Cost-effectiveness of almotriptan and rizatriptan in the treatment of acute migraine

Williams P, Reeder C E

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
Two drugs from the triptan class of migraine agents were compared for the treatment of acute migraine. The drugs chosen were almotriptan and rizatriptan. The dose of almotriptan was 12.5 mg and that of rizatriptan was 10 mg.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The target population for the model were patients presenting with an acute migraine attack.

Setting
The setting was primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was taken from 2001 and 2002. The costs for health service use were taken from 1999. The price year was 1999 for health service use costs and 2003 for drug acquisition prices.

Source of effectiveness data
The effectiveness data were derived from completed studies.

Modelling
A model was constructed to derive the composite health outcome measure used. A simple decision model, with Monte Carlo simulation to evaluate the effect of uncertainty, was used.

Outcomes assessed in the review
The adverse event (AE) rate and sustained freedom from pain rates were derived from a published meta-analysis. These were supplemented with the placebo AE rate using data from a second meta-analysis.

Study designs and other criteria for inclusion in the review
Two meta-analyses were the main sources of the effectiveness data.
Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
The main source of effectiveness evidence was a meta-analysis of 53 clinical trials of oral triptans used for acute migraine (Ferrari et al., see Other Publications of Related Interest).

Methods of combining primary studies
As one meta-analysis (Ferrari et al.) reported the placebo-subtracted AE, the authors added the placebo AE from a second meta-analysis (Roon et al., see Other Publications of Related Interest) since they judged that both should be considered in a real-world scenario.

Investigation of differences between primary studies
Not stated.

Results of the review
The main source of effectiveness provided data on 700 patients treated with almotriptan and 2,800 patients treated with rizatriptan.

For almotriptan (12.5 mg):
the absolute sustained pain-free rate was 25.9%;
the placebo-subtracted AE rate was 1.8%;
the placebo AE rate was 12.0%; and
the calculated absolute AE rate was 13.8%.

For rizatriptan (10 mg):
the absolute sustained pain-free rate was 25.3%;
the placebo-subtracted AE rate was 13.5%;
the placebo AE rate was 27.0%; and
the calculated absolute AE rate was 40.5%.

Methods used to derive estimates of effectiveness
This analysis was based on published data and authors’ assumptions.
Estimates of effectiveness and key assumptions
The authors made several key assumptions in the base-case scenario. It was assumed that efficacy and tolerability were independent. It was also assumed that a migraine attack was treated with only one tablet, consistent with the source of efficacy and AE data in the meta-analysis (controlled clinical trials).

Measure of benefits used in the economic analysis
The measure of benefits used was sustained freedom from pain and no AEs (SNAEs). This is a composite unqualified success measure, defined as the proportion of patients who achieved sustained freedom from pain with no AEs.

Direct costs
The costs for migraine-related health service use (US dollars per migraineur per year) and mean annual attack frequencies were obtained from a 1999 study of the economic burden of migraine in the USA. A prevalence- and diagnosis-weighted mean (weights calculated from information provided by published data) of these gender-specific costs was used when calculating the mean cost-effectiveness ratios (CERs) (Hu et al., see Other Publications of Related Interest).

In the base-case scenario, the authors assumed that the costs for health service use could be apportioned uniformly across attacks. Therefore, the estimated cost per migraine attack was obtained by dividing the annual per-patient health service use costs for physician visits, emergency department visits and hospitalisation by the reported annual attack frequency in a migraine population. In the base-case, the authors assumed that these costs were uninfluenced by the choice of triptan. It was also assumed that a migraine attack was treated with only one tablet.

The authors therefore estimated the total direct cost per attack by adding the drug-acquisition cost (average wholesale price in 2003 US dollars per tablet) to the estimated cost of health service use per attack (1999 price year). Discounting was not carried out. The quantities and the costs were estimated on the basis of published data and authors’ assumptions.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Several areas were explored in the sensitivity and scenario analyses.

The possible non independence of efficacy and tolerability was explored by evaluating different odds ratios (ORs) depicting their association, ranging from strongly negative (OR=0.1) to strongly positive (OR=10).

The possible different costs of health service use, according to initial response to treatment, were explored by repeating the analyses with the assumption that only patients not achieving sustained freedom from pain would incur these costs.

The number of tablets used per attack was explored by evaluating the impact of changing the number of tablets for positive, negative and independent relationships between efficacy and tolerability.

To assess the impact of uncertainty in the efficacy and tolerability estimates, a Monte Carlo analysis was performed. This used distributional data from the meta-analysis to calculate the CERs.
Finally, the authors assessed the probability that almotriptan was cost-effective in comparison with rizatriptan, by totalling across the 10,000 iterations for different values of the OR for the relationship between efficacy and tolerability.

**Estimated benefits used in the economic analysis**
The SNAE rates in the base-case were 22.3% for almotriptan (12.5 mg) and 15.1% for rizatriptan (10 mg).

