Headache - Migraine

PATIENT PRESENTATION

Patient presents with a history suggestive of migraine.

Features **suggestive** of migraine:
- Headache that stops activities
- Untreated duration more than 4 hours
- Sensitivity to head movement, light, noise and smells
- Family history of migraine
- Headache associated with menstruation
- Headache that gets better in pregnancy

Features **against** migraine:
- Headache that is not disabling
- Simple headache with no associated features
- Untreated duration less than 4 hours
- Headache associated with agitation and restlessness

REDFLAGS

Does the patient have any of the following red flags?:

Admission to acute medicine
- Headache and/or vomiting with papilloedema
- Thunderclap headache (seconds to 5 mins)
- Neck stiffness (meningism)
- New headache in patient with history of cancer or HIV infection

Neurology On-call
- New neurological symptoms (e.g. aura lasting < 5 mins or > 1 hour, limb weakness or cognitive disturbance)
- Headache changes with posture or precipitated by physical examination or valsalva manoeuvre

On-call Ophthalmology (Visual Symptoms)
or On-call Neurology (Mainly Headache Symptoms)
Or On-call Rheumatology • Giant Cell Arteritis suspected (obtain FBC, ESR, CRP)

Urgent Suspected Cancer Neurology/Neurosurgery

Neurological deficit:
- Progressive neurological deficit (including personality, cognitive or behavioural change) in the absence of previously diagnosed or suspected alternative disorders (such as multiple sclerosis or dementia)

Seizure:
- Any new seizure
- Seizures which change in character such as post-ictal deficit, headache, increased frequency, etc.

No red flags

CLASSIFICATION

Episodic Migraine
Migraine occurring on less than 15 days per month

ChronicMigraine
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

Menstrual-related Migraine
Females with migraine occurring predominantly between 2 days before and 3 days after the start of menstruation for > 2 out of 3 consecutive menstrual cycles

LIFESTYLE ADVICE

For patients with migraine, maintaining a regular routine is important, including the following:
- Encourage regular meals, adequate hydration with water, sleep and exercise
- Avoid specific triggers if known
- Consider activities that encourage relaxation such as mindfulness, yoga or meditation

Patient information resources:
- SIGN Migraine Patient Information Booklet
- National Migraine Centre – Heads Up Podcast

MANAGEMENT

See page 2 for further management of migraines

Headache - Migraine

MANAGEMENT

See the below treatment options for management of migraines.

ACUTE TREATMENT

Avoid use of opiate medication.

Simple analgesia use should be limited to 2 days per week.

Simple Analgesia
- Aspirin 900mg
- Ibuprofen 400mg-600mg
- Paracetamol 1g

Nausea or Vomiting
(can have analgesic effect)
- Metoclopramide 10mg
- Prochlorperazine 10mg

TRIPTAN TREATMENT

Triptan use should be limited to 2 days per week.

Triptan treatment options include:

First Line Triptan
- Sumatriptan tablets 50–100 mg

Second Line Triptans
- Rizatriptan tablets 10mg (5mg if on Propronolol)
- Almotriptan tablets 12.5mg
- Zolmitriptan tablets or orodispersible 2.5mg

Nausea or Vomiting Unresponsive to Antiemetic
- Zolmitriptan nasal spray 5mg
- Sumatriptansubcutaneousinjection 6mg

Triptans are taken at the start of the headache. If the headache settles but recurs, a second dose of triptan can be taken if it is longer than 2 hours since the last dose. If the headache does not settle with the first dose, don't repeat and use a rescue therapy instead. Choice of rescue therapy will depend on first line acute therapy and may be an oral triptan, subcutaneous or nasal tripan or diclofenac suppository.

Triptan contraindications: uncontrolled hypertension (do not prescribe triptans if blood pressure consistently over 140/90), coronary heart disease, peripheral vascular disease, history of stroke.

Adding a long acting NSAID, such as Naproxen, with a triptan can be an effective combination.

Triptans should generally work for 2 out of 3 attacks.

If two triptans have not worked, consider Rimegepant.

PREVENTATIVE TREATMENT

Consider prophylaxis treatment if migraine is disabling and reducing quality of life – e.g. frequent attacks (> 1 migraine per week on average) or prolonged severe attacks.

Choice of prophylaxis medication to try first will depend on patient comorbidities, drug interactions and patient preference.

Sodium Valproate and Topiramate should not be prescribed in women who may become pregnant.

Start at a low-dose and gradually increase according to efficacy and tolerability. Good response is a 50% reduction in severity and frequency of attacks.

Treatment failure is a lack of response to the highest tolerated dose used for 3 months.

If the patient responds well to prophylactic treatment, a trial of gradual drug withdrawal should be considered after 6-12 months.

