

DRUG UPDATE

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TRIPTANS FOR MIGRAINE RELIEF

Triptans are used at the onset and during the established headache phase of a migraine attack and are the preferred treatment in those who fail to respond to conventional analgesics. The majority of the clinical trial data supports the use of sumatriptan, with 50 mg being the recommended initial dosage. As the patent for sumatriptan has now expired and the potential for further price reductions exists, it is a reasonable first-line choice. If a patient fails to respond to initial treatment with sumatriptan, a trial of an alternative triptan or a higher dose of sumatriptan may be required.

What are they?

Triptans are a group of 5HT (serotonin) agonists which act on the 1B/1D receptors. They are licensed for the treatment of migraine and have been shown to be of considerable value in acute attacks.¹ Sumatriptan may also be of use in the treatment of cluster headaches.¹ There are seven agents available in this class of drugs; almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan, which are available as standard tablets (with some preparations available as oral dispersible tablets and nasal sprays).¹ Sumatriptan is also available as a subcutaneous injection.¹ The patent for sumatriptan expired in May 2006.² This is currently the only member of the triptan group to be available as a generic product.

Which triptan should be used?

Sumatriptan was the first triptan to be licensed and its efficacy has been studied in a large number of randomised controlled trials. The recommended oral dose is 50 mg at the onset of a migraine attack.³ This is supported by trial evidence which has shown similar efficacy for the 50 mg and 100 mg doses, when compared with placebo.^{4,5} The number needed to treat (NNT) has been calculated from clinical trials as 4 (i.e. 4 people need to be treated with sumatriptan rather than placebo in order for one to gain headache relief at two hours) for all strengths of sumatriptan.⁴

Sumatriptan has been used as a comparator in a small number of clinical trials. Meta-analyses of these clinical trials have shown very little or no difference in treatment effect between sumatriptan and the licensed doses of the other triptans.^{4,5}

Eletriptan 20 mg, naratriptan 2.5 mg and zolmitriptan 5 mg have been shown to have similar effects on headache and pain relief at two hours, disability and headache recurrence as sumatriptan 100 mg.⁴ The data comparing rizatriptan 10 mg with sumatriptan are conflicting. In one study, pain-free response and disability at two hours were shown to be statistically significantly in favour of rizatriptan 10 mg when compared with sumatriptan 100 mg (odds ratios [OR] = 0.7, 95% confidence intervals [CI] 0.5 to 0.97 and 0.5 to 0.90, respectively).⁴ However when compared with

sumatriptan 50mg no significant differences in treatment effects or adverse event profile were demonstrated.⁴

One parallel-group study (n = 1,172) compared almotriptan 12.5 mg and sumatriptan 50 mg. Sumatriptan showed a significantly better pain-free response at two hours (OR = 1.5, 95% CI 1.1 to 2.0, NNT = 15).⁴ No significant differences were detected in the other measures of efficacy; however almotriptan was associated with a lower incidence of treatment-related adverse events (16% vs. 9%, p = 0.001).⁴ A smaller (n = 221) randomised, placebo-controlled study examined the efficacy of almotriptan in patients unresponsive to treatment with sumatriptan 50 mg. Of these patients, 47.5% went on to achieve pain relief at two hours after treatment with almotriptan 12.5 mg (compared with 23.2% with placebo, p < 0.001).⁶

The majority of data comparing frovatriptan with placebo are available in abstract form alone.⁵ The efficacy of frovatriptan compared with sumatriptan has not been sufficiently studied to draw conclusions.

A recent review of comparative clinical-effectiveness and cost-effectiveness concluded that there is no compelling economic evidence to support the use of one triptan over another. More comparisons among triptans are required to establish overall differences.⁷

How safe are they?

The most common side-effects are: dizziness, nausea and vomiting, weakness/fatigue, drowsiness, gastrointestinal disturbances, altered sensations (pain, heaviness, pressure or tightness of the throat or chest) and palpitations (affecting between 1% and 10% of patients).^{3,8-13} No differences in chest pain or tightness, or central nervous system effects with eletriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan have been suggested in clinical trials.⁷

When should they be used?

The majority of the clinical trial data relates to the use of sumatriptan, with 50 mg being the recommended dosage. As sumatriptan's patent has expired and its price may fall further, it is a reasonable first-line choice.

If a patient fails to respond to initial treatment with sumatriptan, a trial of an alternative triptan or a higher dose of sumatriptan may be required.

During the last 12 months almost 180,000 prescriptions for triptans were dispensed (at a cost of £7.3M) in the former Northern and Yorkshire region. Corresponding data from Greater Manchester show almost 77,000 prescriptions were dispensed at a cost of approximately £3M. Currently the most commonly prescribed triptan is sumatriptan (47% and 42% of items, respectively).

