Cost-effectiveness of Liple (LipoPGE1) for arteriosclerosis obliterans patients in Japan: an economic evaluation using the EQ-5D instrument
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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 study examined the use of conventional treatment plus alprostadil (LipoPGE1) compared with conventional treatment alone for the treatment of arteriosclerosis obliterans (ASO) patients with pain at rest or ulcers. Alprostadil was administered in a dose of 5 to 10 microg/day, either intravenous injection or drip infusion. The conventional treatment was not described.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised ASO outpatients who experienced pain at rest or had ulcers of the extremities. Patients were excluded if they were hospitalised during the study or if they underwent vascular reconstructive surgery.

Setting
The setting was outpatient care. The economic study was carried out in Japan.

Dates to which data relate
The effectiveness and resource use data related to the period May 1999 to October 2001. The price year was not reported.

Link between effectiveness and cost data
The resource use data were obtained from the same patient sample as that used in the effectiveness study.

Study sample
The authors did not report any power calculations. A total of 2,137 ASO patient case report forms were identified. Of these, 1,374 patients were excluded because of missing data (719), hospitalisation during the study (269), or because they underwent vascular reconstructive surgery (386). The final study sample therefore contained 763 patients with complete data.

Study design
The study was an unblinded before-and-after, within-group comparison. A wash-out period was not relevant.
Analysis of effectiveness
The analysis of effectiveness was based on patients with complete data only. The primary health outcome was the HRQoL, as measured by the EQ-5D.

Effectiveness results
The utility value recorded 2 months after initiation of LipoPGE1 was 0.672 (standard deviation, SD=0.198) compared with 0.616 (SD=0.189) before treatment. The difference was statistically significant, (p<0.05).

Clinical conclusions
The authors concluded that HRQoL improves when LipoPGE1 is added to conventional treatment for ASO patients with pain at rest or ulcers in the extremities.

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). Patients were asked to fill out the EQ-5D, which was then valued using general population preferences from Japan. The utility values were recorded by self-administered questionnaire prior to treatment with LipoPGE1 and 2 months after treatment initiation. To calculate the QALYs, the authors assumed that the duration of drug efficacy after treatment with LipoPGE1 was 0.25 years, 0.5 years or 1 year.

Direct costs
The study included the direct costs of LipoPGE1 only, thus the authors assumed that all other costs were equal. The source of the unit cost data and the price year were not reported. The authors reported the total incremental cost.

Statistical analysis of costs
The cost data were analysed deterministically.

Indirect Costs
Productivity costs were not included.

Currency
US dollar ($). The exchange rate was 110 yen = $1. The year to which the conversion rate related was not reported.

Sensitivity analysis
The authors conducted a one-way sensitivity analysis around the duration of drug efficacy post-treatment. They referred to published studies to support the range tested.

Estimated benefits used in the economic analysis
The authors did not report the incremental QALY gains separately.

Cost results
The total incremental cost of treatment with LipoPGE1 compared with conventional therapy was $1,059. Discounting was not relevant as the costs were incurred over a 2-month time horizon. The authors did not include the costs of adverse events or knock-on costs in the analysis.
Synthesis of costs and benefits
The costs and benefits were synthesised to calculate the cost per QALY gained by adding LipoPGE1 to conventional treatment.

The cost per QALY gained was $18,807 if drug efficacy was assumed to persist for 1 year following the 2-month treatment period, rising to $37,614 if it was assumed to persist for 0.5 years following treatment, and to $75,227 if it persisted for 0.25 years.

Authors' conclusions
The addition of LipoPGE1 to conventional treatment for arteriosclerosis obliterans (ASO) is cost-effective.

CRD COMMENTARY - Selection of comparators
Treatment of ASO with LipoPGE1 was selected to represent current practice in the study setting. It was unclear what was meant by conventional therapy. You must consider whether treatment of ASO in Japan is representative of current practice in your own setting.

Validity of estimate of measure of effectiveness
The estimate of effectiveness was based on a within-group comparison. The authors did not provide a justification for the study design, which was not the most appropriate for the comparison made. The study design means that it is not clear that the change in utility can be attributed to the intervention, so the authors’ conclusions are not fully supported. The authors acknowledged that the large number of patients excluded from the analysis might have introduced some bias into the study results. The authors did not report any power calculations. Overall, given the limitations associated with the study design, the internal validity of the study is likely to be quite low.

Validity of estimate of measure of benefit
The measure of health benefits was calculated on the basis of authors’ assumptions about the duration of drug efficacy post-treatment. The authors stated that the study results were highly sensitive to this assumption.

Validity of estimate of costs
The authors did not specify the study perspective. The cost analysis was based on the additional cost of LipoPGE1 alone, without consideration of other costs such as treatment for adverse effects. This omission may well have affected the authors’ conclusions, and the cost analysis may be regarded as overly simplistic. The price year and the source of the unit costs were not reported, which may limit the generalisability of the study results. As every patient received 2 months of treatment there should have been no variation in the cost of treatment at the patient level.

Other issues
The authors compared their findings with the cost-effectiveness criteria proposed by the National Cholesterol Education Program Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. They did not compare their findings with the published results from other studies in the same area, and the issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively, however, their conclusions cannot be fully supported by the study design.

Implications of the study
The authors recommend that a clinical study be conducted to determine the duration of drug efficacy post-treatment.

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Adolescent; Adult; Aged; Aged, 80 and over; Alprostadil /economics /therapeutic use; Arteriosclerosis Obliterans /drug therapy /economics; Cost-Benefit Analysis; Female; Follow-Up Studies; Humans; Male; Middle Aged; Product Surveillance, Postmarketing /economics; Quality of Life; Retrospective Studies; Treatment Outcome; Vasodilator Agents /economics /therapeutic use

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