European principles of management of common headache disorders in primary care

TJ Steiner¹, K Paemeleire², R Jensen³, D Valade⁴, L Savi⁵, MJA Lainez⁶, H-C Diener⁷, P Martelletti⁸ and EGM Couturier⁹

on behalf of the European Headache Federation and Lifting The Burden: The Global Campaign to Reduce the Burden of Headache Worldwide

¹ Division of Neuroscience and Mental Health, Imperial College London, London, UK; ² Department of Neurology, Ghent University Hospital, Ghent, Belgium; ³ Danish Headache Centre, Department of Neurology, University of Copenhagen, Glostrup Hospital, Glostrup, Denmark; ⁴ Centre d’Urgence des Céphalées, Hôpital Lariboisière, Paris, France; ⁵ Headache Centre, Department of Neurosciences, University of Turin, Turin, Italy; ⁶ Department of Neurology, University Clinic Hospital, Valencia University, Valencia, Spain; ⁷ Department of Neurology, University of Duisberg-Essen, Essen, Germany; ⁸ Department of Medical Sciences, Regional Referral Headache Centre, Saint Andrea Hospital, Rome, Italy; ⁹ Medisch Centrum Boerhaave, Amsterdam, The Netherlands.

These principles are published in J Headache Pain 2007; 8 (supplement 1)
European principles of management of common headache disorders in primary care

Scope and Purpose
Headache disorders are amongst the top 10 causes of disability in Europe. Four of these are important in primary care because they are common and are responsible for almost all headache-related burden. Management of these belongs largely in primary care.

The purpose of these principles is to help primary-care physicians correctly diagnose these few disorders, manage them well, recognise warnings of serious headache disorders and refer for specialist care when appropriate. They aim to give straightforward and easily-followed guidance to physicians who are assumed to be non-expert.

They recognise that availability and regulatory approval of drugs, and reimbursement policies, vary from country to country. For that reason, different possible options are set out wherever appropriate. Otherwise, the emphasis is on unambiguous advice.

These principles are likely to be most useful if read through at least once in their entirety, but are set out in 12 stand-alone management aids in three sections:

Guides to diagnosis (some parts of these will need to be assimilated into routine practice whereas other parts can serve as check lists and aide-mémoires)
1. Headache as a presenting complaint
2. Diagnosis of headache
3. Typical features of the common headache disorders
4. Differential diagnosis of the common headache disorders

Guides to management (these are information sources to be referred to once the diagnosis has been made; management aid #6 includes guidance on information to patients)
5. General aspects of headache management
6. Advice to patients
7. Medical management of acute migraine
8. Prophylactic management of migraine
9. Medical management of tension-type headache
10. Medical management of cluster headache
11. Management of medication-overuse headache

Guide to referral (a reference and reminder)
12. Headache management in primary care: when to refer

These principles are supplemented by the Headache-Attributed Lost Time (HALT) index, a measure of headache burden, and a series of patient information leaflets developed by Lifting The Burden.

Under development by EuroHead (supported by the European Brain Council) is a diagnostic diary and by Lifting The Burden is the Headache Under-Response to Treatment (HURT) index, an outcome measure specifically to guide follow-up in primary care.
Development process

Stakeholder involvement
The initial development group, a collaboration between the European Headache Federation (EHF) and Lifting The Burden: The Global Campaign to Reduce the Burden of Headache Worldwide, were headache specialists from Belgium, Denmark, France, Germany, Italy, Netherlands, Spain and UK. The pilot group were primary care physicians from the same countries. The consultation group were members of the National headache societies within the European Headache Federation representing Albania, Austria, Belgium, Belarus, Bulgaria, Croatia, Denmark, Finland, France, Germany, Greece, Hungary, Israel, Italy, Lithuania, Netherlands, Poland, Portugal, Romania, Russia, Serbia and Montenegro, Slovenia, Spain, Sweden, Switzerland and United Kingdom. Patient representatives and advocates were consulted through the Board of the European Headache Alliance.

Rigour of development
The development process was review of all published treatment guidelines in use in Europe, and harmonization through selection of whatever recommendations within them carried greatest weight.
Evidence-based recommendations were always preferred to those without explicit supporting evidence. Discordance between recommendations was resolved through direct reference to original evidence or, where this was lacking, through consensus of expert opinion.

Clarity and presentation
The aim was to give straightforward and easily-followed guidance to primary care physicians who were assumed to be non-expert. There was recognition that availability and regulatory approval of drugs and reimbursement policies varied from country to country. For that reason, different possible options were considered and are set out wherever appropriate, but otherwise the emphasis was on unambiguous advice.

Applicability
These principles assume that headache services are developed and adequately resourced in all countries in Europe, even though this is not the case at present. Separate initiatives by the European Headache Federation and Lifting The Burden are being undertaken to support better organisation of headache services in all countries in Europe.
These recommendations will be monitored by the pilot group and reviewed annually by the development group.

Editorial independence
The sole funding body supporting development of these principles was European Headache Federation.
Members of the development group declared, as possible conflicts of interest, past or present consultancy agreements with and/or research funding from:

These principles make no recommendations that favour one proprietary medication over another with similar effects.
1. HEADACHE AS A PRESENTING COMPLAINT

Most people have occasional headache, and regard it as normal. Headache becomes a problem at some time in the lives of about 40% of people in Europe. Four headache disorders are common in primary care (table). All have a neurobiological basis. They are disabling and impair quality of life.

