NEUROLOGY:
Migraine Management

Background
This guideline covers advice on the diagnosis and management of migraine in adult patients. It aims to improve the recognition and management of migraine, highlight red flag symptoms, and provide advice on when to refer.

Who?	Adult patients who are experiencing headaches consistent with migraine.
Presentation/ Symptoms	**Red Flags** • New onset migraine in over 50s • New persistent, progressive headache in a patient with prior migraine • Headaches associated with focal neurology, loss or altered consciousness, new cognitive dysfunction • Headache with raised ICP features AND severe vomiting, drowsiness ± papilloedema or visual loss • Headaches associated with systemic features (e.g. worsening headache with fever, meningism or malignant hypertension) or raised ESR/CRP • Sudden onset headache (thunderclap headache) <1 minute to maximum severity • Side locked headache (i.e. migraine only ever affecting one side) • New onset headache in patient with prior history of cancer • Recent head trauma (within last 3 months) • Orthostatic headache • Headache triggered by cough, sneeze, valsalva or exercise • Compromised immunity (HIV or immunosuppressant drugs) • New headache in late pregnancy or early post-partum **<u>Features of/ Symptoms/ Presentation of migraine</u>** Moderate to severe headache (unilateral or bilateral) pounding/throbbing in nature lasting 4 -72 hours. Can be associated with: • Nausea and vomiting • Photophobia • Phonophobia • Aggravated by movement (often preference is to lie still in a dark room) **<u>Examination</u>** • Neurological examination (including fundoscopy) normal **<u>Diagnostics</u>** None required unless have red flags

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Management in Primary Care

After informing the patient of a migraine diagnosis consider signposting for further migraine information e.g. Migraine Trust's website www.migrainetrust.org

Treatment strategies include addressing lifestyle measures for example improving the quality and quantity of sleep, reducing anxiety levels and consideration of dietary triggers (cheese, chocolate, alcohol, caffeine, monosodium glutamate, citrus fruits).

Exclude medication overuse headache (more than 15 days a month for more than 3 months) by reviewing over the counter analgesia use.

Pharmacological treatment options include:

For the acute attack

- Aim to limit acute treatments to no more than 8 days per month to avoid medication overuse headache. Consider preventive treatments if appropriate – see here.
- Adding an antiemetic to acute treatment can improve efficacy unrelated to nausea and/or vomiting by improving gastric motility and aiding drug absorption.
- Avoid opiates including codeine.

- **Simple analgesia:** Ibuprofen 400-600 mg or Paracetamol or Aspirin 600-900 mg.

- **Triptans:** (start with the one with lowest cost unless clinical reasons).
  - **1st line oral sumatriptan** (best evidence with 50mg to 100mg). Triptans not licensed in > 65 years. See here if considering an alternative triptan.
  - With **antiemetic** (see here) or consider alternative route if tablet ineffective e.g. oro-dispersible (more cost effective than melt wafers), nasal spray or injectable.
  - After 2 treatment failures a trial with an alternative triptan is recommended (note triptan considered effective if beneficial for 2 out of 3 attacks). Lack of response to one triptan does not predict response to other triptans.
  - Triptan medication cannot be taken twice for the same migraine attack.
  - Try combination of triptan and paracetamol or NSAID. Combination of a triptan and an NSAID with a long half-life, such as naproxen, is better than monotherapy.

- **2nd line alternative triptans to sumatriptan:** If considering an alternative triptan to sumatriptan prescribe the most cost-effective taking into account preferred formulary choices (sumatriptan and naratriptan are currently the most cost effective triptans).
  In comparison to sumatriptan 100 mg (see BASH guidelines):
    - Lower adverse events: naratriptan 2.5 mg, frovatriptan 2.5 mg and almotriptan 12.5 mg.
    - Better 2-hour pain response: rizatriptan 10mg, eletriptan 80 mg

and almotriptan 12.5 mg tablets.
  - Lower recurrence rate: frovatriptan 2.5 mg or eletriptan 40 mg

For women and girls with predictable menstrual related migraine that does not respond adequately to standard acute treatment consider treatment with naratriptan (2.5 mg twice a day) on the days migraine is expected. If naratriptan not effective, consider frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day).

