Migraine: 10 Top Tips

Non-Medical Prescribing Study Day
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Disclosures

- Speaker Honoraria: Pfizer

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- National Migraine Centre: Online Doctor

- Author Royalties:

- Pulse Articles (2023, 2024), BMJ (2023, 2024), Doctors.net.uk (2024)
- Guidelines in Practice Articles (2020)
- FSRH e-learning Author (2019-2020)
- Oxford Handbook of General Practice 5th Edition (June 2020)

Overview

1 Migraine

- Epidemiology
- Clinical Features
- ‘Red flags’

2 Treatments options

- Lifestyle
- Non-drug
- Acute
- Preventer
- What’s new?

Introduction

- Headache is COMMON
- Lifetime prevalence > 90% (UK)
- 4.4% GP consultations
- 20-30% neurology outpatient consultations

HISTORY IS KEY

CLASSIFICATION

PRIMARY (98%)
- Primary diagnosis
- e.g. migraine, cluster, tension
- International Headache Society classification system http://www.ichd-3.org

SECONDARY (2%)
- Precipitated by underlying condition
- e.g. infectious, neoplastic, vascular, drug-induced

Latinovic R, Gulliford M, Ridsdale L. Headache and migraine in primary care: consultation, prescription, and referral rates in a large population. J *Neurol Neurosurg Psychiatry* 2006;77:385-387; Watson D P. Easing the pain: challenges and opportunities in headache management. *Br J Gen Pract* 2008;58:77-78

Epidemiology: Migraine

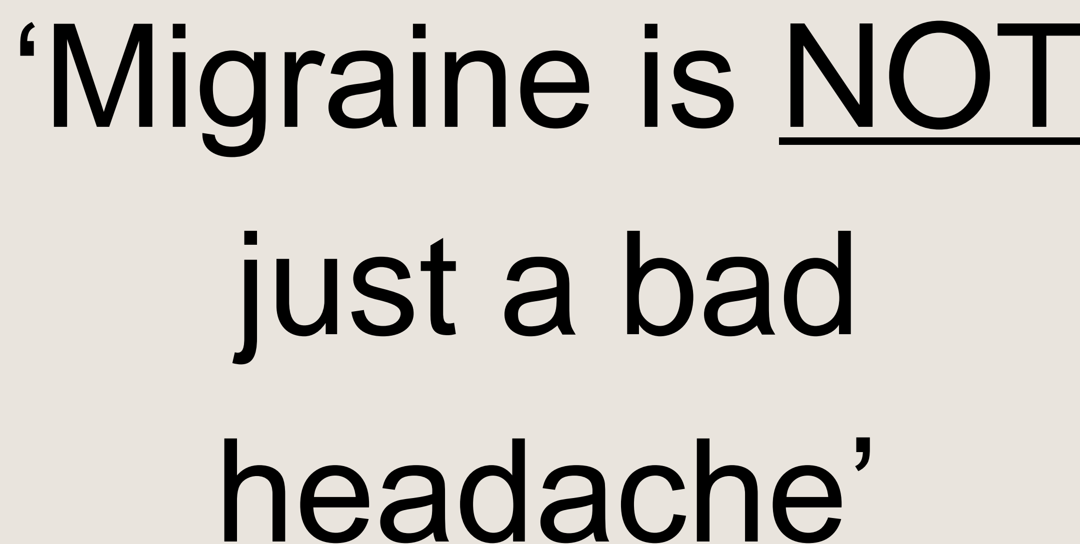
THE **leading** cause of global disability in women aged 15–49[1]

More people live with migraine than **diabetes, asthma and epilepsy** combined[2]

Around **26%** of UK adults aged 15–49 are living with migraine[3]

1. Katsarava Z, et al. *The Lancet* .2021; 397: 1485–95. 2. The Migraine Trust. State of the Migraine Nation Dismissed for too long: Recommendations to improve migraine care in the UK. September 2021. Available at: https://migrainetrust.org/wp-content/uploads/2021/09/Dismissed-for-too-long_Recommendations-to-improve-migraine-care-in-the-UK.pdf; 3. Institute for Health Metrics and Evaluation. GBD Results Tool. 2019. Available at: https://vizhub.healthdata.org/gbd-compare/.

