Treatment of migraine in Canada with naratriptan: a cost-effectiveness analysis
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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 oral naratriptan (2.5 mg) in the treatment of migraine. A strategy of treating mild migraine attacks with the Canadian customary therapy and moderate to severe attacks with naratriptan was compared with the Canadian migraineurs’ customary therapies alone (not including triptans).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised Canadian migraine sufferers. Patients who had used a 5-HT1 agonist in the 3 months prior to the study or who intended to use a 5-HT1 agonist as customary therapy during the trial, were excluded from the study. Also excluded were those who were using prophylactic medications containing ergotamine, derivatives of ergotamine, or methysergide for the treatment of migraine.

Setting
The setting was primary care. The economic study was carried out in Canada.

Dates to which data relate
The costs related to 1998. The dates for the effectiveness and resource use evidence were not reported. Studies published between 1995 and 1997 provided data on resource use, effectiveness and cost parameters.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Model-based costing was carried out retrospectively on a simulated population. The medication use for customary therapy was derived from the Canadian participants under this treatment in the trial, while the use of naratriptan was based on all participants.

Study sample
Approximately 1,000 patients with migraine were reported to have participated. There were no details on the use of power calculations, sample selection methods, or the number of patients in each group.
**Study design**
A multinational, open-label, parallel-group study provided the effectiveness data. The duration of the study was 12 weeks. The loss to follow-up was not reported.

**Analysis of effectiveness**
No details relating to the comparability of the groups or adjustment for confounding factors were provided. The authors did not state whether the analysis was conducted on an intention to treat basis or on treatment completers only. The outcomes estimated were:

the distributions of the annual frequency and the severity of migraine attacks;

the duration of the symptoms per attack;

the time missed from paid work activities;

the time lost from paid work activities due to reduced effectiveness; and

the medication taken to treat symptoms.

The annual frequency of migraine attacks was derived using log-normal probability distributions for men and women. It was fitted to the patients' reported history of attacks at screening. The severity of the attacks was derived from the distribution observed during the trial in men and women, for the naratriptan and customary therapy groups. The probability distributions for the duration of symptoms per attack were calculated according to gender, treatment, and severity of attack. Time-lost distributions were calculated according to treatment and severity. Distributions for non-work time lost were estimated separately for employed and unemployed migraineurs. The number of doses taken per attack, and the type of medications used for each severity level, were also estimated.

**Effectiveness results**
Men had a mean annual attack rate of 37.9 (standard deviation 23.3), while women had an attack rate of 34.8 (standard deviation 18.8).

Men rated more migraines as mild (25.3% in the naratriptan group and 25.6% in the customary therapy group) than did women (15.2% in the naratriptan group and 15.3% in the customary therapy group).

Women rated more migraines as severe (33.7% in the naratriptan group and 34.3% in the customary therapy group) than did men (24.0% in the naratriptan group and 27.3% in the customary therapy group).

Compared with customary therapy (not including triptans), naratriptan led to an annual reduction in symptom duration of 225 hours per patient (37% reduction).

The time lost due to migraine decreased from 117.5 hours with customary therapy to 75 hours with naratriptan.

The other outcomes were not reported numerically.

**Clinical conclusions**
Naratriptan led to a 37% reduction in the annual duration of migraine symptoms and a reduction in the time lost due to migraine.

**Modelling**
A Monte Carlo model was used to simulate a migraineur population with a given set of characteristics (age, gender and employment status). It also simulated their migraine experience over the course of one year, including the severity and duration of the migraine attacks, the days on which the attacks happen, and other related health care used. The model...
processed 10,000 simulated Canadian migraineurs treated with customary therapy and with naratriptan therapy to evaluate the benefits and the costs.

Measure of benefits used in the economic analysis
The measures of benefits used in the economic analysis were the annual duration of migraine symptoms and the activity time lost.

Direct costs
The costs of medications, migraine-related physician visits, emergency department visits, and hospitalisations were analysed. For customary therapy, only those medications used by Canadian participants were included in the analysis. The drug costs were as listed in the Canadian provincial drug formularies. The health care costs were derived using data from the Ontario Case Costing Project (1994 to 1996), Statistics Canada, a report by the Canadian Co-ordinating Office for Health Technology Assessment, and a published profile of emergency department costs by diagnosis. Discounting was irrelevant as the study was carried out over a period of one year. The cost data from before 1998 were adjusted to 1998 using Canadian consumer or health care price indexes.

Statistical analysis of costs
Not conducted.

