Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dovonex 50 microgram/g Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of ointment contains 50 micrograms of calcipotriol.

Excipient with known effect
Contains propylene glycol 100 mg/g.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ointment.

An off-white to yellowish white translucent 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 acitretin, ciclosporin or topical corticosteroids.

4.2 Posology and method of administration

Posology

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 ciclosporin 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 ciclosporin and acitretin.

Paediatric population
Over 12 years: Dovonex Ointment should be applied to the affected area twice daily. Maximum weekly dose should not exceed 75 g.
Aged 6 to 12 years: Dovonex Ointment should be applied to the affected area twice daily. Maximum weekly dose should not exceed 50 g.
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.

Method of administration
For cutaneous use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Due to the content of calcipotriol, Dovonex is contraindicated in patients with known disorders of calcium metabolism (see section 4.4).

4.4 Special warnings and precautions for use

Effects on calcium metabolism:
Due to the content of calcipotriol, hypercalcaemia may occur if the maximum weekly dose is exceeded. Serum calcium is normalised when treatment is discontinued. The risk of hypercalcaemia is minimal when the recommendations relevant to calcipotriol are followed. The maximum weekly dose in adults is 100 g of cream or ointment (equivalent to 5 mg of calcipotriol) or 60 ml of scalp solution (equivalent to 3 mg of calcipotriol). When cream, ointment or cutaneous solution are applied together, the total dose of calcipotriol should not exceed 5 mg per week.

Local adverse reactions:
DovonexOintment should not be applied to the face. The patient must be instructed in correct use of the product to avoid accidental transfer to the face and eyes (see section 4.8). Hands must be washed after each application to avoid accidental transfer to these areas.

Dovonex Ointment should be used with caution in skin folds, as this may increase the risk of developing skin irritation (see section 4.8).

UV exposure:
During Dovonex Ointment treatment, physicians are recommended to advise patients to limit or avoid excessive exposure to either natural or artificial sunlight. DovonexOintment 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).

Unevaluated use:
Due to lack of data, Dovonex Ointment should be avoided in guttate, erythrodermic, exfoliative and pustular psoriasis.

Due to lack of data, Dovonex should be avoided in patients with severe liver and kidney disease.

Adverse reactions to excipients:
Dovonex Ointment contains propylene glycol as an excipient which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interactions

No interaction studies have been performed with Dovonex.

4.6 Fertility, pregnancy and lactation

Pregnancy
Safety for use of calcipotriol during human pregnancy has not been established. When calcipotriol was administered orally in animals, reproductive toxicity has been shown. Calcipotriol should not be used during pregnancy unless clearly necessary.

Breast-feeding
It is unknown whether calcipotriol is excreted in human milk. Caution should be exercised when prescribing Dovonex Ointment to women who breast-feed. The patient should be instructed not to use Dovonex Ointment on the breast when breast-feeding.

Fertility
Studies in rats with oral doses of calcipotriol demonstrated no impairment of male and female fertility.

4.7 Effects on ability to drive and use machines

Dovonex has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The estimation of the frequency of adverse reactions is based on a pooled analysis of data from clinical studies and spontaneous reporting.

The most frequently reported adverse reactions during treatment are pruritus, skin irritation and erythema.

Systemic reactions (hypercalcaemia and hypercalciuria) have been reported. The risk of developing such reactions increases if the recommended total dose is exceeded (see section 4.4).

Adverse reactions are listed by MedDRA SOC and the individual adverse reactions are listed starting with the most frequently reported. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Very common (≥1/10)
Common (≥1/100 to < 1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)

Infections and infestations	
Uncommon (≥1/1,000 to <1/100)	Folliculitis
Immune system disorders	
Rare (≥1/10,000 to <1/1,000)	Hypersensitivity
Metabolism and nutrition disorders	
Rare (≥1/10,000 to <1/1,000)	Hypercalcaemia
Skin and subcutaneous tissue disorders	
Common (≥1/100 to < 1/10)	Psoriasis aggravated Dermatitis Erythema Skin exfoliation Skin burning sensation Skin irritation Pruritus
Uncommon (≥1/1,000 to <1/100)	Rash* Dry skin
Rare (≥1/10,000 to <1/1,000)	Photosensitivity reaction Skin oedema Urticaria Seborrhoeic dermatitis
Unknown frequency	Periorbital or face oedema
Renal and urinary disorders	
Rare (≥1/10,000 to <1/1,000)	Hypercalciuria
General disorders and administration site conditions	
Common (≥1/100 to <1/10)	Application site pain
Uncommon (≥1/1,000 to	Application site pigmentation changes

<1/100)	

* Various types of rash reactions such as rash erythematous, rash maculo-papular, rash morbilliform, rash papular and rash pustular have been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, website: www.hpra.ie.

4.9 Overdose

Use above the recommended dose may cause elevated serum calcium which subsides when treatment is discontinued. The symptoms of hypercalcemia include polyuria, constipation, muscle weakness, confusion and coma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antipsoriatics for topical use.

ATC code: D05AX02

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 metabolised 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 D3.

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/m^2/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.

Calcipotriol has shown maternal and fetal toxicity in rats and rabbits when given by the oral route at doses of 54 µg/kg/day and 12 µg/kg/day, respectively. The fetal abnormalities observed with concomitant maternal toxicity included signs indicative of skeletal immaturity (incomplete ossification of the pubic bones and forelimb phalanges, and enlarged fontanelles) and an increased incidence of supernumerary ribs.

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 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
all-*rac*-α-tocopherol
Liquid paraffin

Macrogol-(2)-stearyl ether
Propylene glycol
White soft paraffin
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

After first opening: 6 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Lacquered aluminium tube with polyethylene screw cap.
Pack sizes: 5g, 15g, 30g, 60g, 100g and 120g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Leo Laboratories Limited
285 Cashel Road
Dublin 12
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0046/061/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25 February 1991

Date of last renewal: 25 February 2006

10 DATE OF REVISION OF THE TEXT

May 2020