

# **Clinical and cost-effectiveness of once-daily versus more frequent use of same potency topical corticosteroids for atopic eczema: a systematic review and economic evaluation**

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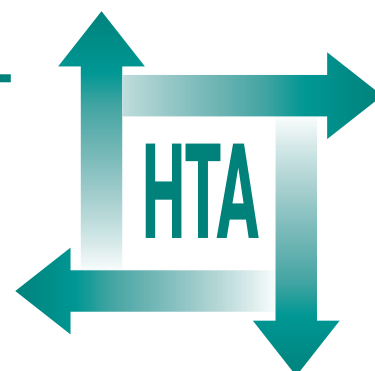
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## ***Executive summary***

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## Executive summary

### Background

Atopic eczema (atopic dermatitis) is a chronic relapsing condition, characterised by frequent flare-ups on the skin (patches of red, dry, scaly and itchy skin), and treatments are aimed at symptom relief and the prevention of complications (e.g. infections), until remission occurs. It is a major public-health problem, thought to affect around 15–20% of school-age children at some stage and 2–10% of adults, giving a likely patient group in excess of two million people in England and Wales.

Atopic eczema is generally classified according to mild, moderate or severe disease, using a range of clinical characteristics, with the majority (over 80%) of patients experiencing mild disease and only a small proportion (around 2–4%) having severe atopic eczema. The condition is associated with considerable morbidity, which varies with disease severity. The physical impact of the condition affects everyday activities (e.g. school, work, sleep), and sufferers may experience distress and anxiety that diminish their psychological well-being and functional capacity.

The mainstay of treatment for atopic eczema is the use of topical corticosteroids, in combination with emollients and soap substitutes. There are a large number of topical corticosteroids available, classified according to potency (mild, moderate, potent or very potent). The frequency of the application of topical corticosteroids in atopic eczema seems to have developed empirically over time, with twice-daily use as the most dominant prescribing strategy.

### Aim of the review

To assess the clinical and cost-effectiveness of once-daily use of topical corticosteroids versus more frequent use of same-potency topical corticosteroids in the treatment of people with atopic eczema.

### Methods

A systematic review of the literature and an economic evaluation were undertaken.

### Data sources

Electronic databases were searched from inception to October 2003. Bibliographies of included studies and related papers were checked for relevant studies and experts were contacted for advice and peer review and to identify additional published and unpublished studies. Manufacturer submissions to the National Institute for Clinical Excellence were reviewed.

### Study selection

Studies were included if they met the following criteria.

- Intervention: once-daily versus more frequent application of topical corticosteroids of the same potency. Studies comparing different potency corticosteroids or compound preparations were excluded.
- Participants: children and adults with atopic eczema (atopic dermatitis). Patients with other types of eczema (e.g. contact dermatitis, seborrhoeic eczema, varicose eczema and discoid eczema) were excluded.
- Design: systematic reviews of randomised controlled trials (RCTs). Controlled clinical trials (CCTs) were considered where no RCT evidence was identified for a given potency group.
- Outcomes: overall response to treatment, impact on clinical features of the condition, relapse/flare-up rate, side-effects, compliance, tolerability, patient preference measures and quality of life.

Studies in non-English languages and studies published only as abstracts were excluded. Titles and abstracts were screened for eligibility by one reviewer and checked by a second reviewer. Inclusion criteria were applied to the full text of selected papers by two reviewers. Any differences in opinion were resolved through discussion or consultation with a third reviewer.

### Data extraction and quality assessment

Data extraction and quality assessment were undertaken by one reviewer and checked by a



second reviewer, with any differences in opinion resolved through discussion. The quality of included systematic reviews was assessed using criteria developed by the NHS Centre for Reviews and Dissemination (CRD) and the quality of RCTs was assessed in accordance with NHS CRD Report 4.

## Data synthesis

The clinical effectiveness data were synthesised through a narrative review with full tabulation of the results of included studies. Meta-analysis was considered inappropriate as the studies were too dissimilar; however, Forest plots with risk ratios were presented for illustration of the most commonly reported outcomes.

## Results

### Number and quality of studies

One systematic review and 10 RCTs were included in the systematic review. One RCT compared moderately potent corticosteroids, eight RCTs compared potent corticosteroids and one RCT compared very potent corticosteroids. No RCTs or CCTs of mild corticosteroids were eligible for inclusion. The systematic review was of good quality. Most of the RCTs were of poor methodological quality, although two RCTs were judged to be of good quality.

### Summary of benefits

#### *Moderately potent corticosteroids*

The one study that compared moderately potent corticosteroids found no significant difference in severity of symptoms between once- and twice-daily application, but the study was small and of poor quality.

#### *Potent corticosteroids*

##### **Numbers responding to treatment**

Overall, studies found little difference in the number of patients responding to treatment between once- and twice-daily application of potent corticosteroids. Some statistically significant differences favouring twice-daily treatment were identified; however, these were inconsistent between outcome assessors (physicians versus patients) and outcomes selected for analysis.

