A comparison of the cost-effectiveness of almotriptan and sumatriptan in the treatment of acute migraine using a composite efficacy/tolerability end point

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of almotriptan 12.5 mg versus two dosing levels of sumatriptan (50 mg and 100 mg) for the treatment of an acute migraine attack.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised male and female patients experiencing an acute migraine attack. No further inclusion or exclusion criteria were provided.

Setting
The setting of the study was primary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness evidence was derived from the results of a meta-analysis that was published in 2001-2002. Health service resource use and costs were obtained from a study published in 1999. The price year was 2004.

Source of effectiveness data
The effectiveness data were derived from a published meta-analysis of completed studies.

Modelling
An ad hoc model was used to estimate the costs and benefits associated with the use of triptans for the treatment of acute migraine attacks. The time horizon was unclear. The major assumption made in this model was that the efficacy and tolerability associated with each agent assessed were independent parameters.

Outcomes assessed in the review
The outcomes assessed were the efficacy of almotriptan and sumatriptan in the treatment of acute migraine (expressed as sustained pain-free rate) and the rate of associated adverse events.

Study designs and other criteria for inclusion in the review
The effectiveness data were derived from a published meta-analysis of 53 double-blinded, randomised controlled clinical trials of oral triptans (Ferrari et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details). This included data on 719 patients treated with almotriptan and 4,715 patients treated with sumatriptan in placebo-controlled trials. Since the study by Ferrari et al. only provided placebo-corrected adverse event rates, the placebo adverse event rates were derived from the results of another study (Roon et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details) which was based on the same meta-analysis.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not relevant.

Methods used to judge relevance and validity, and for extracting data
Not relevant.

Number of primary studies included
Not relevant. The published meta-analysis which provided the data for the economic study included the results from 53 primary studies.

Methods of combining primary studies
Not relevant.

Investigation of differences between primary studies
Not relevant.

Results of the review
The absolute sustained pain-free rate was 25.9% (95% confidence interval, CI: 23 - 29) for almotriptan 12.5 mg, 19.8% (95% CI: 18 - 22) for sumatriptan 50 mg, and 20.0% (95% CI: 18 - 21) for sumatriptan 100 mg.

The placebo-corrected adverse event rate was 1.8% (95% CI: -2.7 - 6.2) for almotriptan 12.5 mg, 7.8% (95% CI: 2.6 - 13.1) for sumatriptan 50 mg, and 13.2% (95% CI: 8.6 - 17.8) for sumatriptan 100 mg.

The placebo adverse event rate was 12% for almotriptan, and 27% for sumatriptan 50 mg and 100 mg.

Methods used to derive estimates of effectiveness
The placebo adverse event rates were added to the placebo-corrected rates to produce estimated absolute adverse event rates.

Estimates of effectiveness and key assumptions
The calculated absolute adverse event rate was 13.8% for almotriptan 12.5 mg, 34.8% for sumatriptan 50 mg, and 40.2% for sumatriptan 100 mg.

Measure of benefits used in the economic analysis
The measure of benefits used was the sustained pain-free and no adverse events (SNAE) end point rate. This was a
composite "unqualified success" measure, expressing the proportion of patients who achieved sustained freedom from pain without experiencing adverse events. Sustained freedom from pain was defined as pain free at 2 hours after taking medication with no recurrence of moderate or severe headache and no rescue medication 2 to 24 hours postdose. For the base-case analysis, efficacy and tolerability were assumed to be independent, so that SNAE was equal to the sustained pain-free rate multiplied by 1 minus the adverse event rate.

**Direct costs**
The direct costs comprised medical costs only. These included costs associated with health service resource use (physician visits, emergency room attendance, and hospitalisation) and medication costs (almotriptan or sumatriptan). The costs and the quantities were not analysed separately in terms of health service resource use. The health service costs were derived from a study published in 1999 that reported the economic burden of migraine in the USA. For the base-case analysis it was assumed that annual migraine-related costs were apportioned uniformly across attacks; the estimated cost per attack was obtained by dividing the annual health service cost per patient with migraine by the annual attack frequency. Therefore, in the base-case analysis, the total health service costs were assumed to be uninfluenced by the choice of triptan.

The drug costs were derived from a national source that provided prices approximating actual managed care pharmacy prices rather than average wholesale prices. It was assumed that every acute migraine attack was treated with one tablet of either almotriptan or sumatriptan. The costs were adjusted to 2004 prices using an annual inflation rate of 3%. Discounting was not necessary as the costs were estimated per episode of attack.

**Statistical analysis of costs**
The costs were treated deterministically. No statistical analysis of the costs was undertaken.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was undertaken to test the robustness of the results under different sets of assumptions. The different scenarios examined in one-way sensitivity analyses involved:

a relationship between efficacy and tolerability;

various odds ratios (ORs) describing this relationship, varying from 0.1 (strongly negative relationship) to 10 (strongly positive relationship); and

the assignment of costs only to patients not achieving sustained freedom from pain.

In addition, threshold analyses examined the number of tablets per attack required so that the agents under evaluation became equivalently cost-effective. This scenario was explored separately for positive, negative and independent relationships between efficacy and tolerability. Finally, a probabilistic analysis was carried out to assess the probability of almotriptan being the cost-effective option. This analysis utilised a range of values for SNAE, determined by the mean values and CIs for efficacy and adverse event rates for triptans that were taken from the published meta-analysis. Separate analyses were undertaken for different values of OR for the relationship between efficacy and tolerability.