<table>
<thead>
<tr>
<th>The common headache disorders in primary care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Migraine</strong></td>
</tr>
<tr>
<td>usually episodic, occurring in 12-16% of the general population, in women more than men in a ratio of 3:1</td>
</tr>
<tr>
<td><strong>Tension-type headache</strong></td>
</tr>
<tr>
<td>usually episodic, affecting &gt;80% of people from time to time; in at least 10% it recurs frequently, and in 2-3% of adults and some children it is chronic, occurring on more days than not</td>
</tr>
<tr>
<td><strong>Cluster headache</strong></td>
</tr>
<tr>
<td>intense and frequently recurring but short-lasting headache attacks, affecting up to 3 in 1,000 men and up to 1 in 2,000 women</td>
</tr>
<tr>
<td><strong>Medication-overuse headache</strong></td>
</tr>
<tr>
<td>a chronic daily headache syndrome occurring in up to 3% of adults, 5 women to each man, and 1% of children and adolescents; this is a secondary headache, but it occurs only as a complication of a pre-existing headache disorder, usually migraine or tension-type headache</td>
</tr>
</tbody>
</table>

One patient may have more than one of these disorders concomitantly.

There are a large number of other secondary headache disorders. Some of these are serious, and they must be recognized (see Management aid #4. Differential diagnosis of the common headache disorders), but overall they account for <1% of patients presenting with headache.
2. DIAGNOSIS OF HEADACHE

Taking a diagnostic history

The history is all-important in the diagnosis of the primary headache disorders and of medication-overuse headache (table). There are no useful diagnostic tests. The history should elicit any warning features of a serious secondary headache disorder.

<table>
<thead>
<tr>
<th>Questions to ask in the history</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How many different headaches types does the patient have?</strong></td>
</tr>
<tr>
<td>A separate history is needed for each.</td>
</tr>
<tr>
<td><strong>Time questions</strong></td>
</tr>
<tr>
<td>• Why consulting now?</td>
</tr>
<tr>
<td>• How recent in onset?</td>
</tr>
<tr>
<td>• How frequent, and what temporal pattern (episodic or daily and/or unremitting)?</td>
</tr>
<tr>
<td>• How long lasting?</td>
</tr>
<tr>
<td><strong>Character questions</strong></td>
</tr>
<tr>
<td>• Intensity of pain?</td>
</tr>
<tr>
<td>• Nature and quality of pain?</td>
</tr>
<tr>
<td>• Site and spread of pain?</td>
</tr>
<tr>
<td>• Associated symptoms?</td>
</tr>
<tr>
<td><strong>Cause questions</strong></td>
</tr>
<tr>
<td>• Predisposing and/or trigger factors?</td>
</tr>
<tr>
<td>• Aggravating and/or relieving factors?</td>
</tr>
<tr>
<td>• Family history of similar headache?</td>
</tr>
<tr>
<td><strong>Response questions</strong></td>
</tr>
<tr>
<td>• What does the patient do during the headache?</td>
</tr>
<tr>
<td>• How much is activity (function) limited or prevented?</td>
</tr>
<tr>
<td>• What medication has been and is used, in what manner and with what effect?</td>
</tr>
<tr>
<td><strong>State of health between attacks</strong></td>
</tr>
<tr>
<td>• Completely well, or residual or persisting symptoms?</td>
</tr>
<tr>
<td>• Concerns, anxieties, fears about recurrent attacks, and/or their cause?</td>
</tr>
</tbody>
</table>
Warning features in the history

Any new headache in an individual patient should be treated with caution. Specific warning features are:

- thunderclap headache (intense headache with “explosive” or abrupt onset), which suggests subarachnoid haemorrhage
- headache with atypical aura (duration >1 hour, or including motor weakness), which may be symptoms of TIA or stroke
- aura without headache in the absence of a prior history of migraine with aura, which may be a symptom of TIA or stroke
- aura occurring for the first time in a patient during use of combined oral contraceptives, which indicates risk of stroke
- new headache in a patient older than 50 years, which may be a symptom of temporal arteritis or intracranial tumour, or in a pre-pubertal child
- progressive headache, worsening over weeks or longer, which may indicate intracranial space-occupying lesion
- headache aggravated by postures or manoeuvres that raise intracranial pressure, which may indicate intracranial tumour
- new headache in a patient with a history of cancer, HIV infection or immunodeficiency

Diagnostic diary

Once serious causes have been ruled out, a headache diary kept over a few weeks clarifies the pattern of headaches and associated symptoms as well as medication use or overuse.

Physical examination of headache patients

Migraine, tension-type headache, cluster headache and medication-overuse headache are diagnosed solely on history. Signs are present in cluster headache patients when seen during attacks.

Physical examination is mandatory when the history is suggestive of secondary headache.

Warning features on examination

- pyrexia associated with headache
- focal neurological signs associated with headache

Investigation of headache patients

Investigations, including neuroimaging, are indicated when history or examination suggest headache may be secondary to another condition.
3. **TYPICAL FEATURES OF THE COMMON HEADACHE DISORDERS**

**Migraine**

Migraine occurs in two principal subtypes, migraine without aura and migraine with aura. One patient may have both.

