Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dovonex Psoriasis 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.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ointment

Off-white to yellowish-white translucent ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dovonex Psoriasis 50 microgram/g ointment is indicated for topical treatment of adults with mild to moderate plaque psoriasis which has been previously diagnosed by a doctor.

Plaque psoriasis (well defined, thickened, scaly, red lesions on trunk and/or limbs) is mild to moderate when the area affected does not exceed 10% of body surface area (for guidance purposes, the body surface area of an arm is approximately 9%).

4.2 Posology and method of administration

Adults (18 years or older):

Dovonex Psoriasis 50 microgram/g ointment should be applied to the affected area once daily. The maximum weekly dose should not exceed 100 g.

Dovonex Psoriasis 50 microgram/g ointment should not be used in children and adolescents aged less than 18 years as supervision by a doctor is needed in these age−groups (see section 4.4 for further information).

Method of administration

Topical use.

Dovonex Psoriasis 50 microgram/g ointment should not be applied to the face, scalp, flexures or genital area.

The patient must be instructed in correct use of the product to avoid accidental transfer to the face and eyes. Hands must be washed after each application to avoid accidental transfer to these areas.

It is not recommended to take a shower or bath immediately after application of Dovonex Psoriasis 50 microgram/g ointment. For advice about duration of treatment, see section 4.4.

4.3 Contraindications

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

The safety of calcipotriol has not been established in pregnancy or breast−feeding. Women who are pregnant or breast−feeding should not use Dovonex Psoriasis 50 microgram/g ointment but should be advised to seek the advice of a doctor (see section 4.6).

Due to the content of calcipotriol, Dovonex Psoriasis 50 microgram/g ointment is contraindicated in patients with known disorders of calcium metabolism (see section 4.4).

4.4 Special warnings and precautions for use

Duration of treatment

The patient should be advised to see a doctor if the condition does not start to improve within 4 weeks of treatment, or becomes worse at any time during treatment.

If within 12 weeks the condition has cleared or is substantially improved and the patient is satisfied with the outcome, the treatment can be stopped. The treatment can be re-started if psoriasis reappears.

If a patient does not reach a satisfactory outcome (e.g. achieves less than 50% reduction in psoriasis) by 12 weeks, this indicates the need for doctor review.

Symptom changes

If a patient develops more extensive skin involvement, the patient should be referred to their doctor.

If a patient develops nail involvement, the patient should be referred to their doctor.

If a patient develops joint pains and/or swelling of joints, the patient should be referred to their doctor.

Patients with psoriasis should see their doctor once a year for a review of their condition.

Effects on calcium metabolism

Due to the content of calcipotriol in Dovonex Psoriasis 50 microgram/g ointment, hypercalcaemia may occur if the maximum weekly dose is exceeded.

Symptoms of hypercalcaemia can include excessive thirst, frequent urination, stomach upset, nausea, vomiting, constipation, muscle weakness, bone pain, confusion, fatigue or lethargy.

If the patient complains of any of the above symptoms or signs associated with hypercalcaemia, the treatment should be suspended and the patient should see their doctor immediately for assessment.

The risk of hypercalcaemia is minimal when the dosage recommendations are followed. The maximum weekly dose in adults is 100 g of Dovonex Psoriasis 50 microgram/g ointment. The patient should be referred back to their doctor if they are using more than 100 g ointment per week.

Dovonex Psoriasis 50 microgram/g ointment should not be covered by any type of occlusive bandage as this may increase the risk of hypercalcaemia.

Local adverse reactions

Dovonex Psoriasis 50 microgram/g ointment should not be applied to the face, scalp, flexures or genital area.

The patient must be instructed in correct use of the product to avoid accidental transfer to the face and eyes. Hands must be washed after each application to avoid accidental transfer to these areas.

Paediatric population

Dovonex Psoriasis 50 microgram/g ointment should not be used in children or adolescents aged less than 18 years as there is an increased risk of hypercalcaemia in this age-group and therefore supervision by a doctor is needed.

UV exposure

Patients should be advised to avoid excessive exposure to either natural or artificial sunlight and avoid the use of UV lamps during treatment with Dovonex Psoriasis 50 microgram/g ointment (see section 5.3).

Other forms of psoriasis

Dovonex Psoriasis 50 microgram/g ointment should not be used on guttate (small, rain drop sized lesions), erythrodermic/exfoliative (merging red inflammatory lesions covering most of body surface area, with large amounts of dead skin being shed) and pustular psoriasis (raised pus filled pustules), except under the supervision of a doctor.

Dovonex Psoriasis 50 microgram/g ointment is not suitable for patients with psoriatic arthritis or nail involvement. These patients should be referred to their doctor.

Concomitant use with other products

Dovonex Psoriasis 50 microgram/g ointment is suitable for use as a monotherapy. Emollients may be used in conjunction with the treatment.

The concomitant use of Dovonex Psoriasis 50 microgram/g ointment with other psoriasis treatments such as other topical products containing calcipotriol, topical corticosteroids, topical retinoids, calcineurin inhibitors or systemic anti-psoriatic therapies should only be undertaken under the advice and supervision of a doctor.

Dovonex Psoriasis 50 microgram/g ointment should not be used concurrently with calcium or vitamin D supplements, or drugs which enhance the systemic availability of calcium.

Unevaluated use

Due to lack of data, Dovonex Psoriasis 50 microgram/g ointment should be avoided in patients with severe liver and kidney disease.

Adverse reactions to excipients

Dovonex Psoriasis 50 microgram/g ointment contains propylene glycol as an excipient which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with Dovonex Psoriasis 50 microgram/g ointment (see section 4.4 Concomitant use with other products).

Dovonex Psoriasis 50 microgram/g ointment should not be used concurrently with calcium or vitamin D supplements, or drugs which enhance the systemic availability of calcium.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of calcipotriol has not been established in pregnancy. Women who are pregnant should not use Dovonex Psoriasis 50 microgram/g ointment but should seek the advice of a doctor (see section 4.3). Studies in animals have shown reproductive toxicity when calcipotriol was administered orally.

Breast-feeding

It is unknown whether calcipotriol is excreted in breast milk. Women who are breast−feeding should not use Dovonex Psoriasis 50 microgram/g ointment and should seek the advice of a doctor.

Fertility

Women who are planning to become pregnant while using Dovonex Psoriasis 50 microgram/g ointment should seek the advice of a doctor.

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

Calcipotriol has no or negligible influence on the ability to drive and to 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
Not known (cannot be estimated from the available data)

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
Not known	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 <1/100)	Application site pigmentation changes

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

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, Earlsfort Terrace, IRL-Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.

Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Due to the content of calcipotriol in Dovonex Psoriasis 50 microgram/g ointment, hypercalcaemia may occur if the maximum weekly dose is exceeded. Symptoms and signs of hypercalcaemia can include excessive thirst, frequent urination, stomach upset, nausea, vomiting, constipation, muscle weakness, bone pain, confusion, coma, fatigue or lethargy.

If the patient complains of any of the above symptoms, the treatment should be suspended and the patient should be referred to their doctor immediately for assessment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: D05A X02

Pharmacotherapeutic group: Other antipsoriatics for topical use

Calcipotriol is a vitamin D derivative. *In vitro* data suggest that calcipotriol induces differentiation and suppresses proliferation of keratinocytes. This is the proposed basis for its effect in psoriasis. A clinical improvement usually starts to become apparent after two weeks' treatment.

5.2 Pharmacokinetic properties

Transdermal absorption of calcipotriol has been shown to be in the range of 1−6% of the administered dose.

Following systemic exposure, calcipotriol is rapidly and extensively metabolised.

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.

Calcipotriol has shown maternal and foetal 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 foetal 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.

There is insufficient pharmacokinetic data available to quantify the safety margin for the embryofoetal effects.

A dermal carcinogenicity study in mice and an oral carcinogenicity study in rats revealed no special hazard to humans.

In a study where albino hairless mice were repeatedly exposed to both ultraviolet (UV) radiation and dermally administered calcipotriol for 40 weeks at dose levels corresponding to 9, 30 and 90 µg/m2/day (equivalent to 0.25, 0.84, 2.5 times the maximum recommended daily dose for a 60 kg adult, respectively), 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

Should not be mixed with other medicinal products.

6.3 Shelf life

Unopened container: 2 years.

After first opening of container: 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 polypropylene screw cap.

Pack size: 60 g

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

LEO Laboratories Limited
Cashel Road
Dublin 12
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0046/064/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 April 2016.

10 DATE OF REVISION OF THE TEXT

December 2016