Resubmission

clobetasol propionate 0.05% shampoo (Etrivex®) No. (434/07)
Galderma (UK) Limited

04 July 2008

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a resubmission

clobetasol propionate 0.05% shampoo (Etrivex®) is accepted for use within NHS Scotland for the topical treatment of moderate scalp psoriasis in adults.

Comparison of clobetasol propionate 0.05% shampoo to another clobetasol formulation demonstrated non-inferiority and costs are similar.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

Topical treatment of moderate scalp psoriasis in adults.

Dosing information

To be applied directly to the dry scalp once daily for 15 minutes before rinsing. Maximum treatment duration is 4 weeks.

Product availability date

September 2007

Summary of evidence on comparative efficacy

Clobetasol propionate is a highly potent corticosteroid. Although the mechanism of action of topical corticosteroids is unclear, it is thought to involve induction of phospholipase A_2 inhibitory proteins thereby reducing the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes.

Three studies tested non-inferiority to comparator, using analysis of covariance and a pre-specified upper non-inferiority margin of a 1.5 point difference in Total Severity Score (TSS). This led to superiority tests in two studies. In all studies, clobetasol shampoo was applied once daily to a dry scalp for 15 minutes before rinsing.

A multicentre, investigator-blinded, active- and vehicle-controlled study investigated the non-inferior efficacy of clobetasol propionate 0.05% shampoo (clobetasol shampoo) to clobetasol propionate 0.05% gel (clobetasol gel), and the superior efficacy of the active shampoo to its vehicle. The study included 144 patients with moderate to severe scalp psoriasis, defined as a global severity score (GSS) ≥3, (indicating at least moderately severe erythema, scaling and plaque thickening), with ≥15% scalp involvement. Patients were randomised in a 3:3:1 ratio to four weeks treatment with clobetasol shampoo, clobetasol gel (once daily to a dry scalp without rinsing) or shampoo vehicle (as for active shampoo). Assessments included change from baseline in TSS (the sum of individual (0 to 3) scores for erythema, scaling and plaque thickening, total range 0 to 9) and in GSS (score 0 (clear) to 5 (very severe) for severity of the same parameters as TSS).

The primary outcome was TSS at four weeks in both the intention to treat (ITT) population (with missing data imputed using last outcome carried forward (LOCF)) and per protocol (PP) populations. The treatment difference between the clobetasol formulations significantly favoured the gel: 0.70, 95% confidence interval (CI) 0.16 to 1.24 (ITT); 0.77, 95% CI 0.25 to 1.29 (PP). Non-inferiority of clobetasol shampoo relative to clobetasol gel was achieved in both populations as the upper limit of the CI was below the pre-specified target of 1.5. Clobetasol gel was also significantly better than clobetasol shampoo in reducing GSS. Clobetasol shampoo was significantly better than vehicle in reducing GSS in the ITT (LOCF) population, but not in the PP population.

A multicentre, investigator-blinded study compared clobetasol shampoo with calcipotriol 0.005% scalp solution in 151 patients with moderate to severe scalp psoriasis. Patients were eligible if they were ≥12 years with moderate to severe scalp psoriasis defined as GSS ≥3 and affected area ≥2cm^2 of scalp. Randomisation was to four weeks treatment with

clobetasol shampoo or calcipotriol 0.005% scalp solution (twice daily to a dry scalp without rinsing).

The primary outcome was mean change from baseline in TSS and GSS at four weeks. Non-inferiority of clobetasol shampoo to calcipotriol scalp solution was demonstrated, leading to the superiority analysis. The mean treatment difference in TSS was -0.51, 95% CI -0.05 to -0.97 (ITT, LOCF) and -0.24, 95% CI -0.66 to 0.18 (PP) and in GSS was -0.43, 95% CI -0.78 to -0.08 (ITT, LOCF) and -0.27, 95% CI -0.59 to 0.06 (PP), both in favour of clobetasol shampoo. Clobetasol shampoo significantly reduced the area of affected scalp compared with calcipotriol solution. The proportions of patients considered "clear" or "almost clear" in global assessment by investigators were 50% vs 28%; and by patients were 47% vs 31% for clobetasol shampoo and calcipotriol solution, respectively.