Top Tip #1



Proposed phases of a migraine attack

Premonitory	Aura	Headache	Postdrome
A few hours to days	5–60 minutes	4–72 hrs	<12–24 hrs
Fatigue Cognitive difficulties Mood changes Food cravings Neck pain Yawning	Visual aura (scotoma, fortification spectrum) Sensory disturbance Speech disturbance Motor symptoms	**Headache** **Nausea with or without vomiting** **Photophobia** **Phonophobia** Osmophobia	Feeling tired or weary Difficulty with concentration Neck stiffness

Headache

Symptoms in **bold** denote criteria in the ICHD-3 classification

ICHD-3=International Classification of Headache Disorders, 3rd edition

Adapted from: Dodick. Lancet 2018;391(10127):1315–1330; Cady et al. Headache 2002;42(3):204–216; Goadsby et al. Physiol Rev 2017;97(2):553–622; Headache Classification Committee of the International Headache Society (IHS). Cephalalgia 2018;38(1):1–211; The American Migraine Foundation. https://americanmigrainefoundation.org/resource-library/timeline-migraine-attack/. Accessed May 2020; Migraine Buddy website. Available at: https://migrainebuddy.com/migraine/2018/11/22/the-stages-of-a-migraine-postdrome-phase. Accessed May 2020

Classification

Aura present or absent?

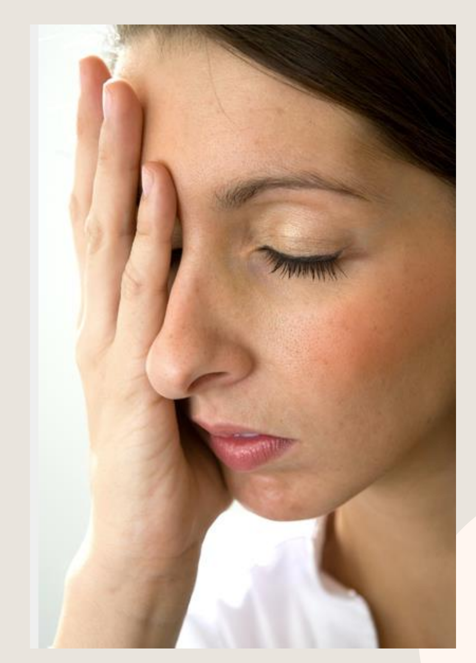
- Migraine with aura
- Migraine without aura

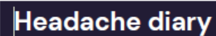
Headache days per month

- Episodic (<15 days per month)
- Chronic (≥15 days per month)

Top Tip #2

‘Headache diary: keep it simple’





National Migraine Centre
Get back to living

Complete your diary for a month (or as long as you can before your appointment). You can use the diary to help you understand your headaches whether you have an appointment or not.

Date	Day M T W Th F S Su	Time headache begins	Pain score 0 – no pain 10 – worst pain	Medication type/time taken	Comments
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					
21					
22					
23					
24					
25					
26					
27					
28					
29					
30					
31					

- Number of headache days or ‘crystal clear’ head days
- Days of acute rescue medication use
- Possible triggers e.g. caffeine, alcohol, exercise, menstrual cycle

https://www.nationalmigrainecentre.org.uk/wp-content/uploads/2023/01/Headache-diary_DIGITAL.pdf

Top Tip #3

‘Consider SNOOP4 red flags’

SNOOP4 Red Flags

	Clinical feature(s)	Need to exclude
S	Systemic symptoms: fever, chills, myalgia, weight loss	Metastasis, infection
N	Neurological symptoms or deficits	Stroke, mass lesion, encephalitis
O	Older age at onset (> 50 years)	Temporal arteritis, glaucoma, mass lesion
O	Onset, thunderclap headache onset	Bleed
P	Papilloedema	Raised intracranial pressure
P	Positional	Intracranial hypotension
P	Precipitated by Valsalva manoeuvre or exertion	Raised intracranial pressure
P	Progressive headache or substantial pattern change	Any secondary cause

