Guidance for the Treatment and Prevention of Acute Migraine (excluding anti-CGRP drugs)

Treatment of Acute Attacks

In general, a triple drug combination taken together works best for the acute treatment of migraine [1]:

- a $5HT_1$ Receptor agonists (known as a 'Triptan') e.g. Sumatriptan or Zolmitriptan
- a Non-Steroidal Anti-inflammatory Drug (NSAID) e.g. Ibuprofen or Naproxen
- *or* Aspirin (this should be avoided in children under 16 years of age) *or* Paracetamol
- an Anti-Emetic e.g. Metoclopramide or Prochlorperazine

Acute treatment can be taken on up to 6 days per month, and not exceeding 10 days per month.

A typical regimen may be:
Zolmitriptan 2.5–5mg Oro-dispersible Tablet as a single dose, Naproxen 500 mg as a single dose, metoclopramide 10mg as a single dose.

The triptan dose should be taken at the onset of the headache.

Some patients achieve sustained headache relief with a single pain-relieving agent [1] e.g. Aspirin 900 mg stat (which should be avoided in children under 16 years of age) or Paracetamol 500mg-1g stat.

Treatment for Prevention of migraine (excluding anti-CGRP drugs)

- Drugs to prevent migraine need to be taken daily to be effective. They are not the same as conventional pain killers. They are pain-modulators which are derived from different drug groups originally designed to treat other diseases.

- In practice they are unlikely to abolish headaches but may reduce the severity and / or frequency of headache. They should be used with lifestyle modifications that can improve headaches including:

    - Getting regular sleep
    - Eating regular meals
    - Taking moderate amounts of exercise
    - Drinking plenty of water
    - Limiting caffeine and alcohol intake
    - Reducing stress

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- Failure to address lifestyle issues can result in a poor response to preventive drugs.

- 'Medication Overuse Headache' can interfere with treatment using preventive or prophylactic drugs: prophylactic drugs are unlikely to work if any combination of acute pain killers is taken regularly on more than 10 days per month.

- All acute analgesia (e.g. paracetamol, co-codamol or tramadol), anti-inflammatory drugs (e.g. ibuprofen or naproxen) or triptans, should be abruptly discontinued for at least 3 weeks to address medication-overuse headache (including triptan-overuse headache). Typically, after 3 weeks the pain is either the same as it was before analgesic use was stopped, or slightly better.

- Prophylactic drugs are not to be used as acute migraine treatments; they should be taken singly rather than in combination.[2]

- Each drug should be started at the lowest possible dose and increased in the smallest dosage steps at weekly / fortnightly intervals, depending on response and tolerability.

- Treatment with a prophylactic drug at the maximum tolerated dose for 3 months is the best way to assess efficacy.

- If treatment is effective, it should be continued for about 6 months before attempting to wean medication.

- A minimum of three drugs should be trialled appropriately in the event of treatment failure with one or more agents.

- The following prophylactic agents are listed in no particular order. Further advice will be provided to GPs by the Consultant Neurologist following consultation with individual patients.

1. Propranolol (Licensed Indication)

- Starting dose: 10 mg daily; Maximum dose: 80 mg twice daily
- Switch to a long-acting formulation, as desired, once a maintenance dose is achieved.
- Possible side effects: dizziness, fatigue, cold extremities, vivid dreams, lowers blood pressure.
- Contraindications: asthma, peripheral vascular disease.

2. Amitriptyline/Nortriptyline (Unlicensed Indication)

- Starting dose: 10 mg at night; Maximum dose: 100 mg at night
- Independent of its anti-depressant effect, these drugs have anti-migraine properties.

- Possible side effects: dry mouth, sedation (Nortriptyline is less sedating than Amitriptyline), blurred vision, constipation and urinary retention.
- Contraindications: heart disease.

