Economic evaluation of famciclovir in reducing the duration of postherpetic neuralgia

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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
Famciclovir therapy for reducing the duration of post-herpetic neuralgia (PHN).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Immunocompetent adults with uncomplicated herpes zoster, diagnosed within 72 hours of onset of rash.

Setting
Primary care centres in the US, Canada and Australia.

Dates to which data relate
Costs estimates were based on data ranging from 1992 to 1996. Effectiveness data were based on a single randomized, controlled trial published in 1995, and an unpublished population database from the UK, 1995.

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

Link between effectiveness and cost data
Costing was not undertaken on the same patient sample as in the study, but was based on a model. Costing of PHN was based on estimates of resource use (physician visits, medications and miscellaneous drug therapy) by a consulting panel of 52 physicians, each of whom treated at least two cases of herpes zoster per month.

Study sample
The study sample comprised 419 immunocompetent adults with clinically diagnosed uncomplicated acute herpes zoster of less than 72 hours duration. Patients were obtained from centres in the US, Canada and Australia. How they were identified was not specified in the report. Sample size calculations were based on an estimated hazard ratio, and provided 80 per cent power to detect a significant difference from placebo. Subjects were randomised to famciclovir 500 mg three times daily for seven days (138 patients), famciclovir 750 mg three times daily for seven days (135 patients) or placebo (146 patients).
Study design
The study was a randomised, double blind, placebo-controlled, multicentre trial. 36 centres were used. The method of patient randomisation was not specified in the report. Patients were followed up for five months after their lesions had healed. Almost 90 percent of patients enrolled in the study were followed for this period.

Analysis of effectiveness
The analysis was based on an intention to treat perspective. The primary outcome measure for the cost-effectiveness analysis was the duration of PHN, defined as the time to resolution of pain after the lesions had healed. Other clinical assessments included duration of viral shedding, time to resolution of lesions and severity of pain, although these were not used as outcome measures in the cost-effectiveness analysis.

Effectiveness results
PHN resolved more quickly in patients who had received famciclovir 500 or 750 mg three times daily for seven days rather than placebo (p = 0.02 and 0.005, respectively). The difference became more significant when limiting the analysis to those over 50 years of age (p = 0.0044 and 0.0030, respectively). The frequency of adverse effects among those treated with famciclovir did not differ significantly from that for placebo.

Clinical conclusions
The use of famciclovir at a dose of 500 or 750 mg three times daily for seven days with uncomplicated acute herpes zoster of less than 72 hours duration significantly reduces the duration of PHN when compared to placebo.

Modelling
A decision-analytic model of the treatment of herpes zoster and PHN was used to compare the cost of PHN between patients treated with oral famciclovir 500 mg three times daily for seven days and patients not receiving any antiviral therapy. The model estimated costs over an 18 month period after the onset of PHN.

Measure of benefits used in the economic analysis
The outcome measure used in this study was the duration of PHN.

Direct costs
Costs were estimated from the perspective of the health care provider under capitated reimbursement. The cost of a course of famciclovir was estimated as the sum of its wholesale acquisition cost (1996, SmithKline Beecham) and a pharmacy dispensing fee of $5 (based on a study published in 1992). To estimate the cost of treating PHN, patients continuing to have pain were assumed to incur monthly costs of physician visits, medications (analgesics, antidepressants, anticonvulsants, corticosteroids and topical agents) and miscellaneous nondrug therapy (pain clinics, nerve blocks, transcutaneous electrical nerve stimulation and physical therapy). Estimates of the frequency of use of the above mentioned items were made by a panel of 52 physicians, each of whom treated at least two cases of herpes zoster per month. Estimation of the duration of PHN was derived from an unpublished population database from the UK (1995). To assign costs of prescriptions to treat PHN, a representative drug was selected from each class and its cost estimated using wholesale acquisition cost plus dispensing fee (Redbook, 1995). Medicare fee schedules (HCFA, 1994) were used to assign costs to visits and therapeutic procedures. Quantities and unit costs were reported separately in the report. The dates to which prices relate included a range of 1992 to 1996 US dollars. Costs were not discounted because of the short time horizon of the analysis (18 months). Costs of adverse effects were not considered for famciclovir because the incidence did not differ from placebo. Costs associated with adverse effects of treating PHN were not considered.