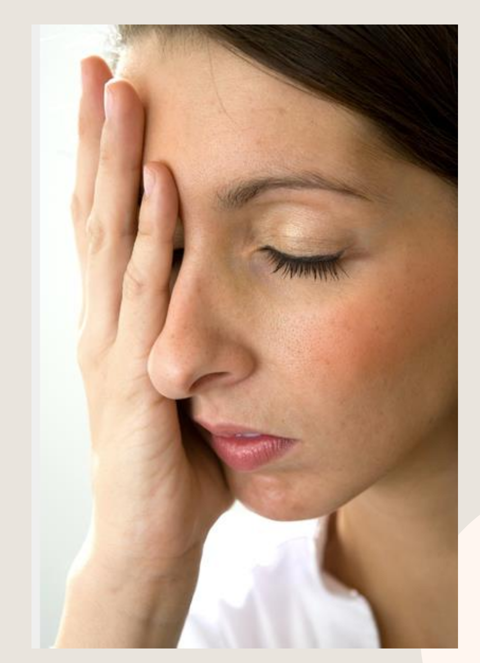
<u>NICE</u>

- impaired consciousness
- recent head trauma (within 3 months)
- new cognitive dysfunction
- vomiting without other obvious cause
- immunosuppression e.g. HIV
- age< 20 and history of malignancy
- history of malignancy known to metastasise to the brain
- change in personality

Lee VME, Ang LL, Soon DTL, Ong JJY, Loh VWK. The adult patient with headache. Singapore Med J. 2018 Aug;59(8):399-406. doi: 10.11622/smedj.2018094. PMID: 30175370; PMCID: PMC6109828.
NICE Headaches in over 12s: diagnosis and management https://www.nice.org.uk/guidance/cg150/chapter/Recommendations

Top Tip #4

‘Take a detailed drug history’



Drug History

- Acute
  - Prescription or over the counter
- Preventer
  - Dose, duration, reason for stopping
- Hormones
  - Contraception, HRT
- Secondary care
  - Botox, anti-CGRP treatments, nerve blocks

- Side-effects:

Vasodilation: nitrates, sildenafil, calcium-channel blockers, alpha 1-blockers

Raised intra-cranial pressure: ciprofloxacin, amiodarone, combined pill

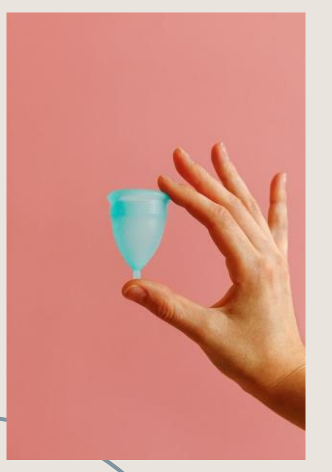
Ferrari A, Spaccapelo L, Gallesi D, Sternieri E. Focus on headache as an adverse reaction to drugs. J Headache Pain. 2009 Aug;10(4):235-9. doi: 10.1007/s10194-009-0127-1. Epub 2009 Jun 4. PMID: 19495934; PMCID: PMC3451740.

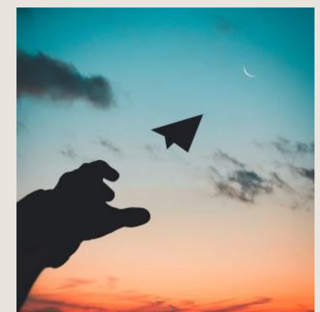
Migraine Management

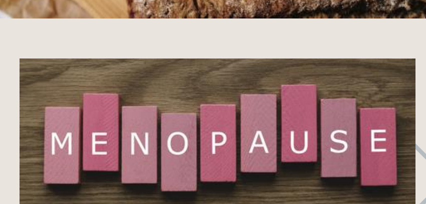
- Diagnose, Empower
- Lifestyle/Triggers
- Alternative therapies
- Acute (Rescue)
- Chronic

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Lifestyle/Triggers: ROUTINE IS KEY



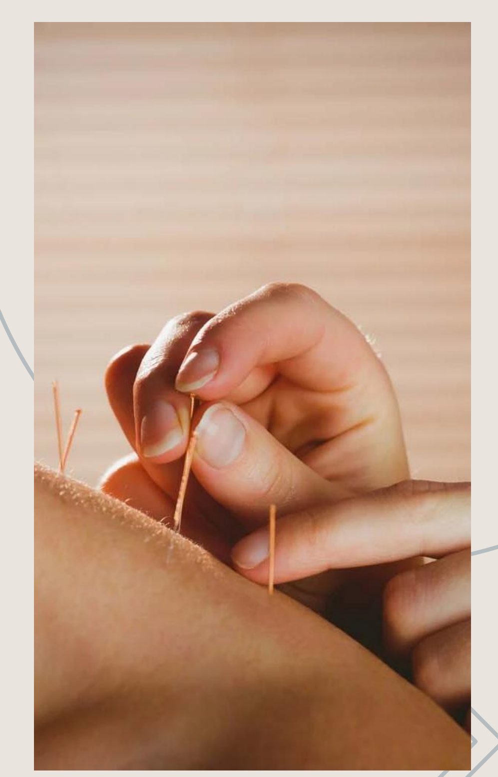




National Migraine Centre. Migraine Triggers Factsheet. https://www.nationalmigrainecentre.org.uk/understanding-migraine/factsheets-and-resources/migraine-triggers/

