Cost-effectiveness of once-daily treatment with calcipotriol/betamethasone dipropionate followed by calcipotriol alone compared with tacalcitol in the treatment of psoriasis vulgaris

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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
Patients with psoriasis vulgaris received once-daily treatment with Daivobet, an ointment containing betamethasone dipropionate (0.5 mg/g) and calcipotriol (50 microg/g), for 4 weeks. This was followed by 4 weeks treatment with calcipotriol. The comparator treatment was to give tacalcitol once daily for 8 weeks.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with a diagnosis of psoriasis vulgaris involving at least 10% of their arms and/or their legs and/or their trunk. The exclusion criteria were described in the earlier effectiveness paper (Ortonne et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details).

Setting
The study took place in France, Germany, Spain and the UK. It was unclear what kind of institution carried out the treatment, although it would appear that the setting was either primary or secondary care. The economic study was carried out in France.

Dates to which data relate
The effectiveness and resource evidence dated from 2001 to 2002. Originally, 2001 prices were used, but the authors then used 2004 prices for the drugs. The price year of other resources was unchanged (2001).

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

Link between effectiveness and cost data
The same patients provided both the effectiveness and the cost data. The costing was carried out prospectively.

Study sample
The power calculations were described in the earlier paper (Ortonne et al. 2004), where it also stated that 190 in each treatment group would give 90% power to detect a difference in the mean change of 10 percentage points, assuming a standard deviation (SD) of 30% and a significance level of 5%. A total of 501 patients were enrolled in the study, of
which 249 were allocated to Daivobet-calcipotriol treatment and 252 to tacalcitol treatment. Half of the participants in the two groups were male (53.8% versus 56.0% in the Daivobet and tacalcitol groups, respectively). The mean age was 50.77 (+/- 14.86) years in the Daivobet group and 51.55 (+/- 15.22) years in the tacalcitol group.

**Study design**
This was a multi-centred, double-blind, randomised controlled trial (RCT) in which patients were studied for 8 weeks. A total of 469 patients (93.6%) completed the 8-week treatment and had a check-up at 8 weeks (96.4% of the Daivobet patients and 90.9% of the tacalcitol patients). Research staff and patients were blinded to the treatment given.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary health outcomes used to assess patients were the percentages of patients achieving at least a 75% reduction in the Psoriasis Area and Severity Index (PASI) at 4 and 8 weeks. Baseline variables showed that the two patient groups were similar.

**Effectiveness results**
At 4 weeks, 46.65% (95% confidence interval, CI: 40.3 to 52.8) of Daivobet patients showed a reduction of 75% in the PASI compared with 13.9% (95% CI: 9.6 to 18.2) of tacalcitol patients, (p<0.001).

At 8 weeks, 44.6% (95% CI: 38.4 to 50.8) of Daivobet patients showed a reduction of 75% in the PASI compared with 23.8% (95% CI: 18.5 to 29.1) of tacalcitol patients, (p<0.001).

**Clinical conclusions**
The authors concluded that 4 weeks' treatment with Daivobet followed by 4 weeks' calcipotriol was more effective for psoriasis sufferers than 8 weeks' treatment with tacalcitol.

**Measure of benefits used in the economic analysis**
No summary measure of benefits was included in the analysis. The costs and effects were left disaggregated and the study was therefore classified as a cost-consequences analysis.

**Direct costs**
Discounting was not carried out since the costs referred to a time period of less than 2 years. The main resource use categories were hospital stay, physician outpatient visits, laboratory and diagnostic tests, procedures and medications (including alternative medication or therapies prescribed after discontinuation of the study medication, and all concomitant medication used for skin disorders). The quantities and the costs were not analysed separately for all resource components. However, the mean costs per patient were given for the following cost components: study medication, alternative treatments for psoriasis, costs relating to adverse events and other medication for skin disorders. The price year was generally 2001. The exception was for drugs, for which 2004 prices were used. The resource data were obtained from the study, while the unit cost data were obtained from the French health care system. Physician fee data were obtained from published statistics in France.

**Statistical analysis of costs**
Statistical analyses of the costs were performed using the Fisher and Wilcoxon rank sum tests, with CIs generated by a bootstrapping method with 1,000 replications.

**Indirect Costs**
Although the authors reported that a societal perspective was adopted, the indirect costs were not considered in the economic study. A rationale for their exclusion was not provided.
Currency
Euros (EUR).

