Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dovonex 50 micrograms/g Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of ointment contains 50 micrograms calcipotriol.

Excipient: Propylene glycol (E1520)

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ointment.

Product sourced from the UK and Greece:
A faint, translucent white to yellowish ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dovonex Ointment is indicated for the topical treatment of plaque psoriasis (psoriasis vulgaris). Dovonex ointment may also be used in combination with phototherapy, acitretin, cyclosporin or topical corticosteroids.

4.2 Posology and method of administration

Adults: The ointment should be applied to the affected area once to twice daily. Twice daily application of the ointment is often preferred initially. Application of the ointment can be reduced to once daily when appropriate. Maximum weekly dose should not exceed 100g.

Twice daily application of Dovonex in combination with phototherapy, cyclosporin or acitretin and once daily application of Dovonex in combination with corticosteroids (e.g. administration of Dovonex in the morning and steroid in the evening) is effective and well tolerated.

The addition of Dovonex twice daily will enhance the efficacy and reduce the dosage of cyclosporin, acitretin and phototherapy.

Children: Over 12 years: Dovonex Ointment should be applied to the affected area twice daily. Maximum weekly dose should not exceed 75g.

Aged 6 to 12 years: Dovonex Ointment should be applied to the affected area twice daily. Maximum weekly dose should not exceed 50g.

Under 6 years: There is limited experience of the use of Dovonex Ointment in this age group. A maximum safe dose has not been established.

4.3 Contraindications

Use in patients with hypersensitivity to any of its constituents.

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

4.4 Special warnings and precautions for use

Dovonex Ointment should not be used on the face. Patients should be advised to wash their hands after applying the ointment and to avoid inadvertent 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 dosage recommendations are followed. Hypercalcaemia may occur if the maximum weekly dose (100g) 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

Safety for use during human pregnancy has not yet been established, although studies in experimental animals have not shown teratogenic effects. Avoid use in pregnancy unless there is no safer alternative. It is not known whether calcipotriol is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Does not apply.

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 sire reaction. Hypercalcaemia and allergic reactions have been reported very rarely.

Based on clinical data for Dovonex ointment undesirable effects occurred in approximately 15% of the patients.

Pruritus, skin irritation, burning and stinging sensation, dry skin, erythema and rash are common. Contact dermatitis, eczema and psoriasis aggravated 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, angiodema, periorbital or face oedema have been reported very rarely. Perioral dermatitis may occur rarely.

Based on post-marketing data the total 'reporting rate' of undesirable effects is very rare being approximately 1:10,000 treatment courses.

The undesirable effects are listed be 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
Dermatitis contact
Psoriasis aggravated
Skin hyperpigmentation
Skin pigmentation
Photosensitivity reaction
Urticaria
Face oedema
Periorbital oedema
Angiodema

*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

Hypercalcaemia may occur in patients with plaque psoriasis who use more than 100g of Dovonex Ointment weekly and has been reported at lower doses in patients with generalised pustular or erythrodermic exfoliative psoriasis.

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 but with less effect on calcium metabolism. This is the proposed basis for its effect in psoriasis.

5.2 Pharmacokinetic properties

Absorption through skin appears to be low but that which reaches the systemic circulation is rapidly metabolized to inactive substances.

5.3 Preclinical safety data

The effect on 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 obstruction uropathy, most probably caused by treatment-related changes in the urinary composition. This is an expected effect of treatment with high dose 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 the calcipotriol may enhance the effect of UV radiation to induce skin tumours. The clinical relevance of these findings is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Disodium phosphate dihydrate
DL-alpha-tocopherol
Liquid paraffin
Polyoxyethylene-(2)-stearyl ether/Macrogol (2) stearyl ether
Propylene glycol (E1520)
Purified water
White soft paraffin

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

Lacquered aluminium tube with polypropylene screw cap, contained in an outer cardboard carton.

Pack size: 30 g or 60 g.

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

Wash hands after use.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

PCO Manufacturing Limited
Unit 10, Ashbourne Business Park
Rath
Ashbourne
Co. Meath

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 0465/132/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 June 2004

10 DATE OF REVISION OF THE TEXT

October 2008