**Estimated benefits used in the economic analysis**
The SNAE rate per acute migraine attack was 22.3% for almotriptan 12.5 mg, 12.9% for sumatriptan 50 mg, and 12.0% for sumatriptan 100 mg. This measure of outcome incorporated both efficacy and adverse event rates associated with each intervention assessed.

**Cost results**
The total cost per acute migraine attack was $18.23 for almotriptan 12.5 mg, $17.14 for sumatriptan 50 mg, and $16.59 for sumatriptan 100 mg.

The health service costs were assumed to be uninfluenced by the choice of triptan. Therefore, any possible differences in costs attributable to the treatment of adverse events were not accounted for in the base-case analysis.

**Synthesis of costs and benefits**
The costs and benefits were combined in the form of cost-effectiveness ratios for each agent separately, and in the form of incremental cost-effectiveness ratios (ICERs) for comparisons between agents.

The cost-effectiveness ratios expressed the cost per attack at which SNAE was achieved. This was $81.75 for almotriptan 12.5 mg, $132.87 for sumatriptan 50 mg, and $138.25 for sumatriptan 100 mg.

The ICERs expressed the incremental cost per attack associated with the use of almotriptan in order to achieve an additional SNAE. The ICERs of almotriptan 12.5 mg versus sumatriptan 50 mg and 100 mg were $11.60 and $15.92, respectively. These ratios were substantially smaller than the cost-effectiveness ratios for both dose levels of sumatriptan. Thus, it was stated that sumatriptan was dominated by the rule of extended dominance.

The results were robust under all scenarios explored in the sensitivity analysis.

The threshold analysis demonstrated that when assuming an OR of 0.1 between efficacy and tolerability, and keeping the number of sumatriptan tablets at one per attack, 1.3 tablets of almotriptan should be used per attack in order for the two agents to be equivalently cost-effective. When assuming an OR of 10 between efficacy and tolerability, 3.6 or 4.3 almotriptan tablets should be used per attack in order for almotriptan to be equally cost-effective with sumatriptan 50 mg and 100 mg, respectively.

The probabilistic analysis showed that the probabilities of almotriptan being more cost-effective than sumatriptan exceeded 99% across the entire range of efficacy-tolerability relationships tested, for both strengths of sumatriptan.

**Authors' conclusions**
Almotriptan 12.5 mg was more cost-effective than sumatriptan 50 mg or 100 mg in the treatment of an acute migraine attack.

**CRD COMMENTARY - Selection of comparators**
It was stated that sumatriptan was selected as the comparator of the analysis because it was the most widely prescribed oral triptan in the USA. Also, it was used as the standard for comparison in the meta-analysis of triptans that served as the source of the effectiveness data for the economic analysis. You should decide whether sumatriptan represents a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The estimate of measure of effectiveness was based on a published meta-analysis of 53 double-blinded, randomised controlled trials of oral triptans. No further details on the methods and conduct of the meta-analysis were provided, although they can be obtained elsewhere (Ferrari et al. 2001). The authors noted that in the meta-analysis there were no differences in the study design or population that could explain the differences in placebo adverse event rates between sumatriptan and almotriptan.
Validity of estimate of measure of benefit
The estimation of benefits was based on the use of a composite measure, which incorporated both efficacy (expressed as sustained pain-free rate) and tolerability (expressed as rate free of adverse events) associated with the agents under assessment. The measure of efficacy used had been described as the ideal measure for assessing response to acute migraine therapy: freedom of adverse events had been stated to be an important outcome to patients. Hence, the measure of benefits used was appropriate for the analysis.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted (US health care payer) were included in the analysis. The costs and the quantities were not reported separately, which hinders the reproducibility of the results. The total annual costs associated with migraine attacks, which were derived from a published study, were evenly apportioned to each migraine attack regardless of the choice of triptan. Therefore, differences in efficacy and adverse event rates between triptans were not considered in the estimation of costs. However, this assumption favoured sumatriptan (because it has a lower efficacy rate and a higher adverse event rate than almotriptan), which proved to be the least cost-effective option. A sensitivity analysis was conducted to test the scenario of apportioning costs only between patients who did not achieve sustained freedom from pain. The drug unit costs used approximated actual managed care pharmacy prices rather than average wholesale prices. Discounting was not necessary, as the costs were estimated per migraine attack, and was not applied. The price year was stated, which increases the generalisability of the results.

Other issues
The authors made appropriate comparisons of their results with those from other studies and found them to be consistent. The issue of generalisability to other settings was not addressed. The authors reported, as a main limitation of the analysis, the key assumption that they made about the relationship between efficacy and tolerability associated with triptans. However, they examined the impact of this assumption in a sensitivity analysis. The results of the study were presented in full. The authors' conclusions reflected the scope of the analysis.

Implications of the study
It can be inferred from the results of the analysis that, in terms of cost-effectiveness, almotriptan should be the preferred option for the treatment of acute migraine attacks. It was suggested that further research on the true nature of the relationship between efficacy and tolerability associated with triptans should be undertaken to inform future analyses on the relative cost-effectiveness of these agents. The authors felt that their findings should influence decision-makers in managed care and those engaged in designing drug formularies, for whom balancing optimal care with value for money is an ongoing challenge.

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Bibliographic details

PubMedID
15228377

Other publications of related interest

Roon KI, Lipton R, Goadsby PJ, Ferrari M. Placebo in triptan trials: efficacy, tolerability and consistency. Cephalalgia


Adelman JU, Belsey J. Meta-analysis of oral triptan therapy for acute migraine: number needed to treat and relative cost to achieve relief within 2 hours. Journal of Managed Care Pharmacy 2003;9:483-90.

Indexing Status
Subject indexing assigned by NLM

MeSH
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