Sensitivity analysis
A sensitivity analysis was carried out. First, the mean cost assessed on the same treatment group for patients who completed the study follow-up, adjusted to the time left to spend until day 56, was applied to the non-observed period. Second, the cost-effectiveness was estimated only for patients who completed the study, defined as those patients for whom medical resource data were captured for 8 weeks.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The average cost of treating psoriasis was EUR 107.53 (95% CI: 98.93 to 116.93) with Daivobet and EUR 113.50 (95% CI: 100.45 to 131.50) with tacalcitol.

The mean cost for treating all skin disorders was EUR 114.09 (95% CI: 104.93 to 124.03) with Daivobet and EUR 119.04 (95% CI: 105.63 to 137.48) with tacalcitol.

The costs of adverse events were dealt with in the costing.

Synthesis of costs and benefits
Treatment with Daivobet was dominant as it was both more effective and less costly than treatment with tacalcitol.

The authors calculated an average cost per successfully treated patient. The average cost of a patient reaching an improvement of 75% or more after 8 weeks was EUR 241.22 with Daivobet and EUR 476.70 with tacalcitol.

The sensitivity analyses showed that the results were robust to variations in the assumptions.

Authors' conclusions
Treatment with Daivobet led to better results for psoriasis patients than treatment with tacalcitol; it was both more effective and less costly.

CRD COMMENTARY - Selection of comparators
The choice of the comparator, tacalcitol, was not explicitly justified. There was an implicit justification that it was a commonly used treatment for psoriasis. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The study design, a double-blind RCT, was appropriate for the hypothesis. There were no other sources of effectiveness data. Given the restrictive inclusion and exclusion criteria, there was no evidence that the results were generalisable to all patients suffering from psoriasis. The analysis of effectiveness was handled credibly. For example, power calculations were conducted, the patient groups were shown to be comparable at analysis, and an intention to treat analysis was undertaken. However, some outcomes were only analysed for the 93.6% of patients who attended the 8-week check-up.
Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The study was, in effect, a cost-consequences analysis. However, the authors reported the average cost per successfully treated patient. This method of presenting the synthesis of costs and outcomes did not result in a clear and informative analysis. The authors underestimated the strength of their results in terms of the advantages of Daivobet-calcipotriol over tacalcitol, which in this study produced better results for patients at a lower cost and was, therefore, the dominant strategy.

Validity of estimate of costs
Although the authors explicitly stated that a societal perspective was adopted in the analysis, in reality it would appear that a health service perspective was adopted. From this cost perspective, all the relevant costs were included in the analysis. The unit costs and the resource quantities were reported separately for some but not all cost components, allowing greater generalisability of the analysis. The resource use quantities were taken from a single study, while the prices were taken from the authors' setting in France and from a published source in France. Statistical analyses of the quantities and mean costs between the two treatment groups were performed, but there was no sensitivity analysis or any other analysis of the quantities. The price year was reported, which will assist any future reflation exercises. Discounting was not carried out, which was appropriate given that the study had a very short-term time horizon.

Other issues
The authors did not compare their results with those from other studies. The issue of generalisability to other settings was not discussed. The authors did not present their results selectively. Overall, the conclusions were an accurate reflection of the results presented and related well to the scope of the study. However, the authors did not make it clear what percentage of psoriasis sufferers would generally meet the inclusion criteria. The authors stated that they made assumptions whenever there was uncertainty about the costs. These underestimated the cost-advantage of Daivobet-calcipotriol, thus strengthening their conclusions that Daivobet is the dominant strategy. The authors did not report any further limitations of their study.

Implications of the study
The authors recommended using Daivobet-calcipotriol for psoriasis sufferers.

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None stated.

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Other publications of related interest
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**MeSH**
Administration, Topical; Adult; Aged; Betamethasone /administration & dosage /analogs & derivatives; Calcitriol /administration & dosage /analogs & derivatives; Confidence Intervals; Cost-Benefit Analysis; Dihydroxycholecalciferols /administration & dosage /economics; Dose-Response Relationship, Drug; Double-Blind Method; Drug Administration Schedule; Drug Combinations; Drug Costs; Europe; Female; Follow-Up Studies; Humans; Male; Middle Aged; Ointments; Probability; Psoriasis /diagnosis /drug therapy; Reference Values; Risk Factors; Severity of Illness Index; Treatment Outcome

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