Migraine Management

Dr Helen Brown
Director of Neurology and Stroke
The Princess Alexandra Hospital
# Referral Criteria for Migraine

## Minimum Referral Criteria

**Does your patient meet the minimum referral criteria?**

| Category 1                  | New onset headache with concerning clinical signs e.g. increasing intracranial pressure; papilloedema, blurred vision  
|                            | Abnormal neurological exam with concerning features on neuroimaging |
|                            | Severe frequent headaches and trial of at least 3 migraine preventers without improvement and/or absent from work or study for more than 4 days per month (list 3 treatments trialled) |
| Category 2                  | Chronic/complicated headache/migraine unresponsive to medical management |
| (appointment within 30 calendar days) |                                                                                 |
| (appointment within 90 calendar days) |                                                                                   |
| (appointment within 365 calendar days) |                                                                                   |

**If your patient does not meet the minimum referral criteria**

- Consider other treatment pathways or an alternative diagnosis
- If you still need to refer your patient:
- Please explain why (e.g. warning signs or symptoms, clinical modifiers, uncertain about diagnosis, etc.)
- Please note that your referral may not be accepted or may be redirected to another service
Migraine Management

- Migraine Diagnosis
- Spot on Health Migraine pathway
- Lifestyle Factors
- Acute/Abortive treatment
- Prophylactic/Preventative treatment
- Goal setting
- Medication overuse management
- Menstrually related migraines
- Advanced therapies
# Features Suggestive of a Potentially Serious Cause of Headache

<table>
<thead>
<tr>
<th>Features</th>
<th>Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sudden onset:</strong></td>
<td></td>
</tr>
<tr>
<td>• Thunderclap (onset over a few seconds)</td>
<td>Subarachnoid Haemorrhage</td>
</tr>
<tr>
<td>• Like a blow to the head</td>
<td></td>
</tr>
<tr>
<td>• Nausea &amp; vomiting soon follows</td>
<td></td>
</tr>
<tr>
<td><strong>Precipitated by coughing, sneezing, exertion, bending, and valsalva</strong></td>
<td>Raised intracranial pressure (<a href="#">check for papilloedema</a>):</td>
</tr>
<tr>
<td>• Venous sinus thrombosis</td>
<td></td>
</tr>
<tr>
<td>• Idiopathic intracranial hypertension</td>
<td></td>
</tr>
<tr>
<td>• Mass lesion e.g. tumour or abscess</td>
<td></td>
</tr>
<tr>
<td><strong>Previous Malignancy</strong></td>
<td>Cancer (especially those which metastasise to the brain: lung, breast, and melanoma)</td>
</tr>
<tr>
<td><strong>New onset headache in a patient &gt;50 years</strong></td>
<td>Giant cell arteritis (GCA)</td>
</tr>
<tr>
<td><strong>Fever, drowsiness, neck stiffness, rash, recent infections</strong></td>
<td>Meningitis or encephalitis</td>
</tr>
<tr>
<td><strong>Atypical aura (&gt; 1 hour duration, or motor weakness)</strong></td>
<td>Stroke or tumour</td>
</tr>
<tr>
<td><strong>Aura occurring for the first time in a patient during use of combined oral contraceptives</strong></td>
<td>Stroke or cerebral venous sinus thrombosis</td>
</tr>
<tr>
<td><strong>Eye symptoms e.g. unilateral painful red eye, visual impairment, nausea and vomiting.</strong></td>
<td>Acute angle closure glaucoma</td>
</tr>
</tbody>
</table>
SpotOnHealth HealthPathways

What is SpotOnHealth HealthPathways?
SpotOnHealth HealthPathways provides clinicians in the greater Brisbane South catchment with web-based information outlining the assessment, management and referral of over 550 conditions.

It is designed to be used at point of care primarily by general practitioners but is also available to specialists, nurses, allied health and other health professionals.

Why HealthPathways?
HealthPathways is an initiative from the Canterbury District Health Board in Christchurch, New Zealand, which provides a ‘whole of system’ approach to effective integration of acute and primary health care services. SpotOnHealth HealthPathways boasts a range of benefits including:

- Best available information on how to assess and manage common clinical conditions, including when and where to refer patients.
- Easy online access to clinical and patient resources for in-consult use, peer-reviewed and localised to our region.
- Integrated, concise, and saving you time.

