



HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

Opinion

21 June 2006

APSOR 4 micrograms/g - topical emulsion

1 × 50 ml high-density polyethylene (HDPE) bottle: 372 202-4

Applicant: Merck Lipha Santé SAS

Tacalcitol monohydrate

List II

Date of Marketing Authorisation: 09 January 2006

Purpose of application: Inclusion on the list of proprietary medicinal products reimbursed by National Health Insurance (NHI) and on the list of products approved for use by hospitals and other public services

Department for the Assessment of Health Procedures and Products

1 PRODUCT CHARACTERISTICS

1.1. Active ingredient

Tacalcitol monohydrate

1.2. Indications

Mild to moderate psoriasis of the scalp.

1.3. Dosage

Adults: 1 daily application to the lesions, preferably in the evening. The maximum weekly dose should not exceed 70 ml.

If used concurrently with Apsor ointment, the total weekly dose of tacalcitol should not exceed 280 µg, e.g. 35 ml of emulsion and 35 g of ointment.

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2005)

D	: dermatologicals
D05	: antipsoriatics
D05A	: antipsoriatics for topical use
D05AX	: other antipsoriatics for topical use
D05AX04	: tacalcitol

2.2. Products in the same therapeutic area

2.2.1. Comparator drugs

Only one proprietary product not containing topical corticosteroids is indicated for topical treatment of psoriasis of the scalp:

- Daivonex 50 micrograms per ml, solution for use on scalp

2.3. Products with the same therapeutic aim

Other topical treatments indicated for the treatment of psoriasis in a pharmaceutical form suitable for the scalp (lotions and gels), particularly topical corticosteroids:

- Betneval (betamethasone) 0.1%, topical emulsion
- Dermoval (betamethasone), gel
- Diprosalic (betamethasone), lotion
- Diprosone (betamethasone) 0.05%, lotion
- Epitopic (difluprednate) 0.05, topical gel
- Locoid (hydrocortisone), lotion, and locoid, topical emulsion
- Synalar (fluocinolone) 0.01%, topical solution
- Topsyne (fluocinolone), topical solution

3 ANALYSIS OF AVAILABLE DATA

3.1. Efficacy

- **H 364 000 –03/96¹**

Randomised, double-blind, placebo-controlled trial to evaluate the efficacy and safety of Apsor 4 µg/g emulsion (one application every evening) in the treatment of psoriasis of the scalp in 266 patients. The patients were treated for 8 weeks.

- **Primary endpoint**

Total psoriasis score (compound score based on erythema, infiltration and desquamation).

- **Inclusion criteria**

- patients aged between 18 and 80 years
- total psoriasis score between 3 and 8 (on a 12-point scale)
- desquamation score between 1 (mild) and 3 (moderate)
- individual score (erythema, infiltration and desquamation) ≥ 1 (corresponding to at least mild psoriasis)

- **Results**

- The total psoriasis score (primary endpoint) was reduced by 53% in the Apsor 4 µg/g group compared with 30% in the placebo group; p < 0.0001 (see table).

Efficacy of Apsor 4 µg/g in psoriasis of the scalp

	Total psoriasis score (ITT analysis)	
	Apsor emulsion n = 133	Placebo n = 133
Day 0	6.2 (3 - 9)	6.1 (3 - 9)
Week 8	2.9 (0 - 9)	4.4 (0 - 9)
Mean reduction by Wk 8	-3.2 (-8 - 3)	-1.8 (-9 - 3)

- The incidence of adverse effects was similar in the two groups (10.3% in the tacalcitol group versus 8.7% in the placebo group). Adverse effects were local, generally transient, reversible on cessation of treatment and similar to those observed with the ointment form: pruritus (1.5%), erythema (3%), and a burning sensation on the skin (3%).
- Comment:
- No study comparing Apsor 4µg/g with Daivonex 50 µg/ml (calcipotriol) solution was included in the dossier. Only an indirect comparison based on published data was submitted (2 studies, one against placebo², the other against betamethasone 17-valerate solution³). This cannot be taken into account because there are no data available on:

¹ Study published in German (2004)

² Green C et al. Comparative effects of calcipotriol (MC903) solution and placebo (vehicle of MC903) in the treatment of psoriasis of the scalp. Br J Dermatol 1994;130:483-7.

³ Klaber MR et al. Comparative effects of calcipotriol solution (50 micrograms/ml) and betamethasone 17-valerate solution (1mg/ml) in the treatment of scalp psoriasis. Br J Dermatol 1994;131:678-83.

- the comparability of the populations included
- the exhaustiveness of the studies taken into account
- any concomitant treatment.

3.2. Conclusion of efficacy and safety

The efficacy and safety of Apsor 4 µg/g emulsion in the treatment of mild to moderate psoriasis of the scalp was assessed against a placebo in 266 patients. After 8 weeks of treatment, the total psoriasis score (primary endpoint) was significantly reduced in the Apsor 4 µg/g group compared with the placebo group.

