Economic impact of tibolone compared with continuous-combined hormone replacement therapy in the management of climacteric symptoms in postmenopausal women

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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 assessed a 3-year treatment course of tibolone, a synthetic steroid that has estrogenic, progestogenic and androgenic properties, in the management of postmenopausal women with climacteric symptoms. Tibolone was taken daily at a dose of 2.5 mg and was taken orally. The treatment was compared with continuous combined hormone replacement therapy, which comprised conjugated equine estrogens (CEE) and medroxyprogesterone acetate (MPA) at daily doses of 0.625 mg and 1.5 mg, respectively.

Type of intervention
Palliative care.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of postmenopausal women, over 50 years old, who were suffering from climacteric symptoms.

Setting
The setting was not described, but it was probably outpatient care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data used to populate the model came from studies published between 1998 and 2004. The dates for the resource use data were not reported. The price year was not reported.

Source of effectiveness data
The clinical data used in the model included:

- the transition probabilities for the different states;
- the cumulative rates of persistence with estrogen replacement therapy, CEE/MPA and tibolone;
- the cumulative rates of amenorrhoea with CEE/MPA and tibolone; and
- the probability of a reduction of climacteric symptoms.

Modelling
A Markov model, based on one developed by Coyle et al. 2003 (see ‘Other Publications of Related Interest’ below for bibliographic details) was used to assess the economic impact of tibolone. The model was subdivided into three related sub-models defined as follows: persistence with treatment, vaginal bleeding, and climacteric symptoms. The health states for each sub-model were reported and the temporal framework for each sub-model was 3 years with a 3-month treatment cycle. Transitional probabilities were presented in full in the study, along with a number of modelling assumptions which were fully justified. A schematic representation of the model was provided.

The clinical outcome data were extrapolated beyond the duration of those trials that provided the clinical estimates, using exponential curves that fitted the data.

Sources searched to identify primary studies
Persistence rates were derived from the published literature. The cumulative rates of amenorrhoea and the probability of a reduction of climacteric symptoms were derived from randomised controlled trials. The rates were extrapolated beyond the end of the trials using statistical techniques.

Methods used to judge relevance and validity, and for extracting data
The process used to identify the data was not reported. No inclusion or exclusion criteria were specified for any of the parameters.

Measure of benefits used in the economic analysis
The measure of benefit used was the quality-adjusted life-years (QALYs). Utility weights were derived from the published literature and, in the absence of documented data, from authors’ assumptions. The benefits were discounted at an annual rate of 3%.

Direct costs
Direct health service costs were included. They were calculated for a 3-year course of therapy and were derived by adding the costs associated with medications and treatment of vaginal bleeding for the persistent patients. The costs included were those for the initiation therapy, the acquisition of CEE/MPA and tibolone, and the treatment of vaginal bleeding. The cost prices were obtained from published sources and national databases. The price year was not stated. The costs were discounted at an annual rate of 3%. The resource quantities, which were based on authors’ assumptions and on published literature, and the unit costs were not reported separately.

Statistical analysis of costs
No statistical analyses of the costs were performed. The costs were treated deterministically.

Indirect Costs
In accordance with the perspective adopted, productivity costs were not included in the analysis.

Currency
Canadian dollars (CAD).

Sensitivity analysis
One-way and two-way sensitivity analyses were performed in order to investigate uncertainty inherent in all parameters and the structural assumptions of the model, and hence to determine their impact on the incremental cost-utility ratio (ICUR).
Estimated benefits used in the economic analysis
Tibolone generated 2.08 QALYs while CEE/MPA generated 2.05 QALYs.

Cost results
The total costs per patient for a 3-year treatment course were CAD 485 with tibolone and CAD 232 with CEE/MPA (difference CAD 253).

Synthesis of costs and benefits
An ICUR of tibolone compared with CEE/MPA was calculated in order to combine the costs and QALYs of the two strategies.

The ICUR of Tibolone compared with CEE/MPA was CAD 9,198 per QALY gained.

The sensitivity analysis showed that the results were robust for changes in most parameters except for the utility values. The ICUR was, in the majority of cases, below the threshold of CAD 20,000 per QALY gained, a threshold below which the authors suggested a strategy can be considered good value.

Authors’ conclusions
Although the results suggested that tibolone is cost-effective compared with conjugated equine estrogens and medroxyprogesterone acetate (CEE/MPA), the authors pointed out that tibolone generates higher costs than CEE/MPA for only a slight improvement in quality-adjusted life-years (QALYs). The authors therefore suggested that CEE/MPA should be recommended as the cost-effective treatment.

CRD COMMENTARY - Selection of comparators
The authors provided a clear justification for their choice of the comparator. CEE/MPA represents one of many regimens of hormone replacement therapy, but they have similar indications and they target the same population. You should decide whether these are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The parameters were derived from published research. The process used to identify the data was not reported. No inclusion criteria were specified for any of the parameters.

Validity of estimate of measure of benefit
The authors used QALYs as the measure of benefit in the economic analysis. Utility weights were derived from published papers and from the authors’ assumptions. The values assigned were reported, but the methods used in the published papers to derive the utilities were not. The impact of using alternative utility estimates was investigated in the sensitivity analysis. Discounting was appropriately conducted.

Validity of estimate of costs
All the categories of costs relevant to the study perspective appear to have been included in the analysis. The sources of resource use and the unit costs were well reported. One or two significant assumptions on resource use were made and these were appropriately tested in sensitivity analyses. The impact of changes in cost was addressed in the sensitivity analysis and discounting was appropriately applied. The price year was not reported, which means the results cannot be adjusted for inflation.

Other issues
The authors compared their findings with those from other studies and, in general, found that the results were in agreement. The authors do not appear to have presented their results selectively, although they did not report the results from the statistical tests they performed. The results of the base-case analysis and the sensitivity analyses were presented clearly. The authors acknowledged a number of limitations to their study, especially those arising from the methodological limitations inherent in a Markov model, the assumptions that were made, and parameter uncertainty.
Furthermore, as this was a short-term assessment, no long-term clinical or economic impacts (such as treatment repercussions on cancer, cardiovascular disease, osteoporosis and others) were taken into account. The authors justified clearly their omission of the long-term risks and benefits. The authors’ conclusions reflected the scope of the analysis.

**Implications of the study**
The authors suggest that the decision to assign a patient to CEE/MPA or tibolone should not be based on the ICUR. As tibolone generates higher costs than CEE/MPA for a slight improvement in QALYs, CEE/MPA should be recommended as the cost-effective option. Tibolone may be an appropriate treatment alternative for patients who cannot tolerate CEE/MPA. The authors made no recommendations for further research.

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**Other publications of related interest**
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**Indexing Status**
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