**Migraine without aura**

**Adults** with this disorder typically describe:

- recurrent episodic moderate or severe headaches which:
  - are often unilateral and/or pulsating
  - last 4 hours to 3 days
  - are often associated with nausea and/or vomiting
  - are aggravated by routine physical activity
- during which they limit activity and prefer dark and quiet
- with freedom from symptoms between attacks.

In **children**:

- attacks may be shorter-lasting
- headache is more commonly bilateral and less usually pulsating
- gastrointestinal disturbance is more prominent.

**Migraine with aura**

affects one third of people with migraine and accounts for 10% of migraine attacks overall. It is:

- characterised by aura preceding headache, consisting of neurological symptoms that develop gradually over >5 minutes and resolve within 60 minutes:
  - hemianopic visual disturbances, or a spreading scintillating scotoma (patients may draw a jagged crescent if asked)
  - and/or unilateral paraesthesiae of hand, arm and/or face
  - and/or (rarely) dysphasia.
- otherwise similar to migraine without aura.

**Typical aura without headache** may occur in patients with a past history of migraine with aura.
**Tension-type headache**

This disorder occurs in three subtypes. Only two of these are medically important: frequent episodic tension-type headache and chronic tension-type headache.

**Frequent episodic tension-type headache**
- occurs in attack-like episodes, at least once a month, lasting hours to a few days
- can be unilateral but is more often generalised
- is typically described as pressure or tightness like a vice or tight band around the head, or is felt in the neck
- lacks the associated symptom complex of migraine.

**Chronic tension-type headache**
- occurs by definition on ≥15 days a month for >3 months and may be daily and unremitting
- otherwise is similar to frequent episodic tension-type headache.

**Cluster headache**

This highly recognisable condition occurs in two subtypes, episodic cluster headache and chronic cluster headache.

Episodic cluster headache occurs in bouts (clusters), typically of 6-12 weeks’ duration, once a year or two years, and then remits until the next cluster.

Chronic cluster headache, which persists without remissions, is less common. It may develop from and/or revert to episodic cluster headache.

Cluster headache:
- mostly affects men
- manifests as strictly unilateral, excruciating pain around the eye
- recurs frequently, typically once or more daily, commonly at night
- is short-lasting, for 15-180 minutes (typically 30-60 minutes)
- has highly characteristic and strictly ipsilateral autonomic features including any of:
  - red and watering eye
  - running or blocked nostril
  - ptosis
- causes marked agitation (the patient, unable to stay in bed, paces the room, even going outdoors).
### Summary of features distinguishing the common headache disorders (NB: two or more may occur concomitantly)

<table>
<thead>
<tr>
<th></th>
<th>Migraine</th>
<th>Tension type headache (TTH)</th>
<th>Cluster headache (CH)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Temporal pattern</strong></td>
<td>recurrent attack-like episodes, lasting 4 hours to 3 days; frequency often 1-2/month but variable from 1/year to 2/week; freedom from symptoms between attacks</td>
<td><strong>Episodic TTH:</strong> recurrent attack-like episodes lasting hours to a few days; 1-14 days affected per month; freedom from symptoms between attacks</td>
<td><strong>Episodic CH:</strong> short-lasting attacks (15-180 minutes) recurring frequently (typically ≥1 daily) in bouts of 6-12 weeks' duration once a year or two years, and then remitting</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Chronic TTH:</strong> ≥15 days affected per month (often daily and unremitting)</td>
<td><strong>Chronic CH:</strong> similar, but without remissions between bouts</td>
</tr>
<tr>
<td><strong>Typical headache characteristics</strong></td>
<td>often unilateral and/or pulsating</td>
<td>can be unilateral but more often generalised; may be felt in the neck; typically described as pressure or tightness</td>
<td>strictly unilateral, around the eye</td>
</tr>
<tr>
<td><strong>Headache intensity</strong></td>
<td>typically moderate to severe</td>
<td>typically mild to moderate</td>
<td>very severe</td>
</tr>
<tr>
<td><strong>Associated symptoms</strong></td>
<td>often nausea and/or vomiting; often photophobia</td>
<td>none</td>
<td>strictly ipsilateral autonomic features: any of red and watering eye, running or blocked nostril, ptosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(mild nausea, but not vomiting, may accompany chronic TTH)</td>
<td></td>
</tr>
<tr>
<td><strong>Reactive behaviour</strong></td>
<td>avoidance of physical activity (maybe bed rest); preference for dark and quiet</td>
<td>none specific</td>
<td>marked agitation</td>
</tr>
</tbody>
</table>
**Medication-overuse headache**

Medication-overuse headache, a chronic daily headache syndrome, is an aggravation of a prior headache (usually migraine or tension-type headache) by chronic overuse of medication *taken to treat headache or other pain*.

All acute headache medications may have this effect. Frequency, regularity and duration of intake are important determinants of risk.

A history can be elicited of increasingly frequent headache episodes, with increasing medication use, over months to many years.

Medication overuse headache
- is associated with:
  - use of simple analgesics on \( \geq 15 \) days a month *and/or*
  - use of opioids, ergots or triptans, or any combination of these, on \( \geq 10 \) days a month
- occurs daily or near-daily
- is present – and often at its worst – on awakening in the morning
- is initially aggravated by attempts to withdraw the medication.

