Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Dovonex Psoriasis 50 microgram/g Ointment (calcipotriol)

Public Consultation

Proposal to make available from Pharmacies without prescription

The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK government agency responsible for regulating medicines and medical devices. We continually review the safety of medicines and vaccines in the UK, and inform healthcare professionals and the public of the latest updates through several means, including public reclassification reports. Suspected side-effects to any drug or vaccine can be reported to MHRA by both healthcare professionals and members of the public via the Yellow Card Scheme (http://www.mhra.gov.uk/yellowcard)

Ref: ARM95

Dovonex Psoriasis 50 microgram/g Ointment (calcipotriol)

Proposal to make available from Pharmacies without prescription

We want to know what you think

- Dovonex Psoriasis 50 microgram/g Ointment is used to treat mild to moderate plaque psoriasis which has been previously diagnosed by a doctor in adults aged 18 years and over.
- Calcipotriol is only at the moment available on prescription (known as Dovonex Ointment).
- We propose to make it available in pharmacies without prescription.
- The Commission on Human Medicines has advised that this product can be available as a pharmacy medicine.
- We want to know what you think about this change.

Please tell us your views – please use the form at the end of this document.

The deadline for comments is **20 April 2017**.

In this document there is:

- A summary of the proposed change and the background
- A copy of the patient information leaflet and label proposed if the change goes ahead
- A form for your response

The full name of the medicine is Dovonex Psoriasis 50 microgram/g Ointment – in this document, we will call it 'Dovonex Psoriasis Ointment.'

Contents:

Product details:

Product name: Dovonex Psoriasis 50 microgram/g Ointment

Active substances: Calcipotriol

Licence holder: Leo Laboratories Limited

Route of sale/supply: Current - on prescription (POM); Proposed - Pharmacy (P)

Indication: Treatment of adults (aged 18 years and over) with mild to moderate plaque psoriasis which has been previously diagnosed by a doctor.

Marketing Authorisation Number: PL 00043/0219 – 0001

Consultation is open from: 30 March 2017 – 20 April 2017

Reference: ARM95

Contact: reclassification@mhra.gsi.gov.uk

1. Background on deciding where medicines are available

The role of MHRA
MHRA regulates medicines and medical devices in the UK, on behalf of the UK Licensing Authority. This means that MHRA decides whether medicines are available:

- on prescription only - 'prescription only medicine' (POM)
- bought from pharmacies - 'pharmacy medicine' (P)
- bought from other shops - 'general sales list medicine' (GSL)

What is re-classification of a medicine?
Making a change on where a medicine is available is called 'reclassification'. This is sometimes referred to as 'switching'. To decide on this change, MHRA may:

- take advice from its committees of external experts
- take advice from a group ('stakeholder group') of health professionals and representatives of people affected by the classification change
- run a public consultation

To be reclassified from POM to P, a medicine must:

- be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
- be generally used correctly (ie not frequently or to a wide extent used incorrectly)
- not contain substances or preparations of substances where the activity of the product or its side effects require further investigation
- not normally be prescribed by a doctor for injection (parenteral administration)

What evidence is needed?
A company or organisation can ask MHRA for a medicine to be available as a pharmacy medicine or a general sale medicine. To do this, they need to get together evidence to show that the medicine

a) is likely to be used appropriately, and
b) with relatively little danger to the public.

This evidence needs to focus on the risk to the public. This includes evidence on the possible abuse or misuse of the medicine. The evidence may include:

- clinical studies
- evidence showing acceptable level of side effects
- advice of experts
- views of relevant health professionals and their professional bodies
- views of relevant public associations and individuals with an interest in the medicine under consideration.

Who makes the final decision?
The final decision on whether to approve a change is made by the MHRA, on behalf of the UK Licensing Authority.

2. About Dovonex Psoriasis Ointment

Dovonex Psoriasis Ointment is a medicine to treat mild to moderate plaque psoriasis which has been previously diagnosed by a doctor for adults aged 18 years and over, for a period of not more than 12 weeks. This medicine is currently a Prescription Only Medicine (known as Dovonex Ointment) used to treat plaque psoriasis (psoriasis vulgaris).

Dovonex Ointment will still be available on prescription under the conditions set out in its marketing authorisation (product licence), in addition to this proposed Pharmacy medicine.

Psoriasis is a condition where your skin develops raised red patches and silver coloured scaly patches.

For this reclassification, plaque psoriasis is considered to be `mild to moderate' when no more than 10% of the patient's body is affected and where the psoriasis is confined to the body and/or limbs only. There are a number of products already available without prescription that are licensed for the treatment of psoriasis. They contain substances such as coal tar, dithranol and salicylic acid. There are also a number of emollients (moisturisers) available, which are used to keep the skin hydrated.

The Commission on Human Medicines (CHM) has advised that this product can be made available as a Pharmacy medicine. This report outlines the background to this decision. Please tell us your views by using the response form at the end of this document (Annex 1). The deadline for comments is **20 April 2017**.

The patient information leaflet, label and summary of product characteristics are provided in Annex 2, 3 and 4.

What is in Dovonex Psoriasis Ointment?
Dovonex Psoriasis Ointment contains calcipotriol.

This is the first application for a medicine containing calcipotriol to be available without prescription.

What is calcipotriol used for?
Calcipotriol is one of a group of medicines called vitamin D analogues. When calcipotriol is applied to skin affected by plaque psoriasis, it can help to reduce the number of cells made by the skin, thereby reducing the silver scaly patches and redness associated with psoriasis.

3. Proposal to make Dovonex Psoriasis Ointment available as a Pharmacy medicine

Who has made the proposal?
The licence-holder for Dovonex Psoriasis Ointment (Leo Laboratories Limited) has applied to make this product available through Pharmacies.

What is the view of the Commission on Human Medicines?
The Commission on Human Medicines has advised that Dovonex Psoriasis Ointment can be available as a Pharmacy medicine. Views on the use of this medicine in practice for adults aged 18 years and over with mild to moderate plaque psoriasis were also sought at an ad hoc stakeholder group meeting, held under auspices of CHM. The members of the stakeholder group consisted of healthcare professionals and patients affected by psoriasis. The views of the stakeholder group were summarised in a report which was considered by CHM.

What are the details of this change?
The application proposes to make Dovonex Psoriasis Ointment available through Pharmacy outlets for:

- topical use (application to the skin)
- treatment of mild to moderate plaque psoriasis which has been previously diagnosed by a doctor in adults aged 18 years of age and over
- application once daily
- maximum weekly dose: 60g ointment
- maximum duration of use: 12 weeks
- pack size: 60g ointment

4. How was the proposal assessed for Dovonex Psoriasis Ointment being available on as a Pharmacy medicine?

To be reclassified from POM to P, a medicine must:

- be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
- be generally used correctly (ie not frequently or to a wide extent used incorrectly)
- not contain substances or preparations of substances where the activity of the product or its side effects require further investigation
- not normally be prescribed by a doctor for injection (parenteral administration)

These criteria are set out in the Human Medicines Regulations 2012, regulation 62(3).

Assessment of suitability for Pharmacy availability

The MHRA assessed the application against the criteria stated above.
The key aspects of the assessment of reclassification are summarised below.

Direct danger

An important risk with the use of calcipotriol, the active ingredient in Dovonex Psoriasis Ointment, without medical supervision is that of developing hypercalcaemia (excessive levels of calcium in the blood).

Calcipotriol has an effect on how the body deals with calcium, and if absorbed through the skin into the bloodstream has the potential to cause hypercalcaemia, although this is rare.

The risk of hypercalcaemia may be increased if the product is used incorrectly, for example by excessive application (over large areas of skin or application too frequently) or by application under occlusion (under a dressing or plaster). The risk of developing hypercalcaemia increases if more than 100g ointment is applied in any one week.

This risk of developing hypercalcaemia when using Dovonex Psoriasis Ointment is minimised as follows:

- Restriction of the indication for the product to adults with mild to moderate plaque psoriasis. Mild to moderate plaque psoriasis is limited to the patient's trunk and/or limbs and covers <10% of their skin surface area (as a guide, the skin surface area of an arm is approximately 9%)
- Limiting frequency of application to once-daily.
- Limiting the amount which may be applied in a week to 60g of ointment

These conditions of use are communicated to the patient via the patient information leaflet and packaging. The patient information leaflet states the signs of hypercalcaemia for the patient and advises them to stop using Dovonex Psoriasis Ointment and see their doctor straight away if they notice any such signs. The patient information leaflet also advises the patient not to use the ointment under occlusion (under a dressing or plaster).

The Licence Holder estimates the usage of Dovonex Ointment on prescription since its international birthdate and up to April 2014 to be 13.5 million treatment courses worldwide and 1,722,338 in the UK.

The most frequently reported adverse effects during treatment with calcipotriol are skin reactions such as pruritis (itchiness), skin irritation and erythema (redness of the skin). Systemic reactions (reactions which occur when calcipotriol is absorbed across the skin and into the bloodstream) such as hypercalcaemia have been reported.

MHRA Yellow Card data (side-effects reported by patients and healthcare professionals) show that between 28 April 1991 and 8 February 2016, 535 reports, consisting of 780 reactions were received for calcipotriol as a single active ingredient in marketed products. Of the 780 reactions reported, the vast majority (530) were skin reactions. 7 reactions recorded hypercalcaemia, for which all patients recovered when they stopped using the product.

There is the potential risk that calcipotriol may increase the effect of UV radiation which could cause skin tumours. There is a warning with this product for patients to limit or avoid excessive exposure to either natural or artificial sunlight. This warning is communicated to the patient on the packaging and in the patient information leaflet.

Dovonex Psoriasis Ointment is intended for use on the skin and, with the exception of emollients (moisturisers), without combination with other topical preparations for psoriasis. There is no evidence of interaction of calcipotriol with other drugs or food and risk of significant drug interactions for the ointment is negligible based on minimal systemic absorption (absorption across the skin into the bloodstream) of calcipotriol. The danger of interactions leading to adverse effects is low for this product.

Indirect danger

Indirect danger to human health, even when the product is used correctly, could occur where treatment might mask or hide an underlying condition requiring medical attention and supervision. Use of the medicine might delay diagnosis and definitive treatment and jeopardise the chance of more successful therapy. Therefore it is important that the condition or symptoms, for which a medicinal product not subject to a medical prescription is indicated, can be correctly assessed by the patient and that the product can be used without medical supervision.

Dovonex Psoriasis Ointment is indicated for plaque psoriasis which has been previously diagnosed by a doctor and therefore, patients wishing to purchase this product from a pharmacy will be aware of their condition. Since plaque psoriasis is a chronic, recurring condition, patients will be familiar with flare-ups and the need to get suitable treatment.

The patient must to speak to their doctor if they have psoriasis covering a large area of the body, psoriasis with pus-filled bumps, if their joints swell or are painful or if they have problems with their nails. These other forms of psoriasis or complications of psoriasis, require treatment under medical supervision. Dovonex Psoriasis Ointment, purchased from a pharmacy, would not be suitable in such cases. Dovonex Psoriasis Ointment should not be applied to the face, scalp, genital area or skin folds since treatment of these areas requires medical supervision. This information is communicated to the patient in the patient information leaflet and on the label.

The patient is instructed, via the label and leaflet, to stop using Dovonex Psoriasis Ointment and seek medical advice if their psoriasis becomes worse at any time or is no better after using Dovonex Psoriasis Ointment every day for 4 weeks. The patient is also advised in the patient information leaflet to see their doctor if they feel their psoriasis has not cleared up by up to 50% after using the medicine for 12 weeks.

Pharmacists and their staff will be provided with training material which will enable them to provide suitable advice to the patient and help the patient decide if Dovonex Psoriasis Ointment is suitable for them. The product outer packaging and the patient information leaflet also include an image of plaque psoriasis which will facilitate both pharmacists and patients in this respect.

There is potential for patients with previous experience of using the prescription product (Dovonex Ointment) twice-daily, to inadvertently or deliberately use the pharmacy product twice daily, instead of once daily as recommended for the pharmacy product. Pharmacy

training materials will specifically include a prompt for the pharmacist to ask patients if they have used Dovonex Ointment previously, and if so at what frequency. The once-daily dosage of Dovonex Psoriasis Ointment will be emphasised by the pharmacist, with patients advised to seek medical advice if they need to use the product twice daily.

Dovonex Psoriasis Ointment is not recommended for use (contraindicated) in patients who are pregnant or breast-feeding unless under supervision of a doctor. Patients are advised via the label and leaflet not to use Dovonex Psoriasis Ointment and to speak to their doctor if they are pregnant or breast-feeding.

Dovonex Psoriasis Ointment is intended for use on the skin and, with the exception of emollients, without combination with other topical preparations for psoriasis.
There is a risk that patients may use topical corticosteroids at the same time as Dovonex Psoriasis Ointment. Many patients with psoriasis may have received such treatment previously under supervision of a doctor and may have topical corticosteroid preparations available to use. In addition, low potency topical corticosteroids are available from pharmacies without prescription. The patient