Indirect Costs
The indirect costs included the cost of time lost from paid work, based on average hourly wages (Statistics Canada earnings information). The wages for part-time employees were assumed to be 20% lower than the wages for full-time employees. The cost of time lost from unpaid work activities was derived from Statistics Canada estimates. No cost for the leisure time lost was incorporated. Discounting was irrelevant as the study was carried out over a period of one year.

Currency
Canadian dollars (Can$).

Sensitivity analysis
Sensitivity analyses were conducted to investigate the following:

the costs of paid, unpaid and leisure time lost;

the cost of naratriptan;

non-prescription medical costs; and

the effectiveness of naratriptan in reducing the time lost.

Analyses were also performed in which only severe migraine attacks were treated with naratriptan, and in which attacks of all severities were treated with naratriptan.

Estimated benefits used in the economic analysis
Naratriptan use led to a 37% reduction in the annual duration of symptoms. This corresponded to 225 hours per patient (from 608.4 hours with customary therapy to 383 hours with naratriptan).

The annual time lost from work was 51.4 hours with customary therapy and 32.8 hours with naratriptan. The annual time lost from unpaid work was 19.9 hours with customary therapy and 12.6 hours with naratriptan. The annual leisure time lost was 46.2 hours with customary therapy and 29.6 hours with naratriptan. Thus, the overall time lost due to
migraine was 117.5 hours with customary therapy and 75 hours with naratriptan.

Cost results
The annual nonpharmaceutical medical costs were Can$90 per patient with naratriptan and Can$223 per patient with customary therapy.

The annual drug costs were Can$489 with naratriptan and Can$75 with customary therapy.

The annual indirect costs were Can$689 with naratriptan and Can$1,080 with customary therapy.

The difference in the indirect costs (Can$391) was due to the time lost dropping from 117.5 hours/year to 75 hours/year.

From the societal perspective, the overall saving was Can$109 per patient per year.

The results were highly sensitive to the cost and effectiveness of naratriptan. When the cost of naratriptan was changed from Can$3 to Can$23, the net costs varied from savings of Can$472 to additional costs of Can$259 per annum. If the time lost with naratriptan was 50% lower, the net savings were Can$467. If the time lost with naratriptan was 50% higher, naratriptan resulted in an additional net cost of Can$236 per person per year. If only the severe migraines were treated with naratriptan, the cost-savings per person became Can$153, whereas if all migraines were treated with naratriptan, the cost-savings were Can$74. If the missed nonwork time was excluded, the cost-savings were Can$78.

Synthesis of costs and benefits
From the health service perspective (only the direct costs were considered), the cost-effectiveness of naratriptan in mild and severe migraine attacks was Can$1.25 per hour of migraine symptoms avoided, or Can$6.62 per avoided hour of total activity time lost.

From the societal perspective (when the indirect costs were also considered), the naratriptan was a dominant strategy as it reduced the time loss due to migraine and resulted in cost-savings.

The results were sensitive to the cost and effectiveness of naratriptan, and the cost of paid work. If only severe migraines were treated with naratriptan, the cost-effectiveness improved.

Authors' conclusions
The use of naratriptan in the treatment of migraine is an economically attractive option. It leads to savings in the overall costs due to a reduction in the duration of symptoms.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparator on the grounds that it was the usual practice in Canada. As the comparator was generally specified from a single unpublished trial, it is unclear whether the mix of services included under the 'customary therapy' strategy was representative of the Canadian practice. The authors acknowledged that they did not perform a head-to-head comparison of naratriptan with specific migraine medications.

Validity of estimate of measure of effectiveness
The measure of effectiveness was derived from a single unpublished open-label parallel-group study. It is unclear whether the study sample was representative of the study population. The groups were treated as comparable, but their comparability was not discussed. The validity of the effectiveness measures is unclear, as the study was non-randomised and non-blinded. The dates during which the trial was performed were not reported.

Validity of estimate of measure of benefit
The estimation of the benefit was modelled. The instrument used to derive a measure of health benefit, a Monte Carlo model of individual patient's experiences, seems to have been appropriate given the details provided.

**Validity of estimate of costs**
The costs were analysed from the societal perspective. All relevant cost categories appear to have been included in the analysis. The costs and the quantities were reported separately. Sensitivity analyses of the major unit costs, effectiveness parameters and modelling assumptions were performed. These improved the internal and external validity of the results.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. The study was designed to be generalisable to the Canadian population. The authors did not present their results selectively. However, some important details of the design and analysis of the effectiveness data were not reported.

**Implications of the study**
The authors conclude that, compared with the patients’ customary therapies, naratriptan reduces symptom duration, time lost, and the economic consequences of migraine. In addition, the tolerability and efficacy profile of naratriptan indicate that it may represent an important treatment option for patients with poor tolerability or inadequate relief with other migraine medications.

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