Diagnosis of medication-overuse headache is confirmed if symptoms improve within 2 months after overused medication is withdrawn.
4. DIFFERENTIAL DIAGNOSIS OF THE COMMON HEADACHE DISORDERS

Each of the primary headaches is in the differential diagnosis of each of the others. Medication-overuse headache is in the differential diagnosis of migraine and tension-type headache.

Otherwise, the differential diagnosis includes a small number of serious secondary headaches that are important to recognise.

Warning features in the history or on examination

- headache that is new or unexpected in an individual patient, or has new features
- thunderclap headache (intense headache with abrupt or “explosive” onset), which may be indicative of subarachnoid haemorrhage
- headache with atypical aura (duration >1 hour, or including motor weakness), which may be symptoms of TIA or stroke
- aura without headache in the absence of a prior history of migraine with aura, which may be a symptom of TIA or stroke
- aura occurring for the first time in a patient during use of combined oral contraceptives, which indicates risk of stroke
- new headache in a patient older than 50 years, which may be a symptom of temporal arteritis or intracranial tumour, or in a pre-pubertal child
- progressive headache, worsening over weeks or longer, which may indicate intracranial space-occupying lesion
- headache associated with or aggravated by postural change or other manoeuvres that raise intracranial pressure, which may indicate intracranial tumour
- new headache in a patient with a history of cancer, HIV infection or immunodeficiency
- otherwise unexplained pyrexia associated with headache, which may indicate meningitis
- focal neurological signs associated with headache
5. **GENERAL ASPECTS OF HEADACHE MANAGEMENT**

The following principles are generally important for all headache disorders managed in primary care.

**Acknowledging impact**

- Recurrent disabling headache is a burden on the person with it, and has an impact on other people. These include the family, work colleagues and employer.
- Recurrent disabling headache may lead to lifestyle compromise, either in response to attacks or in a bid to avoid them. In this way, episodic headache can have continuous impact.

The HALT index, developed by *Lifting The Burden* and currently available in Dutch, English, French, German, Italian, Portuguese and Spanish, is an instrument for assessing burden in terms of lost time.

**Realistic aims of management**

- Headache disorders cannot be cured but can be effectively managed in most cases.
- They usually remit in old age.

**Reassurance and explanation**

- Many people with recurrent headache wrongly fear underlying disease. Appropriate reassurance should never be omitted.
- Explanation is a crucial element of preventative management in patients with migraine or frequent episodic tension-type headache who are at risk of escalating medication consumption.

A series of patient information leaflets developed by *Lifting The Burden* are currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish. They provide basic explanations of migraine, tension-type headache, cluster headache and medication-overuse headache and their treatment.
Causes and triggers

- Whilst patients want to know the cause of their headache, this may not be possible. Both genetic and environmental factors contribute to processes that are not well understood.

- Many patients seek help in identifying triggers. The importance of trigger factors in migraine is over-emphasised. When they are relevant to individual patients, they are usually self-evident. Triggers may be less readily identified when they are cumulative in their effect, jointly contributing to a “threshold” above which attacks are initiated. Even when identified, triggers are not always avoidable.

- Contrary to popular belief, there is no “migraine diet”. The only dietary triggers with evidential support are alcohol and monosodium glutamate.

Follow-up

Every patient to whom treatment is offered, or whose treatment is changed, requires follow-up in order to ensure that optimum treatment has been established.

The use of an outcome measure is recommended. The HURT index is being developed by Lifting The Burden expressly to guide follow-up in primary care.

Diaries and calendars

Diaries are recommended for:

- recording symptoms and temporal patterns that contribute to correct diagnosis
- recording medication use and overuse
- revealing associations with the menstrual cycle and other triggers.

A diagnostic diary is being developed by EuroHead in collaboration with Lifting The Burden.

Calendars are recommended for:

- encouraging compliance with prophylactic medication
- recording treatment effect
- monitoring acute medication use or overuse during follow-up
- charting outcomes.
6. ADVICE TO PATIENTS

Patients with headache disorders commonly request information. Many find or have found misleading information on the internet.

Non-drug treatments

Patients enquiring about the following may be given this advice:

- **Biofeedback and relaxation therapies** can be helpful, and are potentially useful options when drug treatments must be avoided. Their basis requires that only skilled therapists should provide them, but very few skilled therapists are available in most countries.

- **Physiotherapy** has proven benefits in some patients with tension-type headache. It requires skilled and individualised therapy which is not widely available in many countries.

- **Acupuncture** benefits some people with migraine or tension-type headache although large clinical trials have failed to distinguish between acupuncture and sham procedures. It requires skilled and individualised therapy.

- **Transcutaneous electrical nerve stimulation** (TENS) may help in chronic pain but is of unproven value in treating headache disorders.

- **Dental treatment**, including splints and bite-raising appliances, is of unproven value in treating headache and should be discouraged.

- **Spectacles** should be professionally prescribed and worn when needed, but refractive errors are rarely a cause of troublesome headache.

- **Herbals** are mostly not recommended. Butterbur has some efficacy according to clinical trials and is approved for use in some countries but preparations on sale elsewhere are variable in content and have uncertain toxicity. Feverfew preparations on sale everywhere are highly variable in content and their toxicity is not well understood.