Using HealthPathways
The HealthPathways portal is not designed for patient use, therefore a username and password is only provided to clinicians. However, many of the pathways contain patient information which can be printed off and given to patients at the time of consultation.

To obtain the user name and password please visit the SpotOnHealth HealthPathways project site and follow the onscreen, or email the team at spotonhealth@health.qld.gov.au.
Using HealthPathways

- What is HealthPathways?
- Meet the HealthPathways team
- How to use HealthPathways
- How to send feedback on a pathway
- Install shortcuts to HealthPathways

Health System News

15 Feb
General Practice Pain Management Seminar
This full day education seminar will provide an update on a variety of aspects of pain management. Read more...

02 Feb
Need help with codeine addicted patients? Call ADCAS.
On 15 January 2018, Queensland Health began a 12-month pilot of a specialist telephone support service for Queensland medical practitioners. Read more...

30 Nov
Urgent update by RANZCOG – Renewal of National Cervical Screening Program
Do not offer self-collection of samples to women with the commencement of the renewed program on 1 December 2017 until further notice. Read more...

22 Nov
New cervical screening learning modules
To assist healthcare providers in preparing for the new cervical cancer screening changes commencing 1 December 2017, NPS MedicineWise has 6 free online CPD modules now available.

18 Oct
Security alert
Critical vulnerabilities in WPA and WPA2 exposes networks to attacks. Read more...
Migraine Management in Adults

Caution: this pathway is in development

This pathway is for patients diagnosed with migraine according to Headaches In Adults.

About migraine in adults

Management

Managing migraines can be complicated and requires a systematic approach but most patients can be managed well in general practice.

Acute management

Prevention and prophylaxis [Questions for SME]

Pregnant and breastfeeding patients

Request

- Request emergency assessment if status migrainosus or severe vomiting or dehydration requiring IV fluids or further management.
- Request non-acute neurology assessment if:
  - severe, frequent migraines and unsuccessful trial of ≥ 3 prophylactic medications.
  - If the patient has menstrual migraine resistant to treatments above, request non-acute endocrinology assessment.
  - If anxiety or depression, request counselling services through Better Access and GP Mental Health Treatment Plan.
  - Your patient may also wish to consider private referral.

Information

Clinical Resources
Patient Information
References
Migraine without aura

- At least 5 attacks.
- Duration: 4 to 72 hours
- At least 2 of the following characteristics:
  - Unilateral
  - Pulsating
  - Moderate or severe pain intensity
  - Aggravated by physical activity
- During headache at least 1 of:
  - Nausea and/or vomiting
  - Photophobia and phonophobia

Migraine with aura

≥ 2 attacks fulfilling criteria B and C

Criteria B: ≥ 1 of the following fully reversible aura symptoms:
- Visual, sensory, speech and/or language, motor, brainstem, retinal

Criteria C: At least 2 of the following:
- At least one aura symptom spreads gradually over 5 minutes, and/or two or more symptoms occur in succession
- Each individual aura symptom lasts 5-60 minute
- At least one aura symptom is unilateral
- The aura is accompanied, or followed within 60 minutes, by headache
- Not better accounted for by another ICHD-3 diagnosis, and TIA has been excluded.
Visual Aura
Migraine Aura
Lifestyle Factors for Migraine

• Sleep
• Fluid intake
• Stress levels
• Co-Morbid conditions;
  – Obstructive Sleep Apnoea
    • Snoring
    • Early morning headache
    • Epworth sleepiness Scale
  – Treat Hypertension
Step 1 Acute Treatment:
Simple oral analgesic ± anti-emetic

Oral analgesia:
- Aspirin 600-900mg orally STAT OR
- Ibuprofen 400mg (Maximum of 4 doses over 24 hours) AND/OR
- Paracetamol 1g orally every 4 hours (Maximum of 4g over 24 hours) for non-incapacitating headache

Efficacy of analgesia may be improved by giving a pro-kinetic anti-emetic to promote gastric emptying with:
- Metoclopramide 10-20mg ORALLY
- Domperidone 10-20mg orally.