Alternative therapies

- Supplements (3 month trial)
  - Riboflavin (NICE) 400mg a day
  - Magnesium 400mg daily
  - Co-enzyme Q10 150mg daily
  - Vitamin D up to 2000IU daily
- Acupuncture (NICE)



BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019
Ghorbani Z, Togha M, Rafiee P, Ahmadi ZS, Rasekh Magham R, Haghighi S, Razeghi Jahromi S, Mahmoudi M. Vitamin D in migraine headache: a comprehensive review on literature. Neurol Sci. 2019 Dec;40(12):2459-2477. doi: 10.1007/s10072-019-04021-z. Epub 2019 Aug 3. PMID: 31377873.

Current Recommendations: Acute (Rescue pack)

- Simple analgesia
  +/-
- Anti-emetic
  +/-
- Triptan

- Experiment to find the most effective combination
- Try it 3 times

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Simple Analgesia e.g.

1) Paracetamol: 1g QDS

2) NSAIDs e.g.

- Aspirin 900mg QDS
- Naproxen 500mg BD
- Ibuprofen 400-600mg QDS
- Diclofenac 150mg daily divided doses

NSAID issues (PPI cover, renal risk, asthma)

Anti-emetics e.g.

- Metoclopramide 10mg TDS max 5 days

** extrapyramidal disorders and tardive dyskinesia

- Domperidone 10mg TDS max 1 week

** cardiac disease and conduction defects

- Others: Prochlorperazine (Buccastem), Cyclizine, Cinnarizine

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Triptans

- 5HT receptor agonists
- Contraindications (vasoconstriction):
  - ischaemic heart disease
  - cerebrovascular disease
  - previous myocardial infarction
  - uncontrolled or severe hypertension
- Not licenced > 65 years- risk assess

- Lack of response to one does not predict response to others
- 30% do not respond to any triptan
- No need to limit triptan + SSRI prescribing (American Headache Society)

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019
Evans RW, Tepper SJ, Shapiro RE, Sun-Edelstein C, Tietjen GE. The FDA alert on serotonin syndrome with use of triptans combined with selective serotonin reuptake inhibitors or selective serotonin-norepinephrine reuptake inhibitors: American Headache Society position paper. Headache. 2010 Jun;50(6):1089-99. doi: 10.1111/j.1526-4610.2010.01691.x. PMID: 20618823.

Triptans

DRUG	FORMULATION	STRENGTH	SINGLE DOSE	MAX/24 HOURS
ALMOTRIPTAN[168,169]	TABLET	12.5 mg	12.5 mg	25 mg
ELETRIPTAN[170]	TABLET	40 mg	40 mg	80 mg
FROVATRIPTAN[171]	TABLET	2.5 mg	2.5 mg	5 mg
NARATRIPTAN[172]	TABLET	2.5 mg	2.5 mg	5 mg
RIZATRIPTAN[173]	TABLET ORODISPERS LYPOPHILLISATE	5 mg/10 mg 10 mg 10 mg	10 mg 10 mg 10 mg	20 mg 20 mg 20 mg
SUMATRIPTAN[137,174]	TABLET SPRAY SUBCUT INJ	50 mg/100 mg 100 mg/ml or 200 mg/ml 6 mg	50-100 mg 10 - 20 mg 6 mg	300 mg 12 mg
ZOLMITRIPTAN[175-177]	TABLET ORODISPERS SPRAY	2.5 mg/5 mg 2.5 mg/ 5 mg 50 mg/ml	5 mg 5 mg 5 mg	10 mg 10 mg 10 mg

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Menstrual Migraine

DRUG	FORMULATION	STRENGTH
FROVATRIPTAN[255,256]	TABLET	2.5 mg twice daily on the days migraine is expected (generally from two days before until three days after bleeding starts)
NARATRIPTAN[258,259]	TABLET	2.5 mg twice daily on the days migraine is expected (generally from two days before until three days after bleeding starts)
ZOLMITRIPTAN[257]	TABLET	2.5 mg twice or three times a day on the days migraine is expected (generally from two days before until three days after bleeding starts)

*Included in medication days used per month

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Top Tip #5

‘NEVER use codeine’

Why no codeine/ morphine based drugs?