- **Homoeopathy** is of unproven value. There is no arguable case for over-the-counter sales of homoeopathic remedies.

- **Reflexology** has no scientific basis.
• **Devices**: many are on the market, some costly and promoted with unsupportable claims of efficacy. "Testimonials" can be attributed to placebo effect and should be disregarded.

• **Closure of patent foramen ovale (PFO)**: there is insufficient evidence to support the hypothesis that migraine frequency is improved by PFO closure, a procedure which carries a small but relevant risk of serious adverse events including stroke, pericardial tamponade, atrial fibrillation and death. Further prospective trials are underway, and PFO closure should not be undertaken for migraine prophylaxis outside these trials.

• **Other surgical procedures on the face or neck** produce no benefit and are potentially harmful.

### Hormonal contraception and HRT

Headache is often a side-effect of combined oral contraceptives (COCs) and many women report onset or aggravation of migraine after starting them.

The following advice on hormonal contraception may be given to patients with migraine:

- both migraine with aura and the ethinyloestradiol component of COCs are independent risk factors for stroke in young women
- alternatives to COCs are recommended for women with migraine with aura and additional risk factors for stroke (including smoking)
- progestogen-only contraception is acceptable with any subtype of migraine.

Hormone replacement therapy (HRT) is not contraindicated in migraine; decisions about commencing or continuing HRT should be made according to generally applicable criteria.

### Resources for the patient

*Lifting The Burden* has produced a series of patient information leaflets on the common headache disorders and their treatment and one on female hormones and headache. These are currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish.

### World Headache Alliance

WHA is a charitable umbrella organisation. Its website carries much information for people with headache, and links to many other helpful sites including those of its member organisations in 26 countries.

Website: [www.w-h-a.org](http://www.w-h-a.org)
7. MEDICAL MANAGEMENT OF ACUTE MIGRAINE

All adults with migraine should have access to acute medication. Children with short-lasting attacks may respond well to bed-rest without medical treatment.

In adults and children, regular use of acute medication at high frequency (on >2 days/week) risks the development of medication-overuse headache.

Drug intervention

All patients should climb a treatment ladder (stepped management), usually treating three attacks at each step before proceeding to the next. This strategy, if followed correctly, reliably achieves the most effective and cost-effective individualised care.

Step one: symptomatic therapy

- simple analgesia
- plus, if needed, an antiemetic.

<table>
<thead>
<tr>
<th>Analgesics</th>
<th>Antiemetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetylsalicylic acid 900-1000mg (adults only) or ibuprofen 400-800mg or diclofenac 50-100mg or ketoprofen 100mg or naproxen 500-1000mg or (where these are contraindicated) paracetamol 1000mg</td>
<td>domperidone 20mg or metoclopramide 10mg</td>
</tr>
</tbody>
</table>

Local guidelines may recommend trying more than one analgesic in step one before proceeding to step two.

Paracetamol has limited evidence of efficacy and is not first-line treatment.
Principles of step one

- use soluble analgesics, or mouth-dispersible formulations
- take early in the attack, in adequate dosage
- a prokinetic antiemetic inhibits gastric stasis, an early feature of migraine that impairs bioavailability of oral medication
- rectal administration may be preferable in the presence of vomiting:
  - analgesic suppositories (any of diclofenac 100mg, ibuprofen 400mg, ketoprofen 100-200mg or naproxen 500-1000mg)
  - if needed, antiemetic suppositories (either domperidone 30mg or metoclopramide 20mg).

Step one for children (when needed)

- for analgesia: use ibuprofen 200-400mg according to age and weight
- for antiemesis: use domperidone 10-20mg according to age and weight.

Step two: specific therapy

<table>
<thead>
<tr>
<th>Specific anti-migraine drugs, formulations and doses available for step two</th>
<th>(availability varies from country to country)</th>
</tr>
</thead>
<tbody>
<tr>
<td>almotriptan</td>
<td>tablets 12.5mg</td>
</tr>
<tr>
<td>eletriptan</td>
<td>tablets 20mg and 40mg (80mg may be effective when 40mg is not)</td>
</tr>
<tr>
<td>frovatriptan</td>
<td>tablets 2.5mg</td>
</tr>
<tr>
<td>naratriptan</td>
<td>tablets 2.5mg</td>
</tr>
<tr>
<td>rizatriptan</td>
<td>tablets 10mg (and 5mg, to be used only when propranolol is being taken concomitantly); mouth-dispersible wafers 10mg</td>
</tr>
<tr>
<td>sumatriptan</td>
<td>tablets and rapidly dissolving tablets 50mg and 100mg; suppositories 25mg; nasal spray 10mg (licensed for adolescents) and 20mg; subcutaneous injection 6mg</td>
</tr>
<tr>
<td>zolmitriptan</td>
<td>tablets 2.5mg and 5mg; mouth-dispersible tablets 2.5mg and 5mg; nasal spray 5mg</td>
</tr>
<tr>
<td>ergotamine tartrate</td>
<td>tablets 1mg and 2mg; suppositories 2mg</td>
</tr>
</tbody>
</table>
Principles of step two

