IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PPA1328/023/003
Case No: 2034068

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

B & S Healthcare

Unit 4, Bradfield Road, **Ruislip**, **Middlesex**, **HA4 0NU**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Dovonex 50 micrograms/ml Scalp Solution

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **26/03/2007** until **25/01/2012**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dovonex 50 micrograms/ml Scalp Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of solution contains 50 micrograms of calcipotriol (as the hydrate).
Excipient: Propylene glycol (E1520)

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Scalp solution.
Product imported from Greece and the UK:
Clear, colourless, slightly viscous solution with an odour of menthol.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dovonex® Scalp Solution is indicated for the topical treatment of scalp psoriasis.

4.2 Posology and method of administration

Adults: Dovonex® Scalp Solution should be applied twice daily (morning and evening) to the affected areas. Maximum weekly dose should not exceed 60 ml.

When used together with Dovonex® Cream or Ointment, the total dose of calcipotriol should not exceed 5mg in any week.

Children: There is no experience of the use of Dovonex® Scalp Solution in children.

4.3 Contraindications

Known hypersensitivity to any of the ingredients.

Due to the content of calcipotriol, Dovonex® is contraindicated in patients with known disorders of calcium metabolism.

4.4 Special warnings and precautions for use

Dovonex® Scalp Solution should not be used on the face. The patients must be instructed in correct

use of the product to avoid application and accidental transfer to the face. Hands must be washed after each application.

Use of Dovonex® should be avoided in patients with severe renal failure or severe hepatic disorders.
The risk of hypercalcaemia is minimal when the dosage recommendations are followed. Hypercalcaemia may occur if the maximum weekly dose (60 ml) is exceeded. However, serum calcium is quickly normalised when treatment is discontinued.
During Dovonex treatment physicians may wish to advise patients to limit or avoid excessive exposure to either natural or artificial sunlight. Topical calcipotriol should be used with UV radiation only if the physician and patient consider that the potential benefits outweigh the potential risks (See section 5.3)
Propylene glycol may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Pregnancy and lactation

Standard reproduction studies in animals have shown no evidence of drug related abnormality. There is no experience of use in humans in pregnancy and lactation, therefore use should be limited to that considered essential by the physician.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Very common > 1/10
Common > 1/100 and < 1/10
Uncommon > 1/1,000 and < 1/100
Rare > 1/10,000 and < 1/1,000
Very rare < 1/10,000
The most frequently reported undesirable effects are various skin reactions and in particular application site reactions. Hypercalcaemia and allergic reactions have been reported very rarely.

Based on clinical data for Dovonex® Scalp Solution undesirable effects occurred in approximately 25% of the patients.
Burning and stinging sensation are very common. Pruritus, skin irritation, dry skin, erythema and rash are common. Contact dermatitis, eczema and aggravated psoriasis are uncommon.
Systemic effects after topical use may appear very rarely causing hypercalcaemia or hypercalciuria, cf. section 4.4.

Post-market data on Dovonex® cream, ointment and scalp solution
Transient changes in skin pigmentation, transient photosensitivity reactions and hypersensitivity reactions including urticaria, angioedema, periorbital or facial oedema have been reported very rarely.
Perioral dermatitis may occur rarely.
Based on post-marketing data the total 'reporting rate' of undesirable effect is very rare being approximately 1:10,000 treatment courses.
The undesirable effects are listed by MedDRA SOC and the individual undesirable effects are listed starting with the most frequently reported.

Skin and subcutaneous tissue disorders:

Pruritus
Skin burning sensation
Skin stinging sensation
Skin irritation
Skin dry
Erythema
Rash*
Eczema
Contact Dermatitis
Aggravated Psoriasis
Skin hyperpigmentation
Skin depigmentation
Photosensitivity reaction
Urticaria
Facial oedema
Periorbital oedema
Angioedema
* Various types of rash reactions such as scaly, erythematous, maculo-papular and pustular have been reported

Metabolism and nutrition disorders:

Hypercalcaemia
Hypercalciuria

4.9 Overdose

Use above the recommended dose may cause elevated serum calcium which should rapidly subside when the treatment is discontinued.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Calcipotriol is a vitamin D derivative. *In vitro* data suggest that calcipotriol induces differentiation and suppresses proliferation of keratinocytes. This effect is the proposed basis for its effect in psoriasis.

5.2 Pharmacokinetic properties

Calcipotriol is only slightly absorbed from the skin.

5.3 Preclinical safety data

The effect on the calcium metabolism is approximately 100 times less than that of the hormonally active form of vitamin D_3.

A dermal carcinogenicity study in mice showed no indications of increased carcinogenic risks. Calcipotriol solution

was applied topically for up to 24 months at doses of 3, 10 and 30 µg/kg/day (corresponding to 9, 30 and 90 µg/m2/day). The high-dose was considered to be the Maximum Tolerated Dose for dermal treatment of mice with calcipotriol. Survival was decreased at 10 and 30 µg/kg/day, particularly in the males. The reduced survival was associated with an increased incidence of obstructive uropathy, most probably caused by treatment-related changes in the urinary composition. This is an expected effect of treatment with high doses of calcipotriol or other vitamin D analogues. There were no dermal effects and no dermal or systemic carcinogenicity.
In a study where albino hairless mice were repeatedly exposed to both ultraviolet (UV) radiation and topically applied calcipotriol for 40 weeks at the same dose levels as in the dermal carcinogenicity study, a reduction in the time required for UV radiation to induce the formation of skin tumours was observed (statistically significant in males only), suggesting that calcipotriol may enhance the effect of UV radiation in induce skin tumours. The clinical relevance of these findings in unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

hyprolose
isopropyl alcohol
levomenthol
sodium citrate
propylene glycol (E1520)
purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

White HDPE bottles fitted with an LDPE nozzle and blue HDPE screw cap.
Pack size: 30ml and 120 ml

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The alcohol base is flammable.

7 Parallel Product Authorisation Holder

B&S Healthcare
Unit 4
Bradfield Road
Ruislip
Middlesex
HA4 0NU
United Kingdom

8 Parallel Product Authorisation Number

PPA1328/23/3

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation 26th January 2006

10 DATE OF REVISION OF THE TEXT

February 2007