Cost-effectiveness model of topical treatment of mild to moderate psoriasis vulgaris in Germany: a comparison of calcipotriol/betamethasone (Daivobet/Dovobet/Taclonex) once daily and a morning/evening non-fix combination of calcipotriol and betamethasone

Augustin M, Peeters P, Radtke M, Moehling U, Lapp C

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 two first-line treatments for mild to moderate psoriasis.

Treatment 1 was a fixed combination of calcipotriol and betamethasone dipropionate in a common vehicle, to be administered once daily for 4 weeks (followed by calcipotriol for other 4 weeks).

Treatment 2 was a non-fixed combination of calcipotriol and betamethasone dipropionate, administered twice daily at full dose for 8 weeks.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised patients with mild to moderate psoriasis.

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

Dates to which data relate
Clinical estimates and data on resource use were derived from studies published between 1998 and 2004. The price year was not explicitly reported.

Modelling
A Markov model was constructed in order to simulate patient management under the two strategies being studied. The timeframe of the analysis was 48 weeks, with 4-week cycles. Similar pathways were used for both strategies: after the first 4-week cycle on first-line treatment, patients could achieve one of several health states (clearance, marked improvement, moderate improvement, slight improvement or no change, and worsening). The choice to stop or continue treatment after 4 weeks depended on the efficacy of the first cycle (those who reached clearance stopped treatment). Transition patterns and the model structure were reported.

Study designs and other criteria for inclusion in the review
The clinical data used in the decision model were:

- the probabilities of clearance, marked improvement, moderate improvement, slight improvement or no change, and worsening;

- the rates of adverse events;
the proportion of flare-up per cycle; and

the percentage of patients moving from moderate to marked improvement on reduced dose.

Sources searched to identify primary studies
Clinical rates were mainly derived from two published randomised clinical trials (RCTs), the main characteristics of which (study sample, patient characteristics, countries where they were carried out, comparators) were reported. The two patient samples were homogeneous in terms of demographic aspects and duration of psoriasis. The rate of flare-up or relapse was taken from a postal survey conducted in Scandinavia.

Methods used to derive estimates of effectiveness
The primary studies appear to have been identified selectively. Given the lack of head-to-head trials that compared fixed and non-fixed combinations, the study was based on an indirect comparison.

Measure of benefits used in the economic analysis
Two summary benefit measures were used in the analysis. These were the time spent in the state of marked improvement or clearance (disease-controlled days, DCDs) and the time spent in the state of clearance of all lesions. Both measures were estimated using the decision model. No discounting was necessary.

Direct costs
The viewpoint of society was adopted. The direct medical costs considered were study medications, concomitant topical dermatological medications, the treatment of adverse events and rescue ultraviolet B therapy. Specifically, the analysis comprised procedures, tests, hospitalisations and physician consultations. The unit costs and the quantities of resources used were presented separately. Much of the resource use data were derived from the afore-mentioned clinical trials. All resources included patient co-payments and discounts for German pharmacists to reflect the societal perspective. The costs were estimated using German national databases. The costs of medications were taken from the official German price list (Rote Liste). Discounting was not performed but was not relevant given the short time horizon of the analysis. The price year was not explicitly reported, but it might have been 2006.

Statistical analysis of costs
No statistical analyses of the costs or quantities were performed.

Indirect Costs
Productivity costs were not included in the analysis, although they might have been relevant given the societal perspective adopted.

Currency
Euros (EUR).

Sensitivity analysis
Two deterministic sensitivity analyses were carried out to address the issue of uncertainty surrounding some variables. In the first scenario, maximum compliance with the non-fixed combination was assumed in order to bias the analysis against the fixed combination. In the second scenario, the effectiveness of the fixed combination was varied by +/- 10%.

Estimated benefits used in the economic analysis
The number of days that a patient had clearance or marked improvement was 164.60 with the fixed combination and 144.19 with the non-fixed combination.