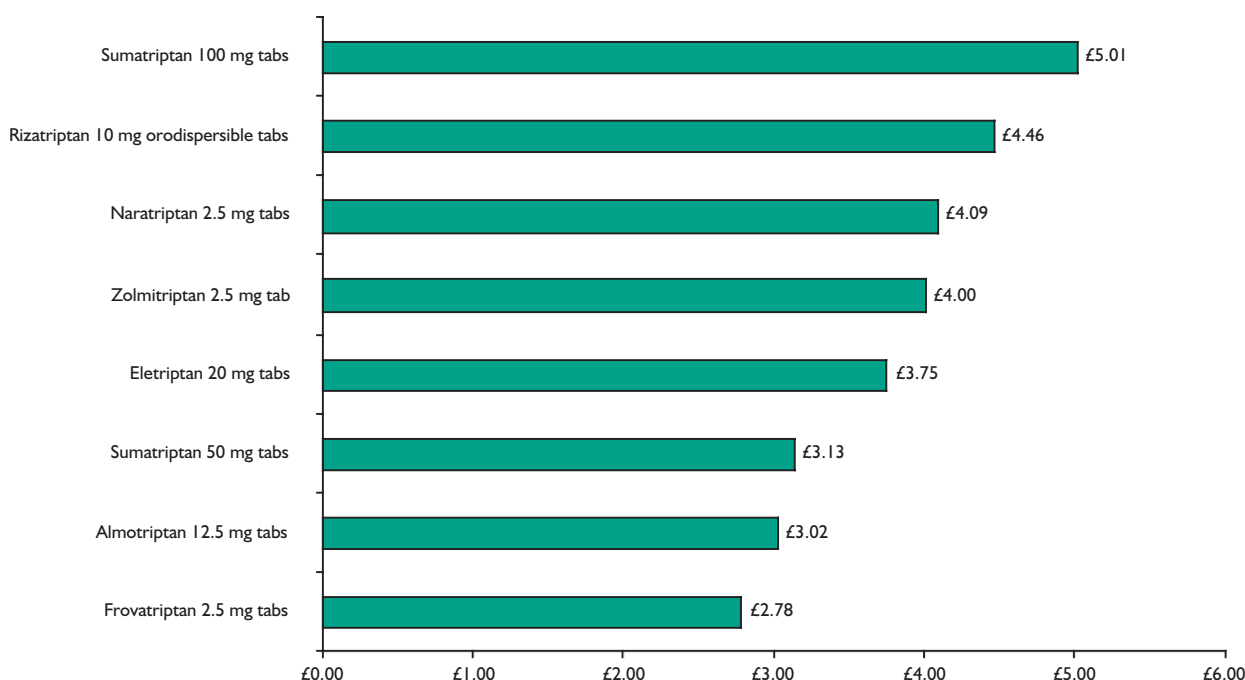
Triptans can be used during the established headache phase of an attack and are the preferred treatment in those who fail to respond to conventional analgesics¹ (e.g. simple analgesics

+/- anti-emetic).¹⁴ They should not be used as preventative therapy.^{3,8-13} A review of migraine treatment should be undertaken and prophylactic treatment offered where:¹⁵

- Acute treatments are being used two days per week on a regular basis or
- More than two attacks per month (that produce disability lasting three days) or
- Less frequent but severe or prolonged attacks or
- Contraindications to, or ineffectiveness of, acute treatments exists.

How much does it cost?

Cost per single treatment dose (Drug Tariff March 2007)



N.B. Doses shown are for general comparison only and do not imply therapeutic equivalence

REFERENCES

1. British Medical Association and Royal Pharmaceutical Society of Great Britain. British National Formulary. No 53, March 2007. www.bnf.org (last accessed 20/03/07).
2. UKMi patents database. www.ukmi.nhs.uk/Med_info/patents/patents_menu.asp (last accessed 20/03/07).
3. GlaxoSmithKlineUK. Summary of Product Characteristics - Imigran tablets 50mg, Imigran tablets 100mg[®]. May 2006. www.medicines.org.uk (last accessed 20/03/07).
4. McCrory DC et al. Oral sumatriptan for acute migraine. Cochrane Database Syst Rev 2003:CD002915. (R)
5. Ferrari MD et al. Oral triptans (serotonin 5-HT_{1B/1D}) agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet 2001;358:1668-75. (MA)
6. Diener HC et al. Almotriptan in migraine patients who respond poorly to oral sumatriptan: A double-blind randomised trial. Headache 2005;45:874-82. (RCT)
7. Canadian Agency for Drugs and Technologies in Health. Triptans for acute migraine: Comparative clinical effectiveness and cost-effectiveness. HTA 2007;76. (R)
8. Pfizer Limited. Summary of Product Characteristics - Relpax 20mg and 40mg[®]. June 2004.
9. A.Menarini Pharmaceuticals UK Ltd. Summary of Product Characteristics - Migard[®]. September 2005.
10. Merck Sharpe and Dohme Limited. Summary of Product Characteristics - Maxalt 5mg, 10mg Tablets, Maxalt Melt 10mg Oral Lyophilisates[®]. February 2004.
11. AstraZeneca UK Limited. Summary of Product Characteristics - Zomig tablets[®]. July 2004.
12. Organon Laboratories Limited. Summary of Product Characteristics - Almogran 12.5mg tablets[®]. September 2005.
13. GlaxoSmithKlineUK. Summary of Product Characteristics - Naramig tablets 2.5mg[®]. June 2006.
14. British Association for the Study of Headache. Guidelines for all doctors in the diagnosis and management of migraine and tension-type headache. 2nd edition. Aug 2004. www.bash.org.uk (last accessed 20/03/07). (G)
15. SCHIN: National Library for Health Clinical Knowledge Summaries - PRODIGY Guidance: Migraine. July 2006. www.cks.library.nhs.uk/migraine (last accessed 29/03/07). (G)

Key: R – review, MA - meta analysis, RCT – randomised controlled trial, G – guideline.

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