For information an prophylaxis options, please see page 3 and page 4

REFERRAL

please consider referral to the headache clinic if still significant patient disability after trying available primary care treatment options

RIMEGEPAN (ACUTE) TREATMENT

Rimegepant is an oral selective calcitonin gene-related peptide (CGRP) receptor antagonist. It is 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.

Before Rimegepant is considered patients should have had an adequate trial of **at least 2 triptans**:

- Ensure triptan has been taken early in the headache phase
- Ensure mode of administration is correct e.g. use nasal or subcutaneous in patients with early vomiting
- Consider combination treatment as detailed in enclosed migraine treatment sheet

Acute treatment dosing regimen
- Rimegepant 75mg taken at the onset of a moderate to severe migraine (maximum 10 days per month or on average 2 days per week)
- The maximum dose in 24 hours is 75mg and a second dose should not be taken if ineffective or pain recurs

Drug Interactions
If patient is prescribed a strong CYP3A4 inhibitor (e.g. Clarithromycin, Itraconazole), then concurrent administration is not recommended. If prescribed with a moderate CYP3A4 inhibitor (e.g. Erythromycin, Fluconazole), a second dose should be delayed for 48 hours.

Side-effects

Rimegepant is generally well tolerated. Nausea is the main adverse effect in 1.2% of patients. Hypersensitivity reactions have been reported but are uncommon occurring in <1%.

Pregnancyand breastfeeding
Rimegepant is not recommended in pregnancy, if planning a pregnancy, or in breastfeeding.

PROPHYLAXIS TREATMENT OPTIONS IN PRIMARY CARE

The following prophylaxis treatment options are appropriate to be started in primary care:

Medication	Dosing Instructions	Additional Information
Propranolol	Starting dose 20mg twice daily, titrated up to 160mg - 240mg in 2-3 divided doses	Side effects in < 10% of patients include: • Gastro-intestinal upset ● Cold hands and feet ● Low blood pressure • Fatigue ● Disturbed sleep ● Impotence Side effects in < 1% of patients include: • Rashes ● Dry eyes
Candesartan	Startingdoseis4mg, titrating upfortnightly to 16mg	Candesartanisusuallywelltoleratedandisagoodtreatmenttoconsiderwhen patients have side effects to other medication or have comorbidities such as depression and fatigue. It can occasionally cause low blood pressure, dizziness and a dry cough.
First Line Amitriptyline Second Line Nortriptyline	Starting dose 10mgs at night, titrated up to 10mg - 150mg depending on efficacy and tolerability	Side effects can include sedation and a dry mouth. They are more likely to give side effects in patients over 65 years age and should generally be avoided. Nortriptyline is generally less sedating than Amitriptyline and is worth considering if patients feel sedated on Amitriptyline.
Topiramate	Starting dose 25mgs at night, titrated by25mgevery 2 weeks (depending on tolerability) to a dose of 50mgs twice a day **Topiramate is now contraindicated in pregnancy and in women of childbearing potential unless the conditions of a Pregnancy Prevention Programmeare fulfilled.** This follows a review by the MHRA which concluded that the use of topiramate during pregnancy is associated with significant harm to the unborn child. **More information [MHRA]**	Sideeffects in >10% of patientsinclude: • Paraesthesia (in ~ 50%) ● Anorexia, nausea ● Weight loss (minor) • Fatigue ● URTI ● Diarrhoea Side effects in < 10% of patients include: • Cognitive effects such as memory, language and somnolence • Depression and mood alteration ● Weight loss (>10% body weight) Side effects in < 1% of patients include: • Acute myopia secondary to angle closure glaucoma (usually occurs in the first month of treatment if it is going to happen) • Choroidal effusions resulting in anterior displacement of the lens and iris **Treatment Safety** • Patients with new onset visual symptoms or signs should have their intra-ocular pressure measured urgently by the community optometrist • Patients should be warned to watch out for significant weight loss and discontinuation of treatment should be considered if weight loss is > 10% • Patients should be monitored for signs of depression and advised to seek medical help immediately if they have suicidal thoughts
Pizotifen	Dose is 1.5mg - 6mg at night	Pizotifen works better in children and teenagers. It can be helpful in patients with dizziness as part of migraine. It can make people sedated so it is taken at night time and it can cause increased appetite.
Sodium Valproate	Starting dose is 200mgs twice daily, titrated up every 2 weeks to 600mg - 1000mg twice daily **Sodium Valproate is contraindicated in pregnancy and in women of childbearing potential unless the conditions of a Pregnancy Prevention Programme are fulfilled.** **More information [MHRA]** **Sodium valproate is contraindicated in males < 55 years of age.** **All men taking valproate and their partners should use effective contraception.** **More information [MHRA]**	Side effects in < 10% of patients include: • Diarrhoea ● Nausea ● Weight gain ● Temporary hair loss Side effects in < 1% of patients include: • Increased alertness ● Tremor
Lamotrigine	Week 1-2 Lamotrigine 25mg once daily Week 3-4 Lamotrigine 50 mg once daily Week 5-6 Lamotrigine 25 mg morning and 50 mg at night Week 7-8 Lamotrigine 50 mg twice daily	Lamotrigine can be helpful in frequent migraine aura or persistent aura (anecdotal evidence). It is not useful for headache. If tolerated can continue to increase daily dose by 25 mg every 2 weeks aiming for a dose of 100 mg twice daily if required for symptom control. Warn patient of risk of rash, fever or any other sign of hypersensitivity reaction. Avoid abrupt withdrawal, taper off over 2 weeks or longer unless serious skin reaction occurs. **Note** – if patient is on Valproate week 1-2 dose is 25 mg on alternative days, then week 3-4 is 25 mg once a day then titration schedule as above (i.e. increase daily dose by 25 mg every 2 weeks).