- **3rd line rimegepant for acute treatment (after triptans and/or simple analgesia)**: Rimegepant 75mg oral lyophilisate (one tablet at onset of migraine) can be considered if over 18 and at least 2 triptans were ineffective or if triptans contraindicated or not tolerated, and simple analgesia are ineffective.
  - Clinician: Supporting Information for Acute Treatment of Migraine
  - Patient Information: Rimegepant for Treating a Migraine Attack

  Note: whilst NICE TA919 has approved rimegepant for this indication and it is Green on the SY TLDL not all GPs will be familiar with prescribing it and may therefore choose not to. Primary care clinicians can seek specialist advice by emailing Sheffield Teaching Hospitals (STH) Headache Clinic: sth.headacheservice@nhs.net.

- **Antiemetics:**
  - Metoclopramide licensed for > 18 years for nausea and vomiting associated with acute migraine. Maximum treatment duration is 5 days. Should not be used regularly due to the risk of extrapyramidal side effects. Metoclopramide safety alert: https://www.gov.uk/drug-safety-update/metoclopramide-risk-of-neurological-adverse-effects.
  - Prochlorperazine (only a buccal preparation of prochlorperazine is licensed for this indication).
  - Domperidone safety alert: https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side-effects (recommended by BASH).

Preventive Treatments

If patients experience 4 or more migraine days a month, consider preventive treatments (recommended by BASH). Treatment involves starting a low dose, with regular titrations upwards according to response, until either headaches improve, side effects intervene, or a maximum dose is reached. Continue for at least 6-8 weeks to adequately assess effect.

Treatment choice will depend on individual patients – on co-morbidities, personal preferences, the side effect profiles and with reference to the patient's current clinical situation and future plans (e.g. pregnancy or contraception).
Offer one of the following after a full discussion of the benefits and risks of each option:

- **Beta-Blockers.** Propranolol 10mg bd - can titrate in 10-20 mg steps (maximum 120mg – 240mg daily) (recommended by BASH). Atenolol 25mg bd daily - can titrate in 50 mg steps (maximum 200mg daily).

  Start at a low dose and increase gradually until migraine frequency improves, side effects intervene or the maximum dose is reached. May

cause worsening of asthma therefore contraindicated. Other side-effects include light-headedness, or bad dreams.
Pregnancy: may cause intra-uterine growth restriction, neonatal hypoglycaemia, and bradycardia.

Note beta-blockers: The maximum dose of rizatriptan in people who are also taking propranolol should be 5 mg due to the risk of interactions. Rizatriptan should not be taken within two hours of taking propranolol.

- **Amitriptyline** starting at 10-25 mg in the evening, increased in 10-25 mg steps after a minimum of 2 weeks with further increases if required to a maximum dose of 150mg at night (usual dose 25 – 75 mg). Doses above 100mg should be used with caution. Can cause tiredness, dry mouth and difficulty passing water. This can be used in combination with beta-blockers.
  Manufacturer advice: not to be used during pregnancy unless clearly necessary and only after careful consideration of the risk/benefit.

- **Topiramate** tablets (capsules more expensive) starting at 25 mg once daily. Can be increased further in steps of 25 mg no sooner than every 2 weeks. The recommended total daily dose is 50 mg bd (can increase to maximum 100 mg bd but care is needed as side-effects more likely).
  Can cause cognitive slowing. This usually improves after the first 6 weeks. Other side effects include drowsiness, confusion, blurred vision, loss of appetite, renal stones. If stopping, need to reduce by 25-50mg every week to avoid rebound headache.

  Topiramate Pregnancy Prevention Programme
  Topiramate is contraindicated for migraine prophylaxis in pregnancy. It is also contraindicated in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme (PPP) are fulfilled. See **here (page 9)** for more details.

- **Candesartan** (off-label use recommended by BASH) starting at 2 mg once a day. This can be increased in 2mg steps up to 8 mg bd if required. Possible side effects include cough, dizziness. Dose increases are every 4 weeks.
  Candesartan is not recommended during first trimester of pregnancy and contraindicated during the second and third trimesters.

- **Riboflavin** (400 mg once a day). **Not recommended on prescription but can be bought OTC (low cost).** May be effective in reducing migraine frequency and intensity. Avoid if planning a pregnancy or pregnant.

Do not prescribe gabapentin nor pizotifen for migraine prophylaxis.

