Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dovonex 50 micrograms/g Cream.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains 50 micrograms of calcipotriol (as the hydrate).
Excipient(s): Cetostearyl alcohol
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.
Product imported from UK:
Soft white cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dovonex Cream is indicated for the topical treatment of plaque psoriasis (psoriasis vulgaris). Dovonex cream may also be used in combination with topical corticosteroids.

4.2 Posology and method of administration

Adults

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

Dovonex Cream in combination with corticosteroids (e.g. administration of Dovonex in the morning and steroid in the evening) is effective and well tolerated.

Children

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

Aged 6 to 12 years
Dovonex Cream 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 Cream in this age group. A maximum safe dose has not been established.

There is no experience of use of Dovonex in combination with other psoriasis therapies 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 cream 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 (100 g) 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).

Cetostearyl alcohol may cause local skin reactions.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Safety for use of Calcipotriol during human pregnancy and lactation has not been established. Studies in animals have not shown teratogenic effects. It is not known whether calcipotriol is excreted in breast milk. Calcipotriol should not be used during pregnancy and lactation unless clearly necessary.

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

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 adverse reactions are various skin reactions, in particular lesional/perilesional irritation. Systemic effects (hypercalcaemia and hypercalciuria) after topical use may appear very rarely, especially if the recommend total dose is exceeded. Allergic reactions have been reported very rarely. Based on clinical data, approximately 25% of the patients treated with Dovonex® cream could experience an adverse reaction. These reactions are usually mild.

Immune system disorders

Very rare:	allergic reactions

Metabolism and nutrition disorders

Very rare:	hypercalcaemia, hypercalciuria

Skin and subcutaneous tissue disorders

Very common:	skin irritation
Common:	rash*, burning sensation, stinging sensation, skin dry, pruritus, erythema, contact dermatitis.
Uncommon:	psoriasis aggravated, eczema.
Unknown frequency:	transient changes in skin pigmentation, transient photosensitivity, urticaria, angioedema, periorbital or face oedema.

*Various types of rash reactions such as scaly, erythematous, maculopapular, pustular, bullous have been reported.

4.9 Overdose

Use above the recommended dose may cause elevated serum calcium, which quickly subsides when treatment is discontinued.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 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/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 30µg/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 to induce skin tumours. The clinical relevance of these findings is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol Cetostearyl Ether
Cetostearyl alcohol
Choroallylhexaminium chloride (Dowicil 200)
Disodium edetate
Disodium phosphate dihydrate
Glycerol 85%
Liquid paraffin
White soft paraffin
Sodium hydroxide
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product is 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

Store below 25°C.

6.5 Nature and contents of container

Aluminium tube with screw cap in a cardboard carton of 120g

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

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

Clear Pharmacy
157-173 Roden Street
Belfast BT12 5QA
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1596/39/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21st December 2010

10 DATE OF REVISION OF THE TEXT

December 2011