For nausea and vomiting (if required):
- Prochlorperazine 5mg orally or Prochlorperazine 25mg suppository
- Domperidone 10mg -20mg orally
- If unable to tolerate either of the above due to prominent nausea and vomiting: Metoclopramide 10-20mg IM or IV STAT
Step 2 Acute Treatment: Prescription NSAID (± anti-emetic as described in step 1)

- **Naproxen 500mg-750mg** with a further 250mg-500mg in 6 hours if required (Maximum dose =1250mg/day).

OR

- **Diclofenac 50-100mg** (maximum 200mg /day). **Diclofenac 100mg suppository** (maximum 100mg BD )

OR

- **Aspalsin 2-3 tablets**
# Step 3 Acute Migraine Treatment: Triptans

<table>
<thead>
<tr>
<th>Triptans</th>
<th>Dose</th>
<th>Grade of Evidence*</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rizatriptan** (Wafer)</td>
<td>10mg Wafer</td>
<td>A</td>
<td>Metabolism is affected by propranolol: an alternate triptan should be considered. No pharmacokinetic interaction was observed with metoprolol. Based on in vitro data, no pharmacokinetic interaction is expected with atenolol.</td>
</tr>
</tbody>
</table>
| Sumatriptan               | 50mg- 100mg  
6mg  
10mg, 20mg into one nostril | A                  | The only triptan with LAM listing                                                                                                                                      |
| Eletriptan** (Tab)        | 40-80mg/dose                              | A                  | Incidence of recurrence lower than other triptans. Best side effect profile                                                                                             |
| Naratriptan** (Tab)       | 2.5mg                                     | A                  | Incidence of recurrence lower than other triptans. Best side effect profile                                                                                             |
| Zolmitriptan** (Tab)      | 2.5-5mg/dose                              | A                  | Incidence of recurrence lower than other triptans. Best side effect profile                                                                                             |
Contraindications to triptans

- If other 5HT agonists or triptans have been used in the preceding 24 hours
- Uncontrolled hypertension
- Vascular disease, including:
  - ischaemic heart disease
  - coronary artery vasospasm
  - peripheral vascular disease
  - stroke or transient ischaemic attack (TIA)
- Pregnancy (eletriptan and sumatriptan are safe in breastfeeding)
- Familial hemiplegic migraine
- Patients receiving:
  - monoamine oxidase inhibitors (MAOIs)
  - tricyclic antidepressants (TCAs)
  - selective serotonin reuptake inhibitors (SSRIs)

due to risk of serotonin syndrome.
Specific anti-migraine medications (triptans)

- Triptan administration and response:
  - Ineffective during aura and most effective when administered as soon as possible at onset of headache.
  - 20 to 50% of patients who initially respond will have a rebound headache within 48 hours. Up to 25% don't respond at all.
  - All triptans generally have equal effect, but patients may prefer a particular triptan.
  - Can be combined with metoclopramide and NSAIDs.
  - Repeat after 2 hours if headache recurs, but not if initial dose was ineffective.
  - Limit to 2 days per week to avoid medication overuse headache.
  - If unsatisfactory response after 3 attacks, trial a different triptan, including dose and route.

- Side effects include:
  - chest or neck or jaw discomfort or tightness ("triptan sensations") – if chest discomfort persists, assess for cardiac cause.
  - paraesthesia.
  - gastrointestinal upset.

For all acute treatments: Aim maximum of twice per week
Migraine Prophylaxis
When to Start?

- ≥ 4 attacks per month
- Failure of, contraindication to, overuse of, or troublesome side effects from acute treatments
- Certain migraine conditions with frequent, prolonged or uncomfortable aura symptoms eg
  - hemiplegic migraine
  - migraine with basilar aura

Under-utilisation of Migraine Prophylaxis

American Migraine Prevalence and Prophylaxis study

- 38.8% of patients met prophylaxis criteria
- 13% of patients were taking prophylaxis

Resetting the Goalposts

• Success for a migraine prophylactic agent is 50% reduction in the frequency and severity of attacks
Migraine Prophylaxis

- Tailor the choice to the patient
- Start low, go slow
- Give each treatment an adequate trial at the maximum recommended (or tolerated dose, if side effects limit up-titration).
- If it doesn’t work move on or add on!
- Set the 50% goals for what is deemed a success
# Migraine Prophylactic Agents