Management in Secondary Care	**Secondary Care initiation of preventive migraine treatment**: 12-week review after initiation by neurology: Headache diary to be kept by patient. **Episodic migraine** (≥ 4 and < than 15 migraine attacks per month), only if at least 3 preventive treatments haven't worked or CI / not tolerated. • **Injection/Infusion Anti-Calcitonin Gene-Related Peptide (CGRP).** - Injection: erenumab, fremanezumab, galcanezumab OR Infusion: Eptinezumab (all RED on SY TLDL) • **Oral Anti-Calcitonin Gene-Related Peptide (CGRP).** - Rimegepant 75mg oral lyophilisate (one tablet on alternate days) Red on SY TLDL or - Atogepant 60mg tablet (one daily) or 10mg once daily for reduced dose Red on SY TLDL. Stop if migraine frequency does not reduce by at least 50% after 12 weeks. **Chronic migraine**: headaches ≥ 15 days/month, with at least 8 of those having features of migraine, choice of: • **Injection Anti-Calcitonin Gene-Related Peptide (CGRP)** - Injection: erenumab, fremanezumab or galcanezumab RED on SY TLDL • **Oral Anti-Calcitonin Gene-Related Peptide (CGRP)** - Atogepant 60mg tablet (one daily) or 10mg once daily for reduced dose RED on SY TLDL. Stop if the migraine frequency does not reduce by at least 30% after 12 weeks.
Monitoring	Titrate preventive medications slowly to an effective or maximum tolerable dose and continued for at least 6-8 weeks to adequately assess effect. A headache diary (see here) may help evaluate response to treatment. Quality of life can be monitored using the HIT- 6 score. Ensure there is no medication overuse – acute treatments should be limited to twice per week - otherwise preventive treatments are less effective and patients are at risk of medication overuse (medication induced) headache. Review the need for continuing migraine prophylaxis 6 months after the start of prophylactic treatment. For topiramate – ensure compliance with the PPP – see here.
Secondary Care Referral Criteria	**Eligibility:** • High frequency migraine persists despite trial of 2 to 3 migraine preventives • Diagnosis of migraine not definite • Migraine with red flags (see above) **Existing Management** In the referral letter the previous preventive drugs used, the maximum doses reached, duration of treatment and reasons for stopping is very helpful.
Clinic Information	If a referral is required, please refer via eRS **Specialty: Neurology** **Clinic Type: General Neurology Clinic** **If there is concern regarding cancer, refer via the 2 week wait pathway.**

Additional information	**Headache Pathway Flowchart Page 7** **Migraine Pharmacological Treatment Pathway in Adults Flowchart Page 8** **Topiramate Pregnancy Prevention Programme Page 9** **Patient Information Page 10**
References	• NICE Guidance. Headaches: Diagnosis and management of headaches in young people and adults. http://www.nice.org.uk/guidance/CG150 • BASH National headache management system for adults 2019 guidelines: https://bash.org.uk/wp-content/uploads/2023/02/01_BASHNationalHeadache_Management_SystemforAdults_2019_guideline_versi.pdf • Medicine manufacturer data sheets (information): https://www.medicines.org.uk/emc • National Neurosciences Advisory Group (NNAG) Clinical pathway for adults for headache & facial pain 2023: www.nnag.org.uk/optimal-clinical-pathway-for-adults-with-headache-facial-pain • MHRA Drug Safety Update: Topiramate (Topamax): start of safety review triggered by a study reporting an increased risk of neurodevelopmental disabilities in children with prenatal exposure. July 22 • MHRA Drug Safety Update: Topiramate (Topamax): introduction of new safety measures, including a Pregnancy Prevention Programme. June 2024

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Headache Pathway Flowchart

Algorithm for migraine management in primary care

Headache consistent with migraine

Are there any red flags?

No

Discuss lifestyle factors including sleep

Consider medication overuse (acute treatment more than twice per week)

Commence acute treatments

Check migraine frequency. If more than 4 per month consider preventive treatments

Monitor with headache diary

Slowly titrate preventive treatment according to response and continue for at least 6-8 weeks to assess effect. All have cautions or contraindications in pregnancy. See manufacturers advice.

Trial of 2 -3 preventives if required

Migraine frequency improves?

Yes

Consider withdrawal of preventive treatment after 6 months of effective treatment.

No

Recheck for medication overuse and if suspected withdraw overused migraine medication.
After 2 -3 preventives consider referral to general neurology clinic.

