Economic impact of different preparations of leuprolide acetate in the management of advanced prostate cancer

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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 considered three different depot formulations (7.5, 22.5 and 45 mg) of leuprolide acetate requiring different dosage intervals (1-, 3- and 6-monthly) in the treatment of advanced prostate cancer. Leuprolide acetate is the most common luteinising hormone-releasing hormone agonist (LHRHa) for hormonal castration in palliative management of prostate cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised 348 patients with localised prostate cancer who were enrolled in three trials. Of these, 332 completed the trials. No significant difference was reported in the baseline and demographic data of the patients.

Setting
The setting was secondary care. The economic analysis was carried out in Germany.

Dates to which data relate
The baseline effectiveness data used to populate the model came from studies published between 2002 and 2006. The price year and the dates to which the resource data referred were not explicitly reported.

Source of effectiveness data
The clinical parameters associated with the model included the proportion of patients who achieved a castration level characterised by testosterone suppression of 20/ng dL, and the proportion of patients with and levels of severity of treatment-related adverse events (mainly hot flushes).

Modelling
A decision tree with a time horizon of 12 months was used to model disease progression. The model was evaluated for twelve different clinical pathways. Model parameters, base-case and ranges were reported in full. The model was based on several assumptions, which were too numerous to be reported in detail here. The reader is therefore referred to the original paper for further details of these assumptions.

Sources searched to identify primary studies
The effectiveness data were derived from three open-label multi-centre trials involving each of the doses. The source of the resource use data was unclear.

**Methods used to judge relevance and validity, and for extracting data**
No details of the methods used to identify or select the estimates included were reported. The authors reported that clinical outcomes from two trials conducted over 6 months were extrapolated to 1 year.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used in the economic analysis as all three preparations had similar clinical outcomes. In effect, a cost-minimisation analysis was carried out.

**Direct costs**
The study reported the direct costs to the national health system. These were doses administered for the three leuprolide acetate preparations, the treatment of adverse events (mainly hot flushes), and hospital or outpatients visits for the purpose of receiving medication. Resource use and unit costs were reported separately. The sources of the cost data were not explicitly stated, but most of the resource use data were based on authors' assumptions. The unit drug costs came from Astellas Pharma Ltd. The costs were reported as the average cost per patient. Discounting was not performed, which was appropriate given the short time period of the cost estimation. The price year was not reported.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
In line with the perspective adopted, no productivity losses were considered.

**Currency**
Euros (EUR).

**Sensitivity analysis**
The authors investigated uncertainty related to variability in the data. One-way sensitivity analyses were performed to investigate the effects of changes in the clinical and cost estimates used in the model. The parameters in these analyses included the proportion of patients receiving 1- or 3-monthly preparations who had severe adverse drug reactions (ADR), the proportion of patients receiving 6-monthly preparations who had severe ADR, the proportion of patients treated in hospital, the number of treatments per year for patients receiving the 6-monthly preparation, and the unit cost of hospital visits.

**Estimated benefits used in the economic analysis**
Not relevant given the cost-minimisation analysis conducted.

**Cost results**
The mean annual treatment costs using the three formulations were:

- EUR 1,567 (standard deviation, SD=205) for the 6-monthly preparation,
- EUR 1,777 (SD=195) for the 3-monthly preparation, and
EUR 2,839 (SD=233) for the 1-monthly preparation.

Thus, the mean annual costs using the 3-month and 1-month preparations were 13% and 81% higher, respectively, than the cost of treatment with the 6-monthly preparation.

Sensitivity analyses demonstrated that the results were robust to all variables tested, except the annual number of treatments per year and the increase in unit cost applied to the 6-monthly preparation.

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant given that a cost-minimisation analysis was carried out.

**Authors' conclusions**
"Despite an increase in the unit cost, the use of the 6-monthly formulation of leuprolide acetate compared with the shorter duration formulations provided the lowest-cost treatment option, the cost-driver being the reduction in the frequency of treatments required."

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear as they represented standard practice in Germany for the treatment of advanced prostate cancer. You should decide whether this applies to your setting.

**Validity of estimate of measure of effectiveness**
The authors used data from three published clinical trials. No systematic search for data was reported. The authors did not report any search methods or inclusion criteria. The details of the clinical trials were sparsely reported as the focus of the paper was the modelling. In addition, the impact of differences between the identified studies was not taken into account when estimating effectiveness. Some estimates of effectiveness were based on authors’ assumptions; however, the authors did not provide any justification for their choice of assumptions. Sensitivity analyses were conducted in order to improve the internal validity of the study.

**Validity of estimate of measure of benefit**
No summary benefit measure was used because of the cost-minimisation design of the analysis. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
The analysis of the costs was consistent with the perspective adopted in the study. The price year and the source of the data were not explicitly stated. Resource consumption reflected the actual pattern of treatment in Germany. Moreover, the cost estimates are likely to be specific to this country although this may, to some degree, have been addressed by the sensitivity analysis. Since the costs were incurred over a short time, discounting was not relevant and, appropriately, was not performed.

**Other issues**
The authors compared their findings with those from previous studies. They stated that this piece of research accorded with the previous trend of 6-monthly leuprolide acetate being a lower-cost treatment option compared with other LHRHα preparations such as buserelin acetate and goserelin acetate. The authors also acknowledged that the 1-year time horizon of this study implies that the long-term clinical benefits, in terms of survival, could not be captured, and nor could secondary aspects of clinical practice such as additional diagnostic tests and additional visits to the hospital or general practitioner. The results of the study do not appear to have been presented selectively and the conclusions appear to be an adequate reflection of the scope of the analysis.

**Implications of the study**
The study results support the switch to the 6-monthly preparation. Switching from the 3-monthly to 6-monthly preparation would save the German authorities EUR 9.1 million a year. The calculated savings would increase to EUR 55.6 million per year if all patients were previously receiving the 1-monthly preparation. The authors also suggested that
countries with health systems such as the Netherlands and the UK would benefit from significant cost-savings as a result of switching from the 3- to 6-monthly preparation of leuprolide acetate in the treatment of prostate cancer patients.

Source of funding
None stated.

Bibliographic details

Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


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