Statistical analysis of costs
Data were presented in a stochastic way, in that averages were reported. No statistical analysis was carried out.
Currency
US dollars ($).

Sensitivity analysis
Sensitivity analysis was conducted for key clinical and economic variables including the frequency of PHN, the effect of famciclovir on the rate of remission of PHN, the duration of follow-up, the monthly cost of physician visits, prescription medications, invasive treatments and the total monthly cost of treating PHN. Most values were varied between the range of 50% and 150% of estimated values. The effect of discounting costs at a rate of 5% per annum was also tested. Although not stated specifically, it appears that a one-way simple analysis method was used.

Estimated benefits used in the economic analysis
According to the model, among those patients who did develop PHN (which included 44% of patients treated with famciclovir 500 mg and 38% of those who received placebo), the use of famciclovir to treat acute herpes zoster was estimated to reduce the duration of PHN by a mean of 1.8 months. When including all patients treated, famciclovir reduced the duration of PHN by an average of 0.5 month per patient.

Cost results
The costs of treating PHN were $294 for famciclovir treated patients, and $379 for placebo treated patient ($85 lower per famciclovir recipient). When adding the cost of famciclovir the net cost of treating PHN was estimated to be $23 per patient. Costs in patients over 50 were $414 in the famciclovir group and $569 in the placebo group ($155 savings in the famciclovir group). Including the cost of famciclovir, the estimated net savings was $47.

Synthesis of costs and benefits
A single course of famciclovir therapy, the net cost of which was estimated to be $23 per patient, reduced the duration of PHN by 0.5 month per patient.

Authors’ conclusions
A model for the use of famciclovir to treat acute herpes zoster showed that treatment reduced the expected duration of PHN and that the cost of such therapy was largely offset by savings in the cost of treating this complication. In the model, these benefits were greatest for older patients, among whom the use of famciclovir may reduce overall health care costs.

CRD COMMENTARY - Selection of comparators
The authors justify the selection of placebo as a comparator by stating that the clinical value of the other two drugs was "unsettled". However, acyclovir and valacyclovir are viable options available to prescribers, and data are available on their respective effects on PHN.

Validity of estimate of measure of benefit
Since PHN is a potential persisting and disabling outcome of herpes zoster infection, which can entail substantial economic cost, duration of PHN is an appropriate measure of benefit for the economic analysis. The existence of PHN was assessed by simply self-reporting the presence or absence of pain, which is appropriate since it is the perception of pain which would motivate resource use.

Validity of estimate of costs
Harder data to support the use of medicinal and other therapies as an alternative to famciclovir would not be necessary in this case as the sensitivity analysis showed that the results of the study changed little with variations in particular
elements of cost. As determined in the sensitivity analysis, the quantitative significance of not discounting costs incurred beyond 12 months was minimal. The method of choosing drugs used in the treatment of PHN was arbitrary. The incidence and cost of adverse effects of these drugs could vary considerably depending on the drug(s) chosen.

Other issues
In general this was a well conducted study. Costing based on resource use and unit cost data derived from the trial would have been preferable to a modelling study based on physician estimates of resource utilisation. However, such a study was not possible in this case since the utilisation and cost of health care services related to PHN were not measured directly in the trial. The incidence of PHN for a period of one year beyond the conclusion of trial was estimated from a data bank of computerised medical records from general practices in the UK, a country not involved in the famciclovir study. The significance of this in terms of the cost estimates is unknown.

Implications of the study
The use of oral famciclovir at a dose of 500 mg three times daily in immunocompetent patients 50 years or older with acute herpes zoster of less than 72 hours duration is likely to lead to net savings in health care expenditure. There is no net cost savings in PHN costs in a similar group of patients aged less than 50 years.

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