Yes

New onset migraine in over 50s. Consider brain imaging* or referral to neurology clinic

New persistent, progressive headache in a patient with prior migraine. Consider brain imaging or referral to neurology clinic

Headaches associated with focal neurology, new cognitive dysfunction or papilloedema. Refer urgently via neurology on call

Headaches associated with systemic features (eg pyrexia) or raised ESR/CRP. Refer urgently to infectious diseases if meningitis being considered. Refer to rheumatology if temporal arteritis being considered (or ophthalmology if have visual symptoms).

Sudden onset headache. Refer urgently via Emergency Department or via neurology on call

Side locked headache (i.e. migraine only ever affecting one side). Consider brain imaging or referral to neurology

New onset migraine in patient with prior history of cancer. Consider brain imaging or referral to general neurology clinic

Recent head trauma (within last 3 months). Consider brain imaging (CT) or referral to general neurology clinic if not available.

Orthostatic headache. Refer via neurology on call or general neurology clinic

Headache triggered by cough, sneeze, valsalva or exercise. Refer via neurology on call or general neurology clinic

Compromised immunity (HIV or immunosuppressant drugs). Consider brain imaging or referral to general neurology clinic

New headache in late pregnancy or early post-partum. Assess for pre-eclampsia. Refer via neurology on call to consider urgent brain imaging including MRV.

* MRI brain unless contraindicated then CT

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Migraine Pharmacological Treatment Pathway in Adults Flow chart

Use headache diary. Success of acute treatment is determined by reduction in bothersome symptoms within 2 hours. Aim to limit acute treatments to no more than 8 days per month to avoid medication overuse headache (MOH).

Primary Care

Acute treatment of migraine with/without aura – offer combination therapy:

1st step:

- **Simple analgesics**: Ibuprofen 400-600mg or Paracetamol or Aspirin 600-900mg (max 10 days per month)
- **Triptan**– 1st line **sumatriptan (best evidence with 50mg to 100mg).** Max 8 days/month to limit MOH. Need to take triptans early in attack to be effective. Only work once headache starts. Contraindicated in people with CVD.
- **Antiemetic** can improve efficacy unrelated to N&V by improving gastric motility and aiding drug absorption.
- If vomiting consider non-oral route triptan (eg nasal, buccal or subcutaneous)
- Do not prescribe opioids (including codeine)

2nd step: No response to first-line triptan.

- Try other triptans. Use for at least 3 migraine attacks at maximum tolerated dose before deciding not effective.

3rd step: Rimegepant for acute treatment of episodic migraine (see page 3)

- Option when at least 2 triptans tried and are ineffective or contraindicated / not tolerated, and simple analgesia are ineffective
- **Rimegepant** (one 75mg oral lyophilisate at onset of migraine). Maximum dose 75mg in 24 hours. Initial trial with 4 tablets, then if successful maximum 8 tablets per month or 2 per week. Rimegepant Supporting Information Acute Treatment and PIL

Preventive treatment: ≥ 4 migraine days per month consider preventive treatment.
Start at low dose and gradually increase according to efficacy and tolerability.
Trial at max tolerated dose for at least 8 weeks before deciding effectiveness.

- **Propranolol** starting dose 10mg BD (maximum 240mg daily) or atenolol.
- **Amitriptyline** starting dose 10mg nocte (usual dose 25 – 75 mg, maximum 150mg daily).
- **Topiramate** target starting dose 25mg OD (maximum 100mg BD). Contraindicated in pregnancy and women of childbearing potential unless using highly effective method of contraception and have signed the annual risk awareness form (see here).
- **Candesartan** off-label use starting dose 2mg OD (maximum 16mg daily). Avoid during pregnancy and breast feeding.
- Riboflavin: NICE CG150 advise patient riboflavin 400mg od can be bought OTC.

Review continued need 6 months after initiation. If having less than 4 migraine days per month try a pause in preventive treatment.
Be alert to MOH (> 15 migraine days per month).

Referral to secondary care if: high migraine frequency e.g. >15 days per month, migraine persists despite trial of 2-3 migraine preventives without satisfactory benefit (<50% reduction in migraine days per month), diagnosis of migraine not definite, migraine with red flags.