- No evidence it works any better
- Side effects e.g. nausea, dizziness
- Increased risk of medication overuse headache (MOH)
- Risk of dependence and tolerance

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Product	Ingredients
NUROFEN PLUS	Ibuprofen 200mg Codeine phosphate 12.8mg
Panadol Ultra	Paracetamol 500 mg Codeine phosphate 12.8 mg
Solpadeine	Paracetamol 500 mg Caffeine 65 mg
Solpadeine MAX	Paracetamol 500 mg Codeine phosphate 12.8 mg
Solpadeine PLUS	Paracetamol 500 mg Codeine Phosphate 8 mg Caffeine 30.0 mg

Product	Ingredients
Syndol	Paracetamol 500mg Caffeine 30mg Codeine Phosphate 8mg
MIGRALEVE	Paracetamol 500mg Codeine phosphate 8mg Buclizine Hydrochloride 6.25mg
Migraleve	Paracetamol 500mg Codeine Phosphate 8mg
PARAMOL	Paracetamol 500mg Dihydrocodeine tartrate 7.46mg
Anadin EXTRA	Aspirin 300mg Paracetamol 200mg Caffeine 45mg
Anadin	Aspirin 325mg Caffeine 15mg

Top Tip #6

‘Rescue packs: only use a maximum of <u>10 days </u>per month’

Medication Overuse Headache (MOH)

- Regular frequent use of acute treatment = exacerbation of pre-existing migraine
- Triptans and opioids are likely to result in MOH more rapidly (10 days + per month) compared with simple analgesics e.g. paracetamol (15 days + per month)
- Medication taken for non-headache pain e.g. joint or back pain, can result in MOH

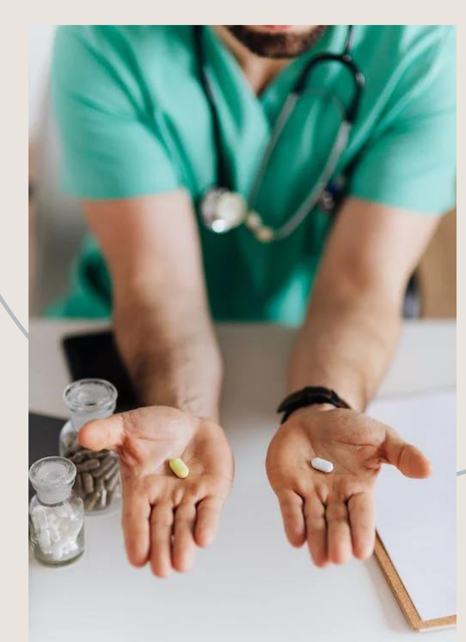
Patient education

- Restrict acute rescue medications to 10 days per month
- Encourage early preventive treatments

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Migraine Prevention Options

- Consider co-morbidities e.g. asthma, mental health
- Consider contraception and pregnancy plans
- Offer to patients with ≥4 migraine days a month
- Not aiming for cure
- Consider gradual withdrawal after 6-12 months if effective i.e. they do not have to be life-long



BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Primary Care Migraine Prevention: Current

Drug	Start dose	Titration	Max Dose	Notes
Amitriptyline (NICE/BASH)	10mg nocte	10mg every 1-2 weeks	75mg	- Drowsiness
Propranolol (NICE/BASH)	10mg BD	10mg BD every 2 weeks	240mg divided doses	- Avoid: Asthma, PVD - Side-effects: sleep disturbed, erectile dysfunction - BP/PR monitoring
Topiramate (NICE/BASH)	25mg nocte	25mg weekly	200mg divided doses	- Side-effects: suicidal thoughts, renal stones, drowsiness, tingling, glaucoma, weight loss - **pregnancy**
Candesartan (BASH)	2mg OD	2mg every 2-3 weeks	16mg	- Renal/BP monitoring

BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

Top Tip #7

‘Preventers: titrate to the maximum tolerated dose and assess after 3 months; Success= 50% improvement’

Others options…

- Lisinopril up to 20mg OD (BASH)

- Flunarizine 5mg OD, up to 10mg OD (BASH)

- Others:

- Pizotifen: Initially 500mcg nocte, increased gradually to 1.5mg OD, alternatively increased gradually to 1.5mg daily in 3 divided doses; increased if necessary, up to 4.5mg daily (max per dose 3mg)

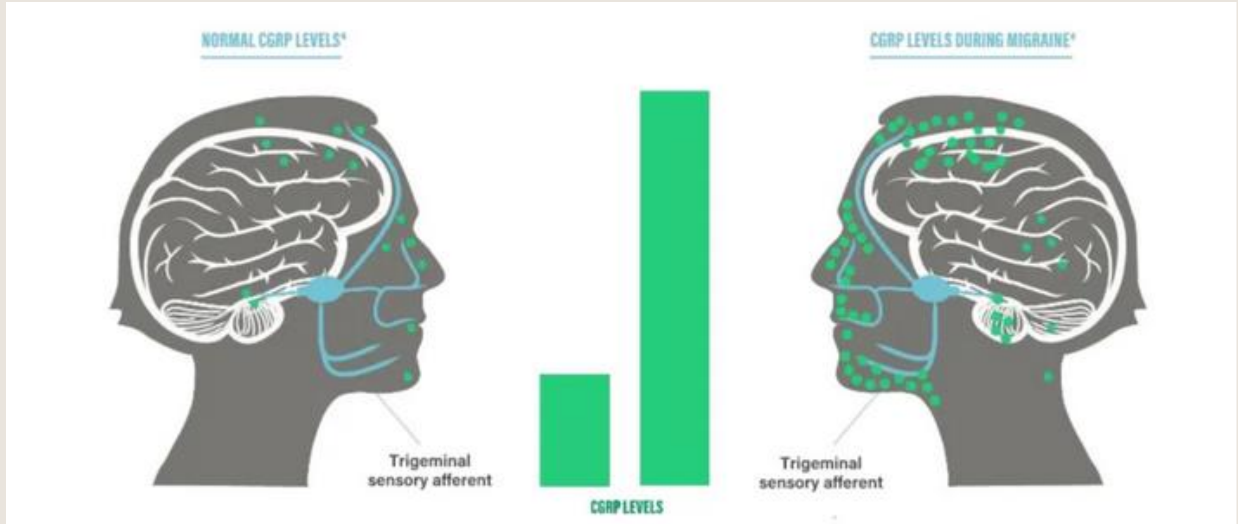
- Venlafaxine: MR 37.5mg OD increase every 2 weeks to max 150mg OD

- Nortriptyline: 10 mg nocte, increased to 75mg OD gradually

Sinclair AJ, Sturrock A, Davies B, et al. Headache management: pharmacological approaches. Practical Neurology 2015;15:411-423.
BASH 2019: https://headache.org.uk/index.php/bash-guideline-2019

What’s New?
Calcitonin- gene related peptide (CGRP)

- Pain signalling neuropeptide important in the migraine pathway
- Blocking CGRP = reduced migraine



https://migrainebuddy.com/cgrp-medications-migraine-prevention-webinar/

Acute GEPANT (Rimegepant)

- Oral CGRP antagonist
- Acute dose: 75mg OD PRN
- Check drug interactions e.g. clarithromycin, fluconazole, erythromycin
- Side-effects: nausea (2%), hypersensitivity (rare)
- Potential: triptan contraindications, or failed effectiveness of rescue painkillers

- Avoid in pregnancy or breast feeding
- No effect on fertility
- Avoid in severe hepatic impairment
- Caution in renal impairment

<u>Check your formulary status**</u>**

NICE accepted for restricted use

<u>Indications:</u>

- inadequate symptom relief with at least 2 triptans or in whom triptans are contraindicated or not tolerated; AND
- inadequate pain relief with NSAIDs and paracetamol

NICE. TA919. Rimegepant for treating migraine

- Preventer dose: 75mg alternate days
- Check drug interactions e.g. clarithromycin, fluconazole, erythromycin
- Side-effects: nausea (2%), hypersensitivity (rare)
- Avoid in pregnancy or breast feeding
- No effect on fertility
- Avoid in severe hepatic impairment
- Caution in renal impairment

Check your formulary status

NICE accepted for restricted use

Prophylaxis of episodic migraine:

- ≥ 4 and <15 migraine days per month, AND
- ≥ 3 failed oral preventers

Stop after 12 weeks if migraine frequency does not reduce by at least 50%

NICE. TA906. Rimegepant for preventing migraine

Preventer GEPANT (Atogepant)