The Committee regretted the lack of any direct comparison with calcipotriol (Daivonex®).

4 CONCLUSIONS OF THE TRANSPARENCY COMMITTEE

4.1. Actual benefit

Psoriasis is a chronic, non-infectious, non-contagious and most often benign inflammatory dermatosis which may, however, have serious psycho-social effects in its severe forms.

- This product provides symptomatic treatment.
- Its ratio of efficacy to adverse effects on the scalp is moderate.
- It is a first-line treatment.
- Alternative treatments are available.

Public health benefit

The public health burden caused by psoriasis is substantial because the disorder is common (see § 4.4) and potentially serious. The burden is however moderate in the population concerned by scalp psoriasis. Moreover, management of patients with mild to moderate psoriasis is not a public health need.

On the basis of clinical trial data, this product is not expected to have any impact on morbidity or quality of life.

However, no public health benefit is expected.

The actual benefit provided by Apsor is substantial.

4.2. Improvement in actual benefit

Apsor 4µg/g (topical emulsion) does not lead to any improvement in the actual benefit (level V) in the management of mild to moderate psoriasis of the scalp.

4.3. Therapeutic use⁴

- Psoriasis treatments depend not only on the severity and extent of the lesions, but also on functional, aesthetic, professional and relational issues, on the psychological impact of the disease, and on the patient's expectations.

⁴ Parier J, Dubertret L. Psoriasis du cuir chevelu. Ann Dermatol Venereol. 2002;129:1405-7.

- Patients with very limited and/or psychologically well-accepted psoriasis are not always treated as a matter of routine.
- The aim of treating the scalp is to stop itching and desquamation, to depigment the lesions, and to maintain this outcome. Intensive therapy is given until a complete clinical response is achieved in order to avoid any early recurrence; this is followed by maintenance treatment.
- Keratolytic preparations containing salicylic acid are used to expose highly keratotic lesions prior to topical treatment. However, few topical treatments are available for psoriasis of the scalp. Topical corticosteroids and vitamin D3 derivatives are the first-line treatments for mild to moderate psoriasis. Emulsion, gel and lotion forms are particularly suitable for treating affected scalp (see table below).

Treatment of scalp psoriasis by topical vitamin D3 derivatives and corticosteroids

Topical product	Comment
Vitamin D3 derivatives	• As effective as potent corticosteroid lotions in superficial psoriasis; ^{5,6} less effective in severe psoriasis⁷ • Reach peak efficacy generally after 4-8 weeks of treatment • Calcipotriol is the gold standard (most effective) • First-line treatment in moderate, essentially keratotic forms of psoriasis • Used for maintenance treatment (topical corticosteroids are sometimes added for short periods)
Corticosteroids	• Initial treatment of choice when the scalp is highly inflamed. A vitamin D derivative is then introduced and the corticosteroids are gradually reduced.
Combination of vitamin D derivatives and corticosteroids	• Used as initial intensive therapy in severe forms of psoriasis

4.4. Target population

Psoriasis affects roughly 2 to 3% of the general population,^{8,9,10} or 1.2 to 1.8 million patients. However, there are no precise data on the prevalence of scalp psoriasis; experts think it is about 50%. The target population for Apsor emulsion would therefore be between 600 000 and 900 000 patients.

⁵ Duweb GA et al. Scalp psoriasis: topical calcipotriol 50 µg/g/ml solution vs betamethasone valerate 1% lotion. Int J Clin Pharmacol Res 2000;20:65-8.

⁶ Thaci D et al. Calcipotriol solution for the treatment of scalp psoriasis: evaluation of efficacy, safety and acceptance in 3,396 patients. Dermatology 200;203:153-6.

⁷ Klaber MR et al. Comparative effects of calcipotriol solution (50 µg/ml) vs betamethasone valerate (1mg/ml) in the treatment of scalp psoriasis. Br J Dermatol 1994;131:678-83

⁸ Farber EM, Nall ML. The natural history of psoriasis in 5,600 patients. Dermatologica. 1974;148:1-18.

⁹ Van de Kerkhof PC et al. Evaluation of topical drug treatment in psoriasis. Dermatology. 1998;197:31-6.

¹⁰ Van de Kerkhof PC et al. Scalp psoriasis, clinical presentations and therapeutic management. Dermatology. 1998;197:326-34.

4.5. Recommendations of the Transparency Committee

The Committee approved the inclusion of this product on the list of proprietary medicinal products reimbursed by NHI and on the list of medicinal products approved for use by hospitals and other public services, subject to the indications and posology stated in the Marketing Authorisation.

4.5.1 Packaging: As required by the prescription.

4.5.2 Reimbursement rate: 65%.