Second line Treatment Options

Medication	Dosing Instructions	Additional Information
Flunarizine	Starting dose is 5mg at night increasing to 10mg *(Hospital only prescription)*	Flunarizine is particularly helpful for migraine patients who get either vertigo or basilar aura. It has a long half life and it can take weeks for an effect to be seen. Flunarizine is usually well tolerated. The most often reported side effects are: . • Drowsiness ● Weight gain ● Nausea ● Insomnia ● Heartburn Patients should be monitored for signs of depression and advised to seek medical help immediately if they have suicidal thoughts. Parkinsonism is a rare side effect. As Flunarizine has a long half life, it can just be stopped and it will usually take a few weeks for the side effects to settle. Flunarizine is not recommended in pregnant or breastfeeding women. Women of childbearing age should take adequate contraceptive precautions and Flunarizine should be stopped for at least 3 months before planning pregnancy.
Botox	Botox has a licence in the UK for chronic migraine (headache occurring on 15 or more days a month for more than 3 months, which has the features of migraine headache on at least 8 days per month and medication overuse headache has been addressed). It is not licensed for episodic migraine. Patients will have to have failed or not tolerated 3 preventers. **Botox Protocol** Patients are given 2 cycles of 31 injections (5 units each injection) 12 weeks apart. Their response is formally assessed at 6 months with patient diary. No further botox is given if either they revert to episodic migraine or have less than a 30% improvement. Injections continue if there is greater than a 30% improvement but they are still chronic migraine. This is re-assessed at every 3 months cycle. Patients who revert back to chronic migraine after stopping botox are eligible for a further series of injection cycles with a slight change in stopping criteria: they will be eligible to continue until less than 10 headache days a month.	
Atogepant	Atogepant 60 mg daily can be if 4 or more migraine days a month and 3 preventers not helpful or tolerated	Atogepant is an oral selective calcitonin gene-related peptide (CGRP) receptor antagonist. It is 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. Acute treatment with Aspirin, NSAIDS, triptans and rimegepant can be considered in patients taking atogepant. Acute treatment should be restricted to 10 days per month to Routine blood monitoring is not required. **Drug Interactions:** If patient is prescribed 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 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. **Side-effects:** Atogepant is generally well tolerated. Side effects noted 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. **Pregnancyand breastfeeding:** Atogepant is not recommended in pregnancy, if planning a pregnancy, or in breastfeeding.
Rimegepant	Rimegepant 75 mg alternate days can be considered for patients with 4-14 migraine days per month	Rimegepant is an oral selective calcitonin gene-related peptide (CGRP) receptor antagonist. It is 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. Àcute treatment with Aspirin, NSAIDS, triptans and rimegepant can be considered in patients taking rimegepant for preventative treatment. Acute treatment should be restricted to 10 days per month to prevent medication overuse headache. For patients prescribed rimegepant as a preventative, rimegepant can be used as an acute treatment on non- preventer dosing days as long as the licensing requirements for acute use are met i.e. triptan failure or lack of tolerability. No blood monitoring is required. **Drug Interactions:** If patient is prescribed a strong CYP3A4 inhibitor (e.g., clarithromycin, itraconazole) then concurrent administration is not recommended. If prescribed 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 **Side-effects:** Rimegepant is generally well tolerated. Nausea is the main adverse effect in 1.2% of patients. Hypersensitivity reactions have been reported but are uncommon occurring in <1%. **Pregnancyand breastfeeding:** Atogepant is not recommended in pregnancy, if planning a pregnancy, or in breastfeeding.
Monoclonal antibodies	**Erenumab** is a humanised monoclonal antibody blocking the calcitonin gene-related peptide receptor inhibiting the function of CGRP at its receptor. Eptinezumab, Fremanezumab and Galcanezumab are humanised monoclonal antibodies that block the CGRP ligand. Monoclonals are licensed as preventer medications for patients with 4 or more migraine a month and 3 preventers not helpful or tolerated	