**Cost results**
For health service use costs, the authors reported a gender-weighted mean, year 1999, of US$1.88 for both agents. Also, for drug acquisition cost per tablet, they reported an average year 2003 wholesale price of $18.44 for almotriptan 12.5 mg and $17.94 for rizatriptan 10 mg. Therefore, the total direct costs per attack reported were $20.32 for almotriptan 12.5 mg and $19.82 for rizatriptan 10 mg.

**Synthesis of costs and benefits**
The mean CER was $91.12 per SNAE for almotriptan 12.5 mg and $131.26 per SNAE for rizatriptan 10 mg.

The incremental CER per additional SNAE was $6.94 for almotriptan. As this incremental CER would be substantially smaller than the mean CER for rizatriptan, according to the principle of extended dominance, almotriptan was economically superior to rizatriptan.

The results of the sensitivity analyses were as follows.

The economic superiority of almotriptan (12.5 mg) over rizatriptan (10 mg) was robust, regardless of the direction or strength of the relationship between efficacy and tolerability.

In terms of health service use costs, the assumption that responders were unlikely to incur emergency department visits and hospitalisation costs did not significantly alter the results (the impact on the CERs was less than $1.00 per SNAE).

In terms of tablets per attack, in the base-case, almotriptan (12.5 mg) remained cost-effective up to the point at which 48% more tablets of almotriptan (12.5 mg) than rizatriptan (10 mg) were used to treat an attack. This margin fell to 8% if the efficacy-tolerability relationship was assumed to be strongly negative (OR=0.1). The margin rose to 228% if the relationship was assumed to be strongly positive (OR=10).

The Monte Carlo simulation showed that the confidence level of the economic superiority of almotriptan exceeded the conventional 95%, except when the relationship between efficacy and AEs was strongly negative.

**Authors’ conclusions**
In the context of the limitations of these analyses, almotriptan 12.5 mg was economically superior to rizatriptan 10 mg for the treatment of an acute migraine attack. This finding was robust across a range of sensitivity analyses.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator was explicitly justified. The justification given for choosing these two agents was based on the results of the TRIPSTAR project. In a dominance hierarchy analysis of the triptan meta-analysis, only two of the 7 triptans (i.e. almotriptan 12.5 mg and rizatriptan 10 mg) were not dominated by any other triptan. You should assess whether these drugs are relevant in your own setting, or whether other comparators from other drug classes could also be relevant.

**Validity of estimate of measure of effectiveness**
The authors used data from published sources only. The main source of effectiveness evidence was a meta-analysis of 53 clinical trials of oral triptans used for acute migraine (Ferrari et al., see Other Publications of Related Interest). The
placebo AE rates were taken from another study (Roon et al., see Other Publications of Related Interest) in order to correct the rates reported in the first study. According to the authors, this meta-analysis was the most comprehensive synthesis of current knowledge in this area. In addition, analyses of this kind are at the top of the hierarchy of evidence. Despite this opinion, it was unclear whether a systematic review of the literature was undertaken. The effectiveness estimates were combined and were derived credibly from the primary studies and the authors' own assumptions. The authors reported the methods used to derive the estimates of effectiveness (ORs) and justified their choice of assumptions with reference to the medical literature. These estimates were investigated in sensitivity analyses using ranges from the literature.

**Validity of estimate of measure of benefit**
The measure of health benefit (SNAE) was proxied directly by a single effectiveness estimate. The choice of estimate was justified in terms of a recommendation from the literature, as it incorporated the features that patients want from treatment. The measure chosen was context specific and can only be compared with other migraine studies (and not with other economic evaluations).

**Validity of estimate of costs**
The authors reported that the costs were estimated from the perspective of a US health care payer. Therefore, the indirect costs were, appropriately, not included. Although some costs could have been omitted from the analysis, these were unlikely to have affected the authors' conclusions since they were common to both therapies.

To estimate the total direct costs, the authors considered the costs of both health service use and drug acquisition. These were taken from different sources and years, and no adjustment was reported. The resource use quantities and prices were taken from published sources. Sensitivity analyses of the quantities were conducted.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability to other settings was not addressed. The authors reported three limitations to this type of cost-effectiveness study and described how they attempted to minimise these limitations. The limitations were those imposed by the data, those imposed by the assumptions, and those inherent in the analytic methods.

The authors reported that they made no attempt to account for possible differences in health service use costs attributable to the treatment of AEs. Such an adjustment (if made) would further favour almotriptan, given its lower AE liability.

**Implications of the study**
The authors recommended that the results of this study, which showed almotriptan to be more cost-effective than rizatriptan, should be considered by physicians treating acute migraine and by managed care organisations obliged to make the most efficient use of their drug budgets. For example, $10,000 spent on the treatment of migraine with a triptan would return 110 successes (i.e. attacks for which SNAE is achieved after treatment) with almotriptan 12.5 mg, compared with 76 successes with rizatriptan 10 mg. Although this study assumed independence between efficacy and tolerability, almotriptan remained superior across the wide range tested.

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**Bibliographic details**
Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
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