- Dose: 60mg daily OR 10mg daily if:
  - Cr Cl < 30 mL/minute
  - Certain concurrent meds e.g. telmisartan
- Check drug interactions e.g. clarithromycin, erythromycin
- Side-effects: reduced appetite/ weight, constipation, drowsiness/ fatigue, nausea
- Avoid in pregnancy or breast feeding
- Avoid in severe hepatic impairment

****Check your formulary status****

NICE accepted for restricted use

Prophylaxis of migraine:
- ≥ 4 migraine days per month, AND
- ≥ 3 failed oral preventers

Stop after 12 weeks if migraine frequency does not reduce by:
- at least 50% in episodic migraine
- at least 30% in chronic migraine

NICE. Atogepant for preventing migraine [ID5090]

Top Tip #8

‘Check if the gepants are available on your local formulary’

Specific Preventive Treatments: CGRP Monoclonal Antibodies

Indication:

Prophylaxis of migraine:

- in adults
- with at least 4 migraine days per month
- AND 3 failed oral preventers

3 are subcutaneous injections:

- Erenumab (Aimovig) 70mg or 140mg SC every 4 weeks
- Fremanezumab (Ajovy) 225mg SC once monthly OR 675mg SC every 12 weeks
- Galcanezumab (Emgality) 240mg SC loading dose, THEN 120mg SC every 4 weeks

One is an IV infusion:

- Eptinezumab (Vyepti) 100mg or 300mg IV infusion every 12 weeks

Side effects

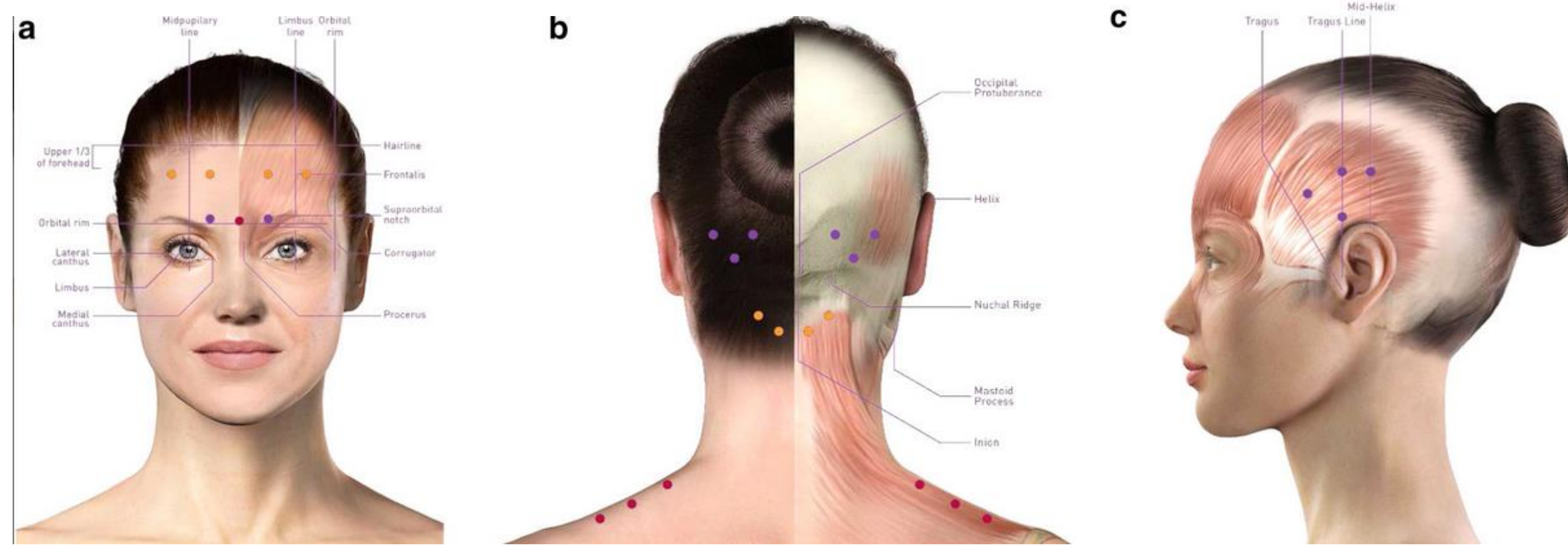
- Monitor blood pressure (Erenumab)
- Constipation
- Injection site reactions
- Rare: allergic reactions
- Flu-like