A multicentre, randomised, investigator-blinded study compared clobetasol shampoo with a tar blend 1% shampoo. The study included 162 adult patients with moderate to severe scalp psoriasis with ≥15% scalp involvement. Patients were randomised in a ratio of 3:1 to clobetasol shampoo, or tar shampoo (twice weekly as per normal shampoo).

The primary objective of non-inferiority of clobetasol shampoo compared to tar shampoo with respect to TSS and GSS at 4 weeks was achieved and superiority analyses followed. There was a significant mean treatment difference for TSS in favour of clobetasol shampoo of -1.84, 95% CI -2.48 to -1.21(ITT, LOCF) and -2.07, 95% CI -2.73 to -1.41 (PP). For GSS, the mean treatment difference in favour of clobetasol shampoo was -1.01 (95% CI -1.36 to -0.66 (ITT, LOCF) and -1.13, 95% CI -1.50 to -0.76 (PP). After four weeks, there was a significant difference between treatments in reduction of affected scalp area, from 48% to 29% with clobetasol shampoo and from 54% to 46% with the tar blend shampoo. Clobetasol shampoo was also significantly better in reducing erythema, plaque thickening, desquamation and pruritus scores. Patients treated with clobetasol shampoo reported a significantly higher rate of cosmetic acceptability when compared to the tar blend shampoo group.

*Other data were also assessed but remain commercially confidential.**

Summary of evidence on comparative safety

The safety and tolerability of four weeks treatment with clobetasol shampoo compared with clobetasol gel was assessed in 26 patients with scalp psoriasis. Study outcomes were the effect on hypothalamic–pituitary–adrenal (HPA) axis function, atrophogenicity and ocular tolerability and other adverse effects (AEs). There was no difference between treatments in any outcome.

In the calcipotriol study described in the comparative efficacy section, 1% patients in the clobetasol shampoo group experienced treatment-related AEs compared with 23% patients in the calcipotriol solution group. Withdrawals due to AEs occurred in 0% and 9% of the clobetasol shampoo and calcipotriol solution groups, respectively.

In the tar shampoo study described in the comparative efficacy section, 8% patients in the clobetasol shampoo group experienced treatment-related AEs compared with 2% in the tar shampoo group. All AEs due to clobetasol shampoo were of mild to moderate severity and included itching, stinging, and burning of the scalp, moderate but unacceptable worsening of psoriasis, and tingling sensation after rinsing hair and headache. Withdrawals due to AEs occurred in 2% and 0% of the clobetasol shampoo and tar shampoo groups, respectively.

Summary of clinical effectiveness issues

Clobetasol shampoo has not been compared to the two other formulations of clobetasol licensed in the UK for scalp psoriasis, clobetasol propionate 0.05% cutaneous foam and clobetasol propionate 0.05% scalp application, so there are no data for these on comparative efficacy, safety or patient acceptability. The dosing frequency and treatment duration of the products currently available differ from the shampoo. Both are applied twice daily and left on the scalp. The cutaneous foam is licensed for a maximum of two weeks compared to four weeks with the shampoo. There is no specified maximum treatment period for the scalp application, but it should be discontinued when control is achieved. There is no evidence that adherence to treatment would be increased with the shampoo compared with the scalp application or cutaneous foam.

Clobetasol shampoo was shown to be non-inferior to a clobetasol gel formulation that is not licensed in the UK.

Clobetasol compared favourably with calcipotriol scalp solution, (used twice daily and left on the scalp) and tar shampoo, (used twice weekly as per normal shampoo). However, in practice, these products are less likely to be direct comparators. If a potent or highly potent corticosteroid were indicated, the choice would depend on the most suitable formulation.

Limitations of the studies include the large margin for non-inferiority in the comparison with clobetasol gel, and the fact that the maximum treatment effect of calcipotriol occurs after four weeks, therefore the four week endpoint favours clobetasol shampoo.

The patient population in all the studies included those with severe scalp psoriasis, although the licensed indication is for moderate disease. It is not known if this affected study results. Although scalp psoriasis is a chronic condition, there is no comparative follow up evidence concerning time to relapse.

There is no evidence that clobetasol shampoo is safer than other clobetasol scalp formulations despite having a short contact time.