Secondary Care

(note Anti-CGRP is Anti-Calcitonin Gene-Related Peptide)

Preventing episodic migraine (≥ 4 and < than 15 migraine attacks per month), only if at least 3 preventive treatments haven't worked or contra-indicated / not tolerated, choice of:

Injection/infusion Anti-CGRP:

- Medications include: **erenumab, fremanezumab, galcanezumab** or **eptinezumab.** RED on SY TLDL

Oral Anti-CGRP:

- **Rimegepant** (one 75mg oral lyophilisate on alternate days for preventing migraine)**.** Red on SY TLDL.
- **Atogepant** (60mg daily) RED on SY TLDL

Stop if migraine frequency does not reduce by at least 50% after 12 weeks or if decision is to continue see below:

Preventing chronic migraine: headaches > 15 days/month, with at least 8 of those having features of migraine, choice of:

Injection/Infusion Anti-CGRP:

- Medications include: **erenumab, fremanezumab, galcanezumab** or **eptinezumab** RED on SY TLDL

Oral Anti-CGRP:

- **Atogepant** (60mg daily) RED on SY TLDL

Stop if migraine frequency does not reduce by at least 30% after 12 weeks, Or

- **Botulinum Toxin (Botox®)**
  155-195 units 12 weekly.
  Stop if migraine frequency does not reduce by at least 30% after 2 treatment cycles or has changed to episodic migraine for 3 consecutive months.

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Topiramate Pregnancy Prevention Programme

Topiramate Pregnancy Prevention Programme

Topiramate is contraindicated for migraine prophylaxis in pregnancy. It is also contraindicated in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme (PPP) are fulfilled.

These conditions are also applicable to female patients who are not sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy – this should be documented in Step 1 of the **Annual Risk Awareness Form**.

Prior to initiation:

- **Assess the potential for pregnancy** and if necessary, discuss the need for the patient to be on the PPP – See **Guide for Healthcare Professionals for Migraine.**
- Ensure the patient is fully informed and understands the **risks related to the use of topiramate during pregnancy** (major congenital malformations, neurodevelopmental disorders and foetal growth restriction).
- Discuss the need to take **highly effective contraception** throughout treatment and for at least four weeks after the last dose of topiramate.
- **Note:** Topiramate can potentially reduce the efficacy of hormonal contraception. Acceptable forms of contraception include an intrauterine method (Cu-ICD or LNG-IUS), or the medroxyprogesterone acetate depot injection PLUS a barrier method. Use of combined hormonal contraception, progestogen-only pills and the etonogestrel implant is not recommended. Pregnancy testing may be required e.g. if there is any reason to suggest lack of compliance or effectiveness of contraception. For more information see MHRA and FSRH: Drug Interactions with Hormonal Contraception.
- **Exclude pregnancy** (by serum pregnancy test).
- Complete the **Annual Risk Awareness Form** with the patient (or responsible person) – give a copy to the patient and upload a copy to their medical notes.
- Provide a copy of the **Patient Guide for Migraine** to the patient (or responsible person).
- Ensure the patient is aware of the need to contact a healthcare professional urgently if they suspect they might be pregnant or wish to plan a pregnancy.
- Ensure appropriate PPP SNOMED codes are assigned. E.g. Pregnancy prevention programme started (1129771000000103)

Following initiation:

- All patients require an annual review, to ensure compliance with the requirements of the PPP and to complete the **Annual Risk Awareness Form.**
  Ensure appropriate PPP SNOMED codes are assigned to all patients. E.g. Pregnancy prevention programme started (1129771000000103)
- Ensure continuous use of **highly effective contraception** in all women of childbearing potential throughout treatment and for at least four weeks after the last dose of topiramate (consider the need for pregnancy testing if not a highly effective method).
- See the patient promptly in case of unplanned pregnancy or if she wants to plan a pregnancy.
- See **Guide for Healthcare Professionals for Migraine** for full details.

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Patient Information

Headache Diary
BASH-diary.pdf

Headache Impact Test
HIT- 6 score
This questionnaire helps the patient describe and communicate the way they feel and what they cannot do because of headaches.

BASH Headache Information Sheet
BASH-selfhelp.pdf

BASH Migraine Medication Patient Information Sheets
Amitriptyline: BASH-amitrip.pdf
Candesartan: BASHCander.pdf
Propranolol: BASHProp.pdf
Topiramate: BASH-tpx.pdf
Triptans: BASH-triptans.pdf

Migraine Trust
https://migrainetrust.org/

Topiramate Pregnancy Prevention Programme
Patient Guide for Migraine