Benefits

- No blood test monitoring
- No significant medication interactions

Unknowns

- No safety data in cardiovascular disease
- Avoided in Raynaud's (case reports of worsening)



Botox Injections
Chronic migraine and at least 3 failed preventers

155–195 units
IM as 0.1 ml (5 units) injections
31- 39 sites
12 weekly

https://headachejournal.onlinelibrary.wiley.com/doi/full/10.1111/head.13074; https://www.nice.org.uk/guidance/ta260

Top Tip #9

‘3 failed preventers? REFER for ? Anti-CGRP/ Botox to secondary care’

National Migraine Centre CHARITY https://www.nationalmigrainecentre.org.uk

- No NHS support or government funding, not-for-profit

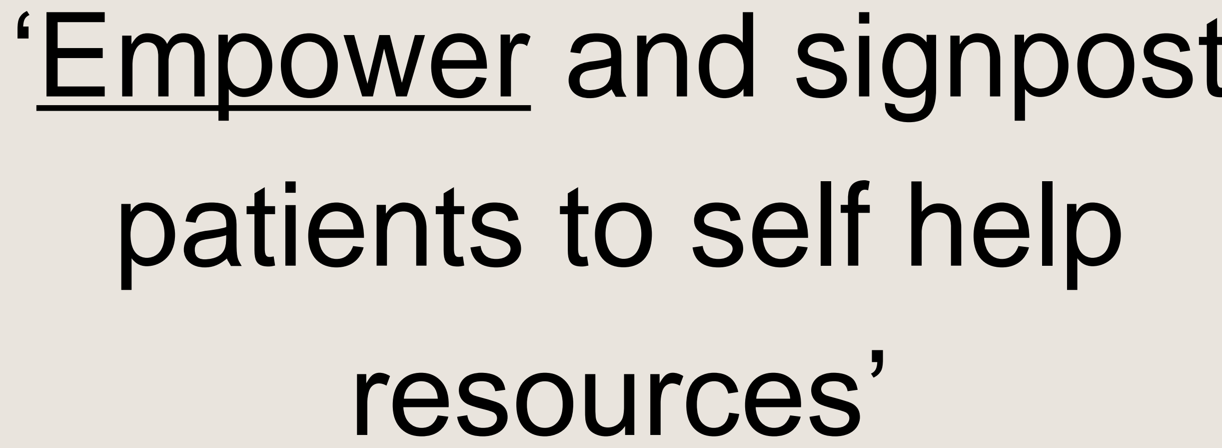
- Offer remote video/phone consultations

- Team of GP headache specialist, neurologists, nurses

- We can see anyone in the UK
  - Children, adults
  - Donation basis OR private-fee basis consultations

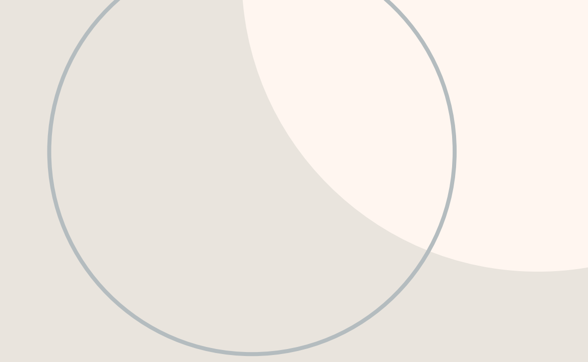
- Private fees: we offer all three SC anti-CGRP, IV anti-CGRP in selected clinics and botox/ nerve blocks

Top Tip #10



Useful Resources and Further Information:

- **'Managing Your Migraine' Dr Katy Munro:** https://www.penguin.co.uk/books/443430/managing-your-migraine-by-munro-dr-katy/9780241514283
- **British Association for the Study of Headache** https://www.bash.org.uk/
- **Heads Up Podcast:** https://www.nationalmigrainecentre.org.uk/understanding-migraine/heads-up-podcast/
- **Migraine and HRT – British Menopause Society:** https://thebms.org.uk/publications/factsheets/migraine-and-hrt/
- **OUCH Charity (cluster): https://ouchuk.org/**
- **The Migraine Trust:** https://migrainetrust.org/
- **The National Migraine Centre:** https://www.nationalmigrainecentre.org.uk/



Thank you!

Any questions?

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