## Table 2-2: Classification of Migraine Preventive Therapies (Available in the United States)

<table>
<thead>
<tr>
<th>Level A: Medications With Established Efficacy (≥ 2 Class I Trials)</th>
<th>Level B: Medications Are Probably Effective (1 Class I or 2 Class II Studies)</th>
<th>Level C: Medications Are Possibly Effective (1 Class II Study)</th>
<th>Level U: Inadequate or Conflicting Data to Support or Refute Medication Use</th>
<th>Other: Medications That Are Established as Possibly or Probably Ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiepileptic drugs</strong></td>
<td><strong>Antidepressants/SSRI/SNRI/TCA</strong></td>
<td><strong>ACE inhibitors</strong></td>
<td><strong>Carbonic anhydrase inhibitor</strong></td>
<td><strong>Established as not effective</strong></td>
</tr>
<tr>
<td>Divalproex sodium</td>
<td>Amitriptyline</td>
<td>Lisinopril</td>
<td>Acetazolamide</td>
<td>Antiepileptic drugs</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>Venlafaxine</td>
<td>Angiotensin receptor blockers</td>
<td>Antithrombotics</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Beta-blockers</td>
<td>Gandesartan</td>
<td>Aceclofenac</td>
<td>Probably not effective</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Atenolol</td>
<td>α-Agonists</td>
<td>Cumarin</td>
<td>Clomipramine</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Nadolol</td>
<td>Clonidine</td>
<td>Picotamide</td>
<td>Possibly not effective</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Triptans (MRM)</td>
<td>Guanfacine</td>
<td>Antidepressants/SSRI/SNRI</td>
<td>Acebutolol</td>
</tr>
<tr>
<td>Timolol</td>
<td>Naratriptan</td>
<td>Triptans (MRM)</td>
<td>Antiepileptic Drugs</td>
<td>Clonazepam</td>
</tr>
<tr>
<td>Frovatriptan</td>
<td>Zolmitriptan</td>
<td>Carbamazepine</td>
<td>Fluoxetine</td>
<td>Nabumetone</td>
</tr>
<tr>
<td>Direct vascular smooth muscle relaxants</td>
<td></td>
<td></td>
<td></td>
<td>Oxcarbazepine</td>
</tr>
<tr>
<td>Cyclandelate</td>
<td></td>
<td></td>
<td></td>
<td>Telmisartan</td>
</tr>
</tbody>
</table>

**Notes:**
- SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant; ACE = angiotensin-converting enzyme; MRM = menstrually related migraine; Ca++ blockers = calcium channel blockers.
- Classification based on original guideline and new evidence not found for this report.
- For short-term prophylaxis of menstrually related migraine.
<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Drug Treatment Strategy</th>
</tr>
</thead>
</table>
| First time strategies (For the patient who has not had prophylaxis before)       | • a. Beta-blocker strategy – propranolol, metoprolol  
• b. Tricyclic strategy – amitriptyline (particularly if poor sleep is an issue) |
| Low side effect strategies                                                       | • a. Drugs – candesartan, lisinopril  
• b. Herbal / vitamin / mineral – magnesium citrate, riboflavin, Coenzyme Q10 |
| Increased body mass index strategy or diabetes strategy                         | Topiramate, candesartan                                                            |
| History of epilepsy strategy                                                     | Topiramate                                                                 |
| Hypertension strategy                                                            | Propranolol, metoprolol, atenolol, candesartan, lisinopril, verapamil               |
| Depression or anxiety strategy or menopause strategy                             | Amitriptyline, venlafaxine, propranolol                                               |
| Poor sleep strategy                                                              | Amitriptyline, pizotifen, topiramate, pregabalin                                      |
| Fibromyalgia or muscular neck tension strategy                                   | Amitriptyline, pregabalin                                                          |
| Additional monotherapy drug strategies                                           | Topiramate, sodium valproate*, gabapentin, pizotifen, verapamil, cyproheptadine, carbamazepine, fluoxetine |
| Refractory patient strategy                                                      | Concomitant use of 2 drugs with different modes of action e.g., antihypertensive plus antidepressant |