3. Topiramate (Licensed Indication)

- Starting dose: 25 mg at night titrated in 25 mg steps every 2 weeks; Maintenance dose: 100 mg daily in two divided doses (offers best trade-off between tolerability and efficacy); Maximum dose: 200 mg daily in two divided doses.
- Possible side effects: somnolence, angle-closure glaucoma, loss of verbal fluency, tingling/numbness in extremities, weight loss, renal stones (ensure adequate fluid intake), foetal malformations.
- Cautions: Topiramate reduces the effectiveness of oral contraceptives; the manufacturer recommends a highly effective method of contraception in women of childbearing age because of the risk to the foetus and does not recommend use for migraine prophylaxis in women of childbearing age.

4. Pizotifen (Licensed Indication)

- Starting dose: 0.5 mg at night; Maximum dose: 4.5 mg daily in two divided doses.
- Possible side-effects: weight gain, dry mouth.
- Evidence for use is limited and weight gain and sedation are often unacceptable side effects of this drug.

5. Gabapentin (Unlicensed Indication)

- Starting dose: 100 mg at night, titrated every 2 weeks; Maximum dose: 1200 mg daily in two or three divided doses.
- Potential side effects: somnolence, weight gain
- Contraindications: Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants, and the elderly may be at higher risk of experiencing severe respiratory depression and dose adjustments may be necessary in these patients https://www.gov.uk/drug-safety-update/gabapentin-neurontin-risk-of-severe-respiratory-depression

6. Candesartan (Unlicensed Indication)

- Starting dose: 4 mg daily; Maximum dose: 24 mg daily (usually 16 mg daily or less is effective)
- Possible side-effects: bodily pain, tiredness, tingling, low heart rate; lowers blood pressure
- Monitoring: regular blood tests for urea & electrolytes (https://cks.nice.org.uk/topics/hypertension/prescribing-information/angiotensin-ii-receptor-blockers/)

7. **Duloxetine (Unlicensed Indication)**

- Starting dose: 30 mg daily, increased every 2 weeks; Maximum dose: 90 mg daily.
- Possible side-effects: nausea, vomiting, constipation/diarrhoea, abdominal pain, dry mouth, insomnia, dizziness, fatigue, dreams, weight changes

8. **Venlafaxine (Unlicensed indication)**

- Starting dose 37.5 mg once daily, increasing in 37.5 mg increments every 2 weeks to a maximum of 375 mg daily in TWO divided doses.
- Only some common side-effects are listed: Anxiety, decreased appetite, arrhythmias, chills, confusion, constipation depersonalisation, dizziness, movement disorders, palpitations, sedation, skin reactions, sleep disorders, weight changes.

9. **Sodium Valproate (Unlicensed Indication)**

- Starting dose: 200 mg at night, titrated every 2 weeks; Maximum dose: 1500 mg daily in two or three divided doses.
- Side effects: weight gain, somnolence, tremor, foetal malformations
- Before initiating valproate in patients younger than 55 years, healthcare professionals should consider all other suitable therapeutic options and consult the findings of the epilepsy medicines in pregnancy review.
    - Valproate: reminder of current Pregnancy Prevention Programme requirements; information on new safety measures to be introduced in the coming months - GOV.UK (www.gov.uk).
- Monitoring: FBC and LFTs at baseline and during treatment.

10. **Riboflavin (Nutritional Product – not on the BLMK Formularies)**

- Whilst UK Guidelines advise that riboflavin may be useful in preventing migraines [3,4], patients should be advised to self-purchase as there is no licensed riboflavin product available in the UK, nor any cost effectiveness data to justify its use on NHS prescription.

You should refer to the patient information leaflet supplied with a medicine for a comprehensive list of potential adverse effects.

All of these drugs are best avoided in pregnancy.

References:

1. Headaches in over 12s: Diagnosis and Management – Overview | Headaches in over 12s: diagnosis and management | Guidance | NICE [last updated 17/12/21 and accessed 10/07/23]
2. Headache Management: Pharmacological Approaches – https://pn.bmj.com/content/15/6/411 [accessed 17/12/23]
3. Items which should not be routinely prescribed in primary care – Guidance for CCGs – NHS England » Items which should not be routinely prescribed in primary care: Guidance for CCGs [accessed 10/07/23]
4. Prophylaxis of migraine headaches with riboflavin: A systematic review - Thompson - 2017 - Journal of Clinical Pharmacy and Therapeutics - Wiley Online Library [accessed 10/07/23]