The number of days in the state of clearance of all lesions was 26.72 with the fixed combination and 14.98 with the non-fixed combination.

Cost results
The total costs per patient were EUR 571.33 with the fixed combination and EUR 705.23 with the non-fixed combination. The difference was mainly due to the higher cost of medication associated with the non-fixed combination (EUR 480.42 versus EUR 352.66).

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios were calculated in order to combine the costs and benefits of the alternative strategies.

The average cost per DCD was EUR 3.47 with the fixed combination and EUR 4.89 with the non-fixed combination.

The average cost per day with full clearance of all lesions was EUR 21.38 with the fixed combination and EUR 47.07 with the non-fixed combination.

The incremental analysis revealed that the fixed combination was both more effective and less expensive than the non-fixed combination, which was dominated.

The sensitivity analysis showed that the base-case results were robust to variations in assumptions around compliance and treatment effectiveness. In all cases the fixed combination dominated the non-fixed combination.

**Authors’ conclusions**
The authors concluded that psoriasis treatment with a fixed calcipotriol-betamethasone combination was more effective than a non-fixed combination, and that it was associated with lower cost of treatment in Germany. This was mainly due to higher compliance with the fixed combination.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear in that two alternative administration modalities of the same therapy were considered. The fixed combination, characterised by a single formulation, was a new option that was compared with standard treatment for mild to moderate psoriasis. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis was based on two published clinical trials. The use of RCTs should have ensured the robustness and validity of the clinical estimates. Furthermore, the authors provided some key details of these trials and showed that the study samples were comparable. However, no information about the approach used to identify these studies was provided. In particular, it was not stated whether they were identified through a review of the literature. A potential limitation of the analysis, as the authors acknowledged, was the fact that the two regimens were not compared directly in a head-to-head clinical trial; instead, indirect comparisons were made. Furthermore, no long-term data were available and the analysis was restricted to a short-term perspective.

**Validity of estimate of measure of benefit**
The benefit measures were specific to the disease considered in the study and would not be comparable with the benefits of other health care interventions. Furthermore, the authors did not investigate the impact of the treatments on quality of life.

**Validity of estimate of costs**
The analysis of costs considered all relevant items from a societal perspective. Thus, discounts and co-payments were included together with direct medical costs. Indirect costs are likely not to be relevant for psoriasis. A breakdown of the cost items was presented for most categories, and extensive information on the unit costs and quantities of resources used was provided, which enhances the possibility of replicating the analysis in other settings. The sources of data, which were reported, were consistent with the German health care system. The price year was not reported, which will limit the possibility of reflating the cost analysis in other time periods. The costs were treated deterministically, and the impact of variations in costs and resources on the results of the analysis was not investigated.

**Other issues**
The authors reported the results from three modelling studies that appeared to support the pharmacoeconomic advantages associated with the fixed combination. The issue of the generalisability of the study results to other settings was not explicitly addressed. Moreover, the limited use of sensitivity analyses limits the external validity of the study. In general, the issue of uncertainty around the model parameters was not addressed adequately since few deterministic sensitivity analyses and no probabilistic analysis were conducted. The analysis referred to patients with mild to moderate psoriasis and this was reflected in the authors’ conclusions. The results of the analysis were satisfactorily reported.

**Implications of the study**
The study results support the use of a fixed combination of calcipotriol and betamethasone dipropionate in a common vehicle to treat mild to moderate psoriasis.

**Source of funding**
Funded by LEO Pharma GmbH.

**Bibliographic details**

**PubMedID**
17823519

**DOI**
10.1159/000106791

**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.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Topical; Adult; Aged; Betamethasone /administration & dosage /analogs & derivatives /economics; Calcitriol /administration & dosage /analogs & derivatives /economics; Cost-Benefit Analysis; Dermatologic Agents /administration & dosage /economics; Drug Administration Schedule; Drug Combinations; Female; Germany; Humans;