Summary of comparative health economic evidence

The manufacturer presented a simple cost-minimisation analysis over a 4 week time horizon of 7.5ml once daily for clobetasol propionate 0.05% shampoo against the comparators of

- 7.5ml twice daily for clobetasol propionate 0.05% gel
- 7.5ml twice daily for betamethasone
- 7.5ml once daily for betamethasone with salicylic acid.
- 60ml per week for calcipotriol

The analysis assumed that demonstrated non-inferiority equated to proof of clinical equivalence. It found clobetasol propionate 0.05% shampoo to be cost saving, the extent of this being £1.72 relative to betamethasone with salicylic acid; £2.62 relative to betamethasone; £12.56 relative to clobetasol propionate 0.05% gel; and, £28.26 relative to calcipotriol.

Summary of patient and public involvement

Patient Interest Group Submission: Psoriasis Scotland Arthritis Link Volunteers (PSALV).

Additional information: guidelines and protocols

The British Association of Dermatologists issued a Psoriasis Guideline in 2006 that for scalp psoriasis a tar-based shampoo should be tried first; this can be combined with the use of either a 2-5% salicylic acid preparation, a coconut oil/tar/salicylic acid combination ointment, a potent topical corticosteroid preparation (e.g. 0.1% betamethasone valerate), calcipotriol scalp application, or more than one of these.

Additional information: previous SMC advice

Following an abbreviated submission, SMC published advice in February 2008: clobetasol propionate 0.05% shampoo (Etrivex®) is not recommended for use within NHS Scotland for the topical treatment of moderate scalp psoriasis in adults. Clinical equivalence to existing topical formulations of clobetasol propionate has not been demonstrated.

Following an abbreviated submission, SMC published advice in July 2006: clobetasol propionate 0.05% cutaneous foam (Clarelux®) is accepted for use within NHS Scotland for short-course treatment of steroid responsive dermatoses of the scalp such as psoriasis, which do not respond satisfactorily to less potent steroids. It offers an alternative to other scalp applications of clobetasol propionate at a similar cost (depending on the rate of application).

Additional information: comparators

The most relevant comparators are the two other formulations of clobetasol propionate 0.05% that are licensed for scalp psoriasis, Dermovate scalp application and Clarelux cutaneous foam.

Cost of relevant comparators

Drug	Dose regimen	Quantity	Cost per course
clobetasol shampoo	**Once daily for up to 4 weeks**	**210ml**	**24**
clobetasol scalp application (Dermovate)	Twice daily until improvement occurs	200ml[#]	22
clobetasol cutaneous foam (Clarelux)	Twice daily for up to 2 weeks (weekly dose up to 50g)	100g	11

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis on 2nd May 2008. Costs calculated based on 7.5ml per application unless licence states maximum quantities; and approximated to most practical pack size eg 210 ml rounded down to 200ml[#]cost for 2 weeks as this reflects total number of applications of the other corticosteroid formulations

Additional information: budget impact

The manufacturer estimated a net drug cost saving of £5k in year 1 given 525 patients switching to the shampoo, rising to £28k by year 5 given 3,150 patients switching to the shampoo. Market share was estimated at 5% in year 1 rising to 30% in year 5. Gross drug costs were not presented.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This assessment is based on data submitted by the applicant company up to and including ***13 June 2008.***

Drug prices are those available at the time the papers were issued to SMC for consideration. These have been confirmed from the eVadis drug database.

** Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/*

The undernoted references were supplied with the submission.

Reygagne P, Mrowietz U, Decroix J, de Waard-van der Spek FB, Acebes LO, et al. Clobetasol propionate shampoo 0.05% and calcipotriol solution 0.005%: a randomized comparison of efficacy and safety in subjects with scalp psoriasis. J Dermatolog Treat 2005; 16(1): 31-36.

Griffiths CE, Finlay AY, Fleming CJ, Barker JN, Mizzi F, et al. A randomized, investigator-masked clinical evaluation of the efficacy and safety of clobetasol propionate 0.05% shampoo and tar blend 1% shampoo in the treatment of moderate to severe scalp psoriasis. J Dermatolog Treat 2006; 17(2): 90-95.

Andres P, Poncet M, Farzaneh S, Soto P. Short-term safety assessment of clobetasol propionate 0.05% shampoo: hypothalamic-pituitary-adrenal axis suppression, atrophogenicity, and ocular safety in subjects with scalp psoriasis. J Drugs Dermatol 2006; 5(4): 328-332.