Table adapted from Pringsheim et al. 2012.
Migraine Prophylaxis during Pregnancy

- Drug avoidance if possible. When necessary, consider:
  - Magnesium
  - Cyproheptadine (pregnancy category A). Caution – insufficient data and may suppress lactation.
  - Pizotifen (pregnancy category B1). Caution – insufficient data and avoid if possible.
  - Propranolol (pregnancy category C). Caution – safety cannot be assured.
## Summary of drug therapy for migraine prophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual titration</th>
<th>Target dose</th>
<th>Precautions and side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antihypertensives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>- 10 to 20 mg twice a day</td>
<td>40 to 80 mg twice a day</td>
<td>Precautions:</td>
</tr>
<tr>
<td>(Grade A evidence)</td>
<td>- Increase by 20 mg twice a day every 2 weeks</td>
<td></td>
<td>- Asthma, diabetes, bradycardia, peripheral vascular disease, depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- For propranolol – co-use of rizatriptan</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>25 to 50 mg twice a day</td>
<td>50 to 100 mg twice a day</td>
<td>Side-effects – hypotension, bradycardia, nightmares, sleep disturbance, fatigue, reduced</td>
</tr>
<tr>
<td>(Grade A evidence)</td>
<td></td>
<td></td>
<td>exercise tolerance, bronchospasm, sexual dysfunction</td>
</tr>
<tr>
<td>Atenolol</td>
<td>- 25 mg a day</td>
<td>50 to 100 mg a day</td>
<td>Precautions – hypotension, renal artery stenosis, HOCM</td>
</tr>
<tr>
<td>(Grade B evidence)</td>
<td>- Increase by 25 mg every 2 weeks</td>
<td></td>
<td>Side-effects – hypotension, dizziness</td>
</tr>
<tr>
<td>Candesartan</td>
<td>- 8 mg a day</td>
<td>16 mg a day</td>
<td>Precautions – hypotension, hereditary angioedema</td>
</tr>
<tr>
<td>(Grade C evidence)</td>
<td>- Increase to 16 mg a day in 2 weeks</td>
<td></td>
<td>Side-effects – hypotension, dizziness, fatigue, non-productive cough, angioedema (rare)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>- 10 mg a day</td>
<td>20 mg a day</td>
<td>Precautions – hypotension, concomitant use of beta-blockers, sick sinus syndrome</td>
</tr>
<tr>
<td>(Grade C evidence)</td>
<td>- Increase to 20 mg a day in 2 weeks</td>
<td></td>
<td>Side-effects – constipation, ankle</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Short acting:</td>
<td>160 to 240 mg a day</td>
<td>Precautions – hypotension, concomitant use of beta-blockers, sick sinus syndrome</td>
</tr>
<tr>
<td>(Grade U evidence)</td>
<td>- 40 mg three times a day for 2 weeks</td>
<td></td>
<td>Side-effects – constipation, ankle</td>
</tr>
<tr>
<td></td>
<td>- Increase to 80 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*HOCM: Hypertrophic obstructive cardiomyopathy*
## Migraine Prophylactic Agents

### Antidepressants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and Titration</th>
<th>Precautions</th>
</tr>
</thead>
</table>
| Amitriptyline (Grade B evidence) | • 10 mg at night  
  • Increase by 10 mg every 2 to 4 weeks                                            | • Precautions – angle closure glaucoma, prostatism, co-use of other anticholinergics  
  • Side-effects – weight gain, drowsiness, confusion, anticholinergic effects (dry mouth, constipation, dry eyes, urinary retention), reduced seizure threshold, sexual dysfunction, cardiovascular effects |
| Venlafaxine MR (Grade B evidence) | • 37.5 mg daily for 2 to 4 week  
  • Increase every 2 to 4 weeks by 37.5 mg                                            | • Precautions – hypertension, MAOI use, angle closure glaucoma  
  • Side-effects – nausea or vomiting, drowsiness, sexual dysfunction, dizziness, blurred vision |
# Migraine Prophylactic Agents