- where available, and unless contra-indicated, triptans should be offered to all patients failing step one
- ergotamine has very low and unpredictable bioavailability, which impairs its efficacy, and complex pharmacology and long duration of action, which lead to poor tolerability
- triptans should not be used regularly on more than 10 days per month to avoid the risk of medication-overuse headache
- triptans differ slightly, but there are large and unpredictable individual variations in response to them; one may work where another has not; patients should try several, in different formulations, and choose between them
- the initial dose of all oral triptans (except, in some cases, eletriptan) is one tablet
- a second dose for non-response is not recommended by most triptan manufacturers but, taken not less than 2 hours after the first, may be effective in some cases
- triptans are more effective when taken whilst headache is still mild (this instruction should be given only to patients who can reliably distinguish migraine from tension-type headache)
- when nausea is present, domperidone 20mg or metoclopramide 10mg may be added
- when vomiting is present, sumatriptan suppositories, zolmitriptan nasal spray (absorbed through the nasal mucosa) or sumatriptan subcutaneous injection may be preferred
- when all other triptans are ineffective, sumatriptan by subcutaneous injection 6mg should be considered
- triptans are associated with return of symptoms within 48 hours (relapse) in up to 40% of patients who have initially responded.

Treatment of relapse

- a second dose of a triptan is usually effective
- this second dose may lead to further relapse (when this happens repeatedly, the triptan should be changed)
- NSAIDs may be an effective alternative.

Avoidance of relapse

- limited evidence suggests that either of the following may prevent some relapses:
  - concomitant use of a triptan and an NSAID
  - use of a triptan followed by an NSAID 6-12 hours later.
**Contraindications to step two**

Pregnancy is a general contraindication to ergotamine and to all triptans. There are specific precautions attached to some triptans (see pharmacopoeia).

All triptans and ergots should be avoided by people with:

- uncontrolled hypertension
- coronary heart disease, cerebrovascular disease and peripheral vascular disease
- multiple risk factors for coronary or cerebrovascular disease.

**Step two for children**

No specific anti-migraine drug has been shown to have efficacy in children (under 12 years old). Failure of step one is an indication for specialist referral.

**Follow-up**

Every patient to whom treatment is offered, or whose treatment is changed, requires follow-up in order to ensure that optimum treatment has been established.

Use of a calendar is recommended to monitor acute medication use or overuse and record treatment effect.

The use of an outcome measure is recommended. The HURT index is being developed by *Lifting The Burden* expressly to guide follow-up in primary care.

**Information for patients**

*Lifting The Burden* has produced an information leaflet on migraine and its treatment. This is currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish.
8. PROPHYLACTIC MANAGEMENT OF MIGRAINE

Any patient whose quality of life is impaired by migraine, whether adult or child, may require prophylaxis in addition to acute medication.

Indications for prophylaxis

Prophylactic therapy may be added when:
- attacks cause disability on two or more days per month, and
- optimised acute therapy does not prevent this, and
- the patient is willing to take daily medication.

Other indications for prophylaxis are:
- risk of over-frequent use of acute therapy, even when it is effective (but prophylactic drugs are inappropriate for medication overuse headache)
- for children with frequent absences from school.

Effective drugs

<table>
<thead>
<tr>
<th>Prophylactic drugs with good evidence of efficacy</th>
<th>(availability and regulatory approval vary from country to country; use of drugs off-licence rests on individual clinical responsibility)</th>
</tr>
</thead>
<tbody>
<tr>
<td>beta-adrenergic blockers without partial agonism</td>
<td>atenolol 25-100mg bd or bisoprolol 5-10mg od or metoprolol 50-100mg bd or propranolol LA 80mg od-160mg bd</td>
</tr>
<tr>
<td>topiramate</td>
<td>25mg od-50mg bd</td>
</tr>
<tr>
<td>flunarizine</td>
<td>5-10mg od</td>
</tr>
<tr>
<td>sodium valproate</td>
<td>600-1500mg daily</td>
</tr>
<tr>
<td>amitriptyline</td>
<td>10-100 mg nocte</td>
</tr>
</tbody>
</table>
All of these drugs have contra-indications and side-effects (refer to pharmacopoeia).

**Principles of prophylaxis**

- A calendar should be kept by every patient on prophylaxis to assess efficacy and promote compliance.
- Poor compliance is a major factor impairing efficacy of migraine prophylactics; once-daily dosing is associated with better compliance.
- The dose of any drug should start low in the suggested range and be increased in the absence of troublesome side-effects.
- Drugs that appear ineffective should not be discontinued too soon; 2-3 months may be the minimum to achieve and observe efficacy.
- Tapered withdrawal may be considered after 6 months of good control, and should be considered no later than after 1 year.
- Amitriptyline may be preferred when migraine coexists with tension-type headache, depression or sleep disturbance.
- Propranolol has best evidence of safety during pregnancy.

**Prophylaxis in children**

- Beta-blockers (dosage adjusted according to body weight) or flunarizine (dosage adjusted according to age) may be tried.

**Follow-up**

Every patient to whom prophylactic treatment is offered, or whose treatment is changed, requires follow-up in order to ensure that optimum treatment has been established.

Use of a calendar is recommended to encourage compliance with prophylactic medication and record treatment effect.

The use of an outcome measure is recommended. The HURT index is being developed by *Lifting The Burden* expressly to guide follow-up in primary care.