##### **Severity of symptoms**

Once-daily mometasone furoate (Elocon<sup>®</sup>) compared with twice-daily application of a different active compound was found to result in a greater percentage improvement in total atopic dermatitis

scores in one study and an improvement in pruritus only in another study, whereas a third study found no statistically significant differences. Again, these studies were of poor quality. One good-quality study favoured twice-daily application of fluticasone propionate ointment (Cutivate<sup>®</sup>) whereas other studies found no significant difference or an improvement in one symptom but not others with twice-daily application. The validity and reliability of the severity scales used were not reported in any of the studies, and the clinical meaning of these scores is not clear.

#### **Very potent corticosteroids**

Only one study considered very potent corticosteroids, comparing once- versus three-times daily application. This study found a statistically significant difference in comparative clinical response in favour of three-times daily treatment but no significant difference in the number of patients with at least a good response.

#### **Adverse effects**

The extent of reporting of adverse effects was variable between studies. There appears to be little difference in the frequency or severity of short-term adverse events between once-daily and more frequent application of potent or very potent topical corticosteroids; however, data are limited. No data on late onset adverse events such as skin atrophy were available.

#### **Cost-effectiveness**

A search of the literature revealed no published cost-effectiveness studies comparing frequency of application of same-potency topical corticosteroids. Given that our review of clinical effectiveness has shown that outcomes from the comparators are similar, the relative cost-effectiveness of once- versus more frequent application of topical corticosteroids becomes a case of cost minimisation, where the least cost alternative should be favoured, all else being equal. A review of the topical corticosteroid products available revealed a wide range of products and a wide variation in the price of these products; the cost per 30 g/30 ml for topical corticosteroids included in this review varies between £0.60 (for generic hydrocortisone) and £4.88 (for mometasone furoate, Elocon<sup>®</sup>). Specific decisions on the least cost alternative, between once-daily and more frequent application of products, will be determined by the relative price of the products being compared. In the case of the 10 RCTs included in this review, on the basis of response to treatment, six of these comparisons would favour the once-daily option as 'least cost',



and three of the comparisons would favour the 'twice-daily' option as the 'least cost' treatment option. In the remaining RCT, the clinical effectiveness findings favoured the twice-daily treatment regimen, with a greater number of patients classed as successful treatment responders, at an additional cost. Given the relatively small costs associated with treatment per patient, it is difficult to imagine that such additional costs are not a cost-effective use of NHS funds, where a successfully treated flare-up is regarded as a good thing.

Where patients can be appropriately prescribed once-daily treatment of a similarly priced product, a reduction in the quantity of topical corticosteroid used will be expected. Therefore, it is feasible that a move to once-daily application of topical corticosteroids will result in some cost savings to the NHS. However, in the absence of information on the quantity of product used by treatment regimen and on the present prescribing patterns, it is not possible to make reliable estimates of potential cost savings. Furthermore, issues related to pack size for prescribed products and subsequent waste (unused product) could easily erode any potential saving. The potential cost savings on prescribed products are very small at a patient level, although given the large numbers of patients with atopic eczema, cost savings in theory could be substantial. The presence of specifically marketed 'once-daily' topical corticosteroids, which are relatively expensive (per unit price), may result in additional costs to the NHS should there be a general recommendation in favour of once-daily use of topical corticosteroids compared with more frequent use.

## Conclusions

The literature to inform on the clinical effectiveness of once-daily versus more frequent application of topical corticosteroids is very limited. The available literature indicates that the clinical effectiveness of once-daily and more frequent application of potent

topical corticosteroids is very similar, but it does not offer a basis for favouring either option. The cost-effectiveness of once-daily versus more frequent use of topical corticosteroids will depend on the generalisability of the findings to the specific treatment decision and the relativities in product prices.

The trials included in this review generally refer to moderate to severe atopic eczema, whereas most patients have mild disease, and furthermore most of the included trials report on potent topical corticosteroids (eight of 10 RCTs); therefore, the generalisability of the findings presented in the review is severely limited.

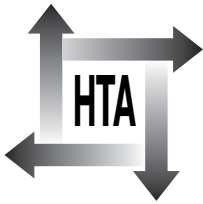
## Recommendations for further research

Further research is required on the clinical and cost-effectiveness of once-daily versus more frequent use of same-potency topical corticosteroids, across a broader range of patient groups and across a broader range of topical corticosteroids. Specifically, further information is needed on the effectiveness of mild potency products (e.g. hydrocortisone products) for the treatment of mild to moderate atopic eczema, by frequency of application (i.e. once-daily versus more frequent use).

Research is particularly required to inform on areas of expected benefit related to a reduction in the use of topical corticosteroids (e.g. improved compliance, impact on quality of life).

## Publication

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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