## Antiepileptics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Information</th>
<th>Precautions</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topiramate (Grade A evidence)</td>
<td>25 mg a day (best to start with dose at night)</td>
<td>Precautions – renal stones, angle closure glaucoma, pregnancy, depression</td>
<td>Side-effects – gastrointestinal (nausea, anorexia), renal calculi (ensure adequate hydration), paraesthesia, acute glaucoma, CNS (dizziness, tremor, sedation, cognitive impairment, depression), weight loss, metabolic acidosis</td>
</tr>
<tr>
<td></td>
<td>Increase by 25 mg every 2 to 4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25 to 100 mg a day (divided into two doses or a single dose at night)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium valproate* (Grade A evidence)</td>
<td>200 mg a day (best to start at night)</td>
<td>Precautions – obesity, liver disease, PCOS, pregnancy and women of childbearing age</td>
<td>Side-effects – weight gain, alopecia, contraindicated in females of childbearing age due to teratogenicity, nausea/vomiting, tremor</td>
</tr>
<tr>
<td></td>
<td>Increase by 200 mg every 2 to 4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>200 to 600 mg twice a day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin (Grade U evidence) Non-PBS for this indication.</td>
<td>300 mg a day</td>
<td>Precaution – epilepsy.</td>
<td>Side-effects – drowsiness, dizziness</td>
</tr>
<tr>
<td></td>
<td>Increase by 300 mg every 5 to 14 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1200 to 1500 mg a day divided into 3 doses</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Migraine Prophylactic Agents

### Other agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Description</th>
<th>Precaution</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pizotifen (serotonin antagonist)</td>
<td>0.5 mg at bedtime for 2 to 4 weeks</td>
<td></td>
<td>Precaution – epilepsy</td>
</tr>
<tr>
<td></td>
<td>Increase by 0.5 mg every 2 to 4 weeks if needed</td>
<td></td>
<td>Side-effects – drowsiness, weight gain</td>
</tr>
<tr>
<td></td>
<td>0.5 mg to 3 mg at night or in divided doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyproheptadine (antihistamine) (Grade C evidence)</td>
<td>4 mg at night for 4 weeks</td>
<td></td>
<td>Precaution – lactation</td>
</tr>
<tr>
<td></td>
<td>Increase to 8 mg at night</td>
<td></td>
<td>Side-effects – drowsiness, dizziness, ataxia, hallucinations, blurred vision</td>
</tr>
<tr>
<td></td>
<td>8 mg at night</td>
<td></td>
<td>Hypotension anticholinergic effects (dry mouth, constipation, dry eyes, urinary retention)</td>
</tr>
</tbody>
</table>

### Vitamins / Minerals / Herbal medicine

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Dosage Description</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium citrate</td>
<td>300 mg (elemental magnesium) twice a day</td>
<td>Side-effects – diarrhoea, gastrointestinal upset</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>200 mg twice a day</td>
<td>Side-effects – yellow discolouration of urine (benign), gastrointestinal upset</td>
</tr>
<tr>
<td>Coenzyme Q10</td>
<td>100 mg a day</td>
<td>Side-effects – gastrointestinal upset</td>
</tr>
<tr>
<td></td>
<td>300 mg a day (or 100 mg three times a day to minimise side-effects)</td>
<td></td>
</tr>
</tbody>
</table>

*Valproate is teratogenic – avoid in women of childbearing potential.*

*Table adapted from Siberstein et al. 2012* and Pringsheim et al. 2012.
Pure Menstrual Migraine Prophylaxis; Non-hormonal options

• For all 3 agents; start 2 days before menstruation and continue x 5 days
• Peri-menstrual NSAIDS;
  – Naproxen 500 mg bd
• Peri-menstrual triptans:
  – Naratriptan 1.25mg twice daily (1/2 x 2.5mg tablet). Risk of post treatment migraine.
  – Zolmitriptan 2.5mg bd. Risk of post treatment headache has not been assessed.
Pure Menstrual Migraine Prophylaxis; Hormonal Options

• Continuous Hormonal Option
  – Continuous administration of an oestrogen-progesterone oral contraceptive.
  – A low oestrogen dose (ie 20mcg ethinyl oestradiol) recommended to reduce risk of stroke.
  – Allow up to 4 withdrawal bleeds per year.
Pure Menstrual Migraine Prophylaxis; Hormonal Options

• Peri-menstrual oestrogen; For women having a natural cycle, who do not need or wish to use a COCP:

  • apply a 100 microgram oestrogen patch about 3 days before the anticipated onset of bleeding, and leave in place for 7 days, or

  • give 2 mg oestradiol valerate (Progynova) daily for 7 days, starting 2-3 days before the period, or

  • apply oestradiol gel 1.5 mg (1.5g gel) transdermally daily for 7 days, starting 2 days before expected onset of migraine.
Medication Overuse Headache (MOH)

- Often a featureless daily headache (or >15 days/month)
- Most commonly presents as a complication of migraine:
  - Increased frequency and severity of a pre-existing migraine
  - Reduced response to preventative and/or acute treatments
- It accounts for up to 60% of GP referrals
- Due to regular overuse (> 3 months) of acute migraine treatments:
  - >10 days/month Codeine containing painkillers or triptans
  - >15 days/month: Non-opioid/simple analgesics (NSAIDs)
  - A combination of any of the above >15 days per month
Medication Overuse Headache Treatment

STEP 1: Patient education and withdrawal of offending agent.
- Need to forewarn that withdrawal will initially aggravate their symptoms and it should be planned in advance.