**If prophylaxis fails**

- failure may be due to subtherapeutic dosage or insufficient duration of treatment
- review the diagnosis
- review compliance
- review other medication, especially for overuse
- when prophylaxis still fails to have clear benefit, discontinue it.
Information for patients

*Lifting The Burden* has produced an information leaflet on migraine and its treatment. This is currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish.

Hormonal contraception and HRT

Many women report onset or aggravation of migraine after starting combined oral contraceptives (COCs). Others report improvement of pre-existing migraine.

The following advice on hormonal contraception may be given:

- both migraine with aura and the ethinyloestradiol component of COCs are independent risk factors for stroke in young women
- alternatives to COCs are recommended for women with migraine with aura and additional risk factors for stroke (including smoking)
- progestogen-only contraception is acceptable with any subtype of migraine.

Hormone replacement therapy (HRT) is not contraindicated in migraine. Decisions about commencing or continuing HRT should be made according to generally applicable criteria.

*Lifting The Burden* has produced an information leaflet on female hormones and headache.

Botulinum toxin (Botox)

Patients may ask about this treatment.

There is insufficient evidence to support the efficacy of Botox in migraine prevention. This treatment is not recommended.

Patent foramen ovale (PFO) and migraine

Patients may ask about this treatment.

There is insufficient evidence to support the hypothesis that migraine frequency is improved by PFO closure. This procedure carries a small but relevant risk of serious adverse events including stroke, pericardial tamponade, atrial fibrillation and death. Further prospective trials are underway. PFO closure should not be undertaken for migraine prophylaxis outside these trials.
9. MEDICAL MANAGEMENT OF TENSION-TYPE HEADACHE

Drug therapy has limited scope in tension-type headache but is effective nevertheless in many patients.

Either acute medication or prophylaxis may be indicated.

Acute medication should be used with care when headache is frequent because of the risk of medication overuse.

**Acute intervention**

- Symptomatic treatment with over-the-counter analgesics is appropriate for episodic tension-type headache occurring on ≤2 days per week:
  - acetylsalicylic acid 600-1000mg (adults only)
  - ibuprofen 400-800mg
  - paracetamol 1000mg is less effective.
- Episodic tension-type headache on >2 days per week is an indication for prophylaxis in place of, rather than in addition to, acute intervention.
- These treatments are unlikely to be effective in chronic tension-type headache and put the patient at risk of medication overuse headache.

**Principles of acute intervention**

- Opioids should be avoided; in particular:
  - codeine and dihydrocodeine
  - dextropropoxyphene
  - combination analgesics containing any of these.
- Barbiturates have no place in the treatment of tension-type headache.
- As the frequency of headaches increases, so does the risk of medication overuse.
Prophylaxis

- Amitriptyline, 10-100mg at night, is the drug of choice for frequent episodic or chronic tension-type headache.
- Nortriptyline causes fewer anticholinergic side-effects but has less good evidence of efficacy (amitriptyline can be replaced by nortriptyline at the same dose).

Principles of prophylaxis

- Intolerance is reduced by starting low (10mg) and incrementing by 10-25mg each 1-2 weeks.
- A calendar should be kept to assess efficacy and promote compliance.
- Prophylaxis that appears ineffective should not be discontinued too soon; 2-3 months may be the minimum to achieve and observe efficacy.
- Tapered withdrawal may be considered after 6 months of good control, but prolonged treatment is sometimes indicated.

Follow-up

Every patient to whom treatment is offered, or whose treatment is changed, requires follow-up in order to ensure that optimum treatment has been established.

Use of a calendar is recommended to monitor acute medication use or overuse, or to encourage compliance with prophylactic medication, and to record treatment effect.

The use of an outcome measure is recommended. The HURT index is being developed by Lifting The Burden expressly to guide follow-up in primary care.

If prophylaxis fails

- failure may be due to subtherapeutic dosage or insufficient duration of treatment
- review the diagnosis
- review compliance (patients who are not informed that they are receiving medication often used as an antidepressant, and told why, may default when they find out)
- review other medication, especially for overuse
- when prophylaxis still fails to have clear benefit, discontinue it.
**Pain management**

Despite best efforts, chronic tension-type headache is often refractory to medical treatment.

Patients in this situation require a pain management programme with emphasis on psychological approaches.

**Information for patients**

*Lifting The Burden* has produced an information leaflet on tension-type headache and its treatment. This is currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish.

**Botulinum toxin (Botox)**

Patients may ask about this treatment.

There is insufficient evidence to support the efficacy of Botox in tension-type headache. This treatment is not recommended.
10. MEDICAL MANAGEMENT OF CLUSTER HEADACHE

Cluster headache management is usually better left to experienced specialists who see this disorder frequently.

The objective in both episodic and chronic cluster headache is total attack suppression. This is not always achievable.

Both acute medication and prophylaxis have a role in management, but preventative drugs are the mainstay of treatment in most cases.

Acute therapies

- Sumatriptan 6mg subcutaneously is the only proven highly-effective acute treatment, but cannot be recommended for use more than twice a day.
- Oxygen 100% at ≥7 l/min for up to 15 min (requires a non-rebreathing mask and regulator) helps some people and may be used as frequently as needed.
- Analgesics, including opioids, have no place in treating cluster headache.

