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INVESTIGATIVE REPORT

Cost-effectiveness of Maintenance Treatment with a Barrier-strengthening Moisturizing Cream in Patients with Atopic Dermatitis in Finland, Norway and Sweden

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Atopic dermatitis is a chronic skin disorder with high prevalence, especially in the Nordic countries. Effective maintenance therapy during symptom-free episodes may prolong the time to eczema relapse according to a previously published clinical trial. The present study evaluates the cost-effectiveness of a barrier-strengthening moisturizer containing 5% urea, compared with a moisturizer with no active ingredients during eczema-free periods. A health economic microsimulation model, based on efficacy data from the randomized clinical trial, analysed the cost-effectiveness of the barrier-strengthening treatment in Finland, Norway and Sweden. The barrier-strengthening moisturizer was cost-saving compared with the moisturizer with no active ingredients in all 3 countries. The result was confirmed in all but one sensitivity analysis. In conclusion, the barrier-strengthening moisturizer is cost-effective as maintenance therapy for patients with atopic dermatitis compared with a moisturizer with no active ingredients. ***Key words: atopic dermatitis; cost-effectiveness; model simulation; moisturizer; maintenance treatment; Nordic countries.***

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Atopic dermatitis (AD) is a chronic, inflammatory, relapsing skin disorder. The severity of the disease can vary with the seasons and may require frequent medical visits, special clothing and topical treatment, all of which impact on health-related quality of life (HRQoL) (1).

Conventional long-term therapy for AD consists of both treatment of eczema and maintenance treatment during eczema-free episodes. Maintenance treatment is based on emollients (moisturizing creams), sometimes combined with low doses of more potent drugs, e.g. tacrolimus ointment (2, 3).

In 2009, a barrier-strengthening moisturizing cream containing 5% urea was shown to lengthen the time interval between eczema episodes for AD patients compared with no treatment (4). A health economic analysis, based on the results of this study, indicated that the barrier-strengthening cream was cost-effective compared with no treatment (5). The same barrier-strengthening moisturizing cream was evaluated in a double-blinded clinical study of patients with AD in 2015 (6). The new study compared the barrier-strengthening moisturizing cream containing 5% urea with a moisturizer with no active ingredients, showing that the study cream significantly prolonged the eczema-free time compared with the reference cream and reduced the risk of eczema relapse (6).

The aim of this health economic analysis was to assess whether maintenance treatment with the study cream (6) was cost-effective, compared with a reference cream with no active ingredients, for patients with AD during symptom-free periods in Finland, Norway and Sweden.

METHODS

Health economic analysis

A cost-utility analysis was performed to evaluate the cost-effectiveness of maintenance treatment with the study cream compared with the reference cream for patients with AD in a Nordic setting. The cost-utility analysis is a health economic method used when the treatment benefits of both treatment alternatives are measured with a unified generic utility measure, such as quality-adjusted life years (QALYs) (7). The analysis had a societal perspective, including both direct and indirect costs and was performed according to present guidelines for health economic studies (7–10). Separate cost analyses were carried out for Finland, Norway and Sweden to ensure alignment with country-specific conditions. National unit costs are presented in Appendix S1[1], where the unit costs of the reference cream and the steroid creams refer to mean prices of creams available in each country. Costs are presented as 2014 Euros, adjusted to 2014 price levels using the consumer price index (CPI) when necessary (11–13). The average exchange rates in 2014 were €1 = SEK 9.0968 and €1 = NOK 8.3534 (14, 15).

Data on treatment efficacy, i.e. time-to-relapse, and measures of HRQoL were retrieved from the randomized clinical trial (RCT) population (6). The trial included 172 patients (198 screened) from 15 dermatological clinics. The average patient had moderate AD according to Rajka & Langeland criteria (16). Additional patient characteristics are shown in Table I.

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Upon inclusion, ongoing eczemas were treated with corticosteroids during a 3-week initiation phase. A hydrocortisone cream 1% was used for sensitive body areas, while a mometasone furoate cream 0.1% was used for all other eczemas. Eczema-free patients were then randomized to maintenance treatment with either the study cream or the reference cream. The patients were followed until eczema relapse or for a maximum of 6 months. An eczema relapse was defined as an episode that, according to the patient, required escalation of treatment (6). The estimated median time-to-relapse was 22 days with the study cream and 15 days with the reference cream. A larger proportion of patients treated with the study cream remained eczema-free during the full follow-up period.

All analyses were performed using STATA 13 (Stata Corp. 2013. Stata Statistical Software: Release 13. College Station, TX, USA: Stata Corp LP).