<table>
<thead>
<tr>
<th>Medication Overused</th>
<th>Expected time to improvement post cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triptans</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Simple Analgesics</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>Narcotics</td>
<td>2-4 weeks</td>
</tr>
</tbody>
</table>
Management of Withdrawal Headache

• Expert opinion suggests managing withdrawal headaches using naproxen which should be taken regularly as per the following reducing schedule in order to break the habit of responding to pain with mediation;

• Naproxen 500mg scored tablet
  – 1 tablet bd x 2 weeks; ½ tablet bd x 2 weeks; ½ tablet daily x 2 weeks, then cease.
  – And/or introduce a prophylactic agent concurrently
## Medication Overuse Headache Treatment

### Step 2: Assess recovery post withdrawal
- Review after 2-3 weeks to ensure withdrawal has been achieved.
- Recovery continues slowly for weeks to months.

### STEP 3: Review and reassess the underlying primary headache disorder
- Most patients revert to their original headache type within 2 months.
- Overused medications (if appropriate) may be reintroduced after 2 months, with explicit restrictions on frequency of use.
- Decide re need for a prophylactic agent for their migraine

### STEP 4: Prevent relapse
- Relapse rate of approx. 40% within 5 years.
- Risk factors for relapse include: male sex, intake of combined analgesic drugs, tension-type headache as the primary headache.
- Behavioural therapies (CBT, stress reduction, biofeedback) may help.
Migraine Prophylaxis: Advanced Therapies

- Botox
- Cephaly Device
- Calcitonin Gene Related Peptides monoclonal antibodies
Botox for Chronic Migraine

CHRONIC MIGRAINE: THE FACTS

More than a headache

3.2 million Americans* live with Chronic Migraine—a neurologic condition that amounts to much more than just frequent headaches and migraines.

People with Chronic Migraine have:
- 15 or more headache days a month
- At least 8 headache days a month associated with migraine
- Each headache lasts 4 hours or more per day

See how BOTOX® can help

*TThis was determined by taking the publication’s Chronic Migraine prevalence rate and applying it to 2010 US population estimates for those 18 or more years of age (n = 234,504,070).
Chronic Migraine

• Episodic migraines can convert to chronic migraine at the rate of 2.5% per year

• Risk factors for conversion:
  – Higher headache frequency & greater disability
  – Obesity
  – Snoring
  – Allodynia
  – Depression, Anxiety
  – Poor response to acute treatment

• Opioids have a 44% increase in the risk of chronic migraine
Botox for Chronic Migraine

**The appointment**

The injections take about 15 minutes, and are done right in your doctor's office. The needles used for BOTOX® treatment are very small. People say that the injections feel like tiny pinpricks.

BOTOX® is injected into shallow muscles, not too deeply beneath the skin. Each treatment involves 31 injections in 7 key areas of the head and neck.

PREEMPT trial protocol (Phase 3 Research Evaluating Migraine Prophylaxis Therapy trials) of 31 injection sites
# Botox for Chronic Migraine

## Safety & Side Effects

**Side effects of BOTOX® in clinical studies**

The most common side effect was neck pain, which was experienced by 6% of BOTOX® patients (vs 3% for placebo).

[See all side effects in clinical studies](#)

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>BOTOX® (In 607 patients)</th>
<th>Placebo (In 692 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Migraine</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Partial facial paralysis</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Drooping eyelids</td>
<td>4%</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Neck pain</td>
<td>9%</td>
<td>3%</td>
</tr>
<tr>
<td>Musculoskeletal stiffness</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>4%</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

These are not all the side effects of BOTOX®. Please see the Important Safety Information at the link below and talk to your doctor about the Summary of Information about BOTOX®.
Cephaly Device
Cephaly Device

• Supraorbital transcutaneous nerve stimulation
• PREMICE Study
  – Randomised, double blinded, sham control (n=67)
  – Daily sham versus neurostimulation x 20 minutes
  – Primary outcome: Change in monthly migraine days; 50% responder rate

(Schoenen et al, Neurology 2013)
A BACKGROUND TO CGRP* AND ITS RECEPTOR

*CALCITONIN GENE-RELATED PEPTIDE
What is Calcitonin Gene-Related Peptide (CGRP)?

CGRP is a 37-amino acid neuropeptide derived from the gene encoding calcitonin. It is a potent vasodilator and also functions as a messenger in nerve cells.

CGRP exists in two forms in humans

α-CGRP is the predominant form
- Found in the peripheral and central nervous systems.
- Formed from alternative splicing of the calcitonin/CGRP gene on chromosome 11.

β-CGRP is found in the enteric nervous system. This differs in 3 amino acids.

CGRP levels are increased in migraine sufferers

- During migraine attacks (with or without aura) CGRP levels increase in the extracerebral circulation (external jugular blood)
- Only CGRP levels are elevated; there is no change in other peptides thought to be involved in pain transmission

Triptans suppress CGRP release from trigeminal nerves

Sumatriptan acts via presynaptic 5-HT1B/D receptors to suppress CGRP release from trigeminal nerves.

Treatment with sumatriptan normalized the increase in CGRP levels seen in acute migraine, with relief of headache pain.

## Summary of development of CGRP therapeutic monoclonal antibodies

<table>
<thead>
<tr>
<th></th>
<th>Erenumab (AMG 334)</th>
<th>Eptinezumab (ALD 403)</th>
<th>Galcanezumab LY2951742</th>
<th>Fremanezumab TEV-48125</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>CGRP receptor</td>
<td>CGRP</td>
<td>CGRP</td>
<td>CGRP</td>
</tr>
<tr>
<td><strong>Migraine types studied</strong></td>
<td>Episodic, Chronic</td>
<td>Episodic, Chronic</td>
<td>Episodic, Chronic Cluster headache</td>
<td>Episodic, Chronic</td>
</tr>
<tr>
<td><strong>Route of administration</strong></td>
<td>SC (monthly)</td>
<td>IV</td>
<td>SC (2-weekly or monthly)</td>
<td>SC (monthly)</td>
</tr>
<tr>
<td><strong>Half-life (days)</strong></td>
<td>21</td>
<td>31</td>
<td>28</td>
<td>45</td>
</tr>
<tr>
<td><strong>Current development phase</strong></td>
<td>Phase 3 (both)</td>
<td>Phase 3 (Episodic Migraine), Phase 2 (Chronic Migraine)</td>
<td>Phase 3</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>
Calcitonin Gene Related Peptide (CGRP) antibodies

Acknowledgements

• Dr Azimi Portelli
• Naomi Subat
• Christine Mc Cormack
Senior Medical Officer - General Practitioner with Special Interest (GPwSI) - Neurology

Queensland Health (Organisation site (http://www.health.qld.gov.au/))
Princess Alexandra Hospital, Woolloongabba

The Neurology Department are looking for a Senior Medical Officer - General Practitioner with Special Interest (GPwSI) - Neurology to join their team. This role will provide clinical services and care within the agreed scope of their experience and qualifications, under the supervision and guidance of consultant neurologists so as to further develop their diagnostic and management skills of neurological conditions.

**Job ad reference:** PA02269118
**Role title:** Senior Medical Officer - General Practitioner with Special Interest (GPwSI) - Neurology
**Status:** Temporary part time position (up to June 2019, 16 hours per fortnight)
(Future vacancies of a temporary, full time or part time nature may be accommodated within this role)
**Unit:** Department of Neurology
Division of Medicine
**Health Service:** Metro South Hospital and Health Service
**Location:** Princess Alexandra Hospital, Woolloongabba
**Classification level:** L13 – L17
**Salary level:** (see remuneration explained page 3)
**Closing date:** Friday, 16 March 2018
(Applications will remain current for 12 months)
*Please note: No third party applications will be accepted*

**Contact:** Dr Helen Brown
**Telephone:** (07) 3176 2782
**Online applications:** www.smartjobs.qld.gov.au
If you are unable to apply online, please contact Medical Employment Services on (07) 3176 7901

**Deliver application:** Hand delivered applications will not be accepted