Prophylaxis

Principles

- Drugs in the table are used by specialists, balancing efficacy against toxicity
- Prophylaxis of episodic cluster headache should begin as early as possible after the start of a new cluster bout and (except for prednisolone, which is used in short courses only) should be discontinued by tapering 2 weeks after full remission
- For chronic cluster headache, treatments may need to be continued long-term
- Failure of one drug does not predict failure of others
- Combinations may be tried, but the potential for toxicity is obviously high.
Drugs used by specialists in cluster headache prophylaxis

(all are potentially toxic: refer to pharmacopoeia)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>verapamil</td>
<td>240-960mg daily</td>
</tr>
<tr>
<td></td>
<td>ECG monitoring is advised</td>
</tr>
<tr>
<td>prednisolone</td>
<td>60-80mg od for 2-4 days, discontinued by dose reduction over 2-3 weeks</td>
</tr>
<tr>
<td></td>
<td>may need repeating because of relapse during dose reduction</td>
</tr>
<tr>
<td>lithium carbonate</td>
<td>600-1600mg daily</td>
</tr>
<tr>
<td></td>
<td>levels must be monitored</td>
</tr>
<tr>
<td>ergotamine tartrate</td>
<td>2-4mg daily per rectum</td>
</tr>
<tr>
<td></td>
<td>usually omitted every 7th day</td>
</tr>
<tr>
<td></td>
<td>may not be used concomitantly with sumatriptan</td>
</tr>
<tr>
<td>methysergide</td>
<td>1-2mg tds</td>
</tr>
<tr>
<td></td>
<td>usage interrupted for at least 1 month in every 6 months</td>
</tr>
<tr>
<td></td>
<td>not recommended to be used concomitantly with sumatriptan</td>
</tr>
</tbody>
</table>

Follow-up

Every patient with active cluster headache requires frequent follow-up both to ensure that optimum treatment is maintained and to monitor for treatment toxicity.

Information for patients

*Lifting The Burden* has produced an information leaflet on cluster headache and its treatment. This is currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish.
11. MANAGEMENT OF MEDICATION-OVERUSE HEADACHE

Medication-overuse headache is an aggravation of a prior primary headache by chronic overuse of medication taken to treat it.

Once this condition has developed, early intervention is important. The long-term prognosis depends on the duration of medication overuse.

Management

- Prevention, through education, is better than cure.
- The only effective treatment of established medication-overuse headache is withdrawal of the suspected medication(s).

Objectives

There are four separate objectives in the complete management of MOH, and all are important:

- the first is to achieve withdrawal from the overused medication
- the second, which should follow, is recovery from MOH
- the third is to review and reassess the underlying primary headache disorder (migraine or tension-type headache)
- the fourth is to prevent relapse.

Principles

- Clear explanation that the “treatment” a patient is taking for headache is actually the cause of it is vital to success.
- Patients may be reassured that the outcome of withdrawal is usually good.
- With forewarning, withdrawal is most successfully done abruptly; admission to hospital is rarely necessary.
- Withdrawal leads initially to worsening headache, so should be planned to avoid unnecessary lifestyle disruption (1-2 weeks’ sick leave may be needed).
- After 1-2 weeks, usually, headache shows signs of improvement
- Recovery continues slowly for weeks to months.
Follow-up

- Every patient withdrawing from medication requires follow-up in order to provide support and observe outcome.
- First review is advised after 2-3 weeks to ensure withdrawal has been achieved.
- Use of a calendar is strongly recommended to record symptoms and medication use during withdrawal, and to record changing headache pattern.
- Most patients revert to their original headache type (migraine or tension-type headache) within 2 months; this will need review and appropriate management.
- Further follow-up is important to avoid relapse, and most patients require extended support: the relapse rate is around 40% within five years.

Re-introducing withdrawn medication

- Withdrawn medications should subsequently be avoided as far as is possible.
- When needed, they may be cautiously reintroduced after 2 months.
- Frequency of use should never exceed 2 days/week on a regular basis.

Information for patients

*Lifting The Burden* has produced an information leaflet on medication-overuse headache and its treatment. This is currently available in Danish, Dutch, English, French, German, Italian, Portuguese and Spanish.
12. HEADACHE MANAGEMENT IN PRIMARY CARE: WHEN TO REFER

Most primary headaches, and medication-overuse headache, can best be managed in primary care.

**Reasons for specialist referral:**

- diagnostic uncertainty after due enquiry
- diagnosis of cluster headache (most cases are best managed by specialists)
- suspicion of serious secondary headache, or cases where investigation may be necessary to exclude serious pathology (referral may need to be immediate):
  - any headache that is new or unexpected in an individual patient, but especially:
    - newly-occurring thunderclap headache (intense headache with abrupt or “explosive” onset)
    - new headache in a patient older than 50 years
    - new headache in a pre-pubertal child
    - new headache in a patient with a history of cancer, HIV infection or immunodeficiency
  - unusual migraine aura, especially:
    - aura with duration >1 hour
    - aura featuring motor weakness
    - aura without headache in the absence of a prior history of migraine with aura
    - aura first occurring with use of combined oral contraceptives
  - progressively worsening headache over weeks or longer
  - headache associated with postural change indicative of high or low intracranial pressure
  - headache associated with unexplained fever
  - headache associated with unexplained physical signs
- persistent management failure
- comorbid disorders requiring specialist management
• presence of risk factors for coronary heart disease may warrant cardiological referral prior to use of triptans.