Model and model inputs

Modelling is a standard method for evaluation of healthcare interventions. For the analysis, a health economic discrete-event model including 2 health states (eczema and eczema-free) was developed using Microsoft® Excel. The model simulates 10,000 patients with AD during a 1-year time-period in respect of eczema relapses.

All patients were assumed to be eczema-free and started treatment with maintenance therapy, i.e. either the study cream or the reference cream, at model entry. In order to embody clinical practice in each country, a representative mix of moisturizers with no active ingredients available in Finland, Norway and Sweden were used as comparators in the model. Upon the event of an eczema relapse the patient was modelled to receive a 3-week course of corticosteroid treatment, after which the patient returned to the eczema-free state with maintenance therapy. The same sequence of events was repeated until one year had passed.

While the RCT (6) followed patients only to their first eczema recurrence, the model allowed for multiple relapses. As most patients in the RCT experienced eczema relapse within the first few weeks of maintenance therapy each modelled patient could have several eczema episodes during the analysed year. This is in line with the number of relapses during the previous 12 months reported by patients in the RCT (Table I).

The modelled time-to-relapse directly represented RCT data (Kaplan–Meier curves) during the initial 6 months, while the subsequent 6 months were parametrized with a Weibull curve (Fig. 1).

Each health state was associated with a utility (QALY weight) based on HRQoL data from the RCT (6). The mean utility of the eczema-free state was 0.938 and the eczema health state corresponded to a disutility of –0.108.

The model uses a maintenance cream consumption that corresponds to the data from the RCT (6), where patients applied maintenance cream twice daily (mean 11.8 g/day). A corresponding cream consumption of a once daily application was assumed for the corticosteroid treatment during the eczema episodes (5.9 g/day).

Table I. *Patient characteristics from the randomized clinical trial (6)*

Characteristic	Study cream (n=87)	Reference cream (n=85)	Total (n=172)
Age, years, median (min–max)	30 (18–66)	28 (18–82)	28 (18–82)
Females, *n* (%)	49 (56.3)	52 (61.2)	101 (58.7)
Years since AD diagnosis, median (min–max)	26 (0–64)	24 (0–62)	25 (0–64)
Patient reported relapses during previous 12 months, *n*, median (min–max)	5 (0–20)	4 (1–96)	4 (0–96)

AD: atopic dermatitis.

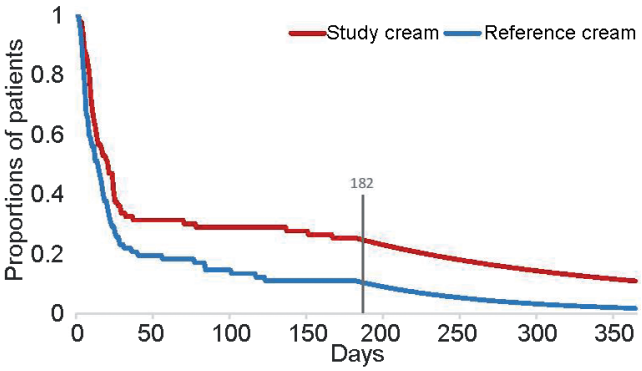

Fig. 1. Proportion of eczema-free patients over time per treatment alternative, where the Kaplan–Meier survival curve based on randomized clinical trial (RCT) data (6) is used for the initial 182 simulation days and extrapolated using a parametric Weibull curve for the subsequent 183 simulation days. This reflects the distribution of time-to-relapse used in the model.

In line with a previous study, we assumed that 25% of the patients visited a general practitioner (GP) and 25% visited a specialist/dermatologist, while 50% of the patients consulted a physician over the phone or did not visit a doctor upon eczema relapse (5). A 2 h production loss from work absenteeism per physician visit was assumed and the cost of production loss was estimated according to the human capital approach.

Sensitivity analyses were performed according to health economic praxis to explore the stability of the results. Additional details on the model, resource use, model inputs and sensitivity analyses are presented in Appendix S1[1].

RESULTS

Results from the cost calculations of the base case analysis are shown in Table II. The results state that maintenance treatment with the study cream during symptom-free periods results in a decrease in costs of €260 in Finland, €145 in Norway and €508 in Sweden compared with the reference cream for patients with AD. The study cream also resulted in a QALY gain of 0.016 compared with the reference cream in all countries (data not shown). Thus, treatment with the study cream is both cost-saving and more effective than the reference cream.

The result is explained by fewer episodes of eczema, resulting in 55 fewer days with eczema, in the study cream group during the simulated year (data not shown).

The results of the sensitivity analyses confirmed the base case results and are presented in detail in Appendix S1[1].

DISCUSSION

This health economic analysis assessed the cost-effectiveness of a barrier-strengthening moisturizing cream containing 5% urea compared with a moisturi-

Table II. *Base case results. The cost of atopic dermatitis (AD) treatment in Finland, Norway and Sweden*

	Study cream €	Reference cream €	Difference €
Finland			
Maintenance therapy	151	92	60
Steroids	157	250	–93
Physician visits	231	370	–139
Indirect costs	146	234	–87
Total	686	946	–260
Norway			
Maintenance therapy	272	174	98
Steroids	92	147	–55
Physician visits	134	215	–81
Indirect costs	176	282	–106
Total	673	818	–145
Sweden			
Maintenance therapy	141	158	–17
Steroids	78	124	–46
Physician visits	550	880	–330
Indirect costs	132	212	–79
Total	901	1,373	–472

Euro is given in 2014 price level.

zer with no active ingredients as maintenance therapy during eczema-free periods for patients with AD, in Finnish, Norwegian and Swedish settings. The study was conducted using a health economic model with a 1-year time-horizon that simulated 10,000 patients. The base case results indicate that the study cream is both cost-saving and more effective compared with the reference cream.

Although the QALY difference between the treatment alternatives is relatively small, treatment with the study cream results in fewer eczema relapses and fewer days with eczema than the reference cream during the analysed period, i.e. the study cream is more effective. As the relapse episodes are more costly than eczema-free periods (primarily due to the cost of physician visits) the study cream is a less costly treatment alternative in all 3 countries.

In the sensitivity analysis we increased the price of the study cream by 10% and varied the price of the reference cream to the minimum and maximum prices found on the national markets. These variations had no influence on the cost-effectiveness of the results.

The study cream remained a cost-saving maintenance therapy, compared with the reference cream in all but one sensitivity analysis. The exception was a Norwegian sensitivity analysis that assumed a maximal amount of maintenance cream consumption (the maximum usage at 2 full-body applications, i.e. 36 g/day). However, the cost per QALY gained was €3,637, which is well below the commonly cited Norwegian threshold of approximately €60,000 (NOK 500,000) (17).

This analysis is based on efficacy data from a previously published RCT and the included comparators reflect the comparators in the RCT. The results thus refer to the costs and effects of the barrier-strengthening moisturizer containing 5% urea compared with moisturizers with no active ingredients. No other potential alternative maintenance therapies for AD were analysed as we have not found any publications of clinical trials comparing the barrier-strengthening moisturizing cream containing 5% urea with any other similar moisturizer. It is not possible to compare the cost-effectiveness with other similar products, since we have no information about similarities or differences in clinical efficacy.

There are different severity levels of AD. The patient population included in the RCT had moderate and persistent AD, representing approximately 25% of adult patients with AD (18, 19).The results primarily apply to patients with moderate and persistent AD.

A strength of the present health economic analysis is that it is based on Nordic data both regarding efficacy and costs. It is known that environmental factors affect AD (19) and that the highest prevalence is found in the Nordic countries (20). The region-specific perspective therefore provides high internal validity.

Previous research has shown that 34% of patients with AD reported sick-leave due to AD during their lifetime (19). Furthermore, 15% had changed occupation due to their AD. These findings indicate that the societal costs of AD and, consequently, the cost reduction of maintenance treatment with the study cream, may be underestimated in the present analysis.

The model considers only one eczema health state and one eczema-free health state and disregards the severity of the eczema. As the severity level of AD may drive the use of steroids, maintenance therapy and medical consultation, the fact that the severity of eczema was disregarded may be a drawback of the present analysis.

Another shortcoming of this study may be that it does not fully control for the seasonal variation in recurrence of eczema. As all inclusions in the RCT (6) occurred during the winter season no seasonal variation in time-to-relapse was detected in the efficacy data.

In 2009, Hjalte et al. (5) showed that a barrier-strengthening moisturizing cream containing 5% urea was a cost-effective maintenance therapy during eczema-free periods compared with no treatment. To our knowledge, there has been no previous research on the cost-effectiveness of the study cream compared with a moisturizer with no active ingredients.

In conclusion, this cost-utility analysis indicates that a barrier-strengthening moisturizing cream containing 5% urea is a cost-effective maintenance therapy during symptom-free periods for patients with AD compared with a reference cream with no active ingredients.

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The authors declare no conflicts of interest.

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