product license.

Erenumab is delivered as a subcutaneous injection using a pre-filled syringe or pen. The dose is either 70mg or 140mg monthly.

Galcanezumab is delivered as a subcutaneous injection using a pre-filled pen. The recommended regimen is a 240mg loading dose, followed by 120mg monthly.

Fremanezumab is delivered as a subcutaneous injection using a pre-filled syringe. The dose is either 225mg monthly or 675mg quarterly.

Eptinezumab is delivered by intravenous infusion. The dose is 100mg quarterly.

Occipital nerve block

There is currently conflicting evidence about the benefit of greater occipital nerve blocks in migraine headache. There are four small randomised controlled trials that assessed the short-term benefit of GON blocks in people with migraine. They all used different regimens of treatment. Three of them found a reduction in headache frequency compared to placebo whereas the fourth showed no difference. In the negative study, however, the placebo group received a small dose of lidocaine so this may have been a confounding factor.

Recommendation

GON blocks may be used in migraine as a transitional treatment (short term effect to “switch off” a headache bout or provide temporary headache relief) in certain situations when the severity and frequency of the headaches is significant and other acute or preventive options are not available (i.e. pregnancy) or effective. It may also be used as a temporary relief in the context of medication overuse headache when withdrawal of acute medication results in unbearable rebound headache.

References and further resources

SIGN 155 Pharmacological management of migraine – updated March 2023; includes clinician and patient guidelines

url: Pharmacological management of migraine (sign.ac.uk)

British Association for the Study of Headache (BASH) National Management System 2019; includes clinician and patient portals

url: Headache UK

NICE Technology Appraisal Guidance TA260)

Overview | Botulinum toxin type A for the prevention of headaches in adults with chronic migraine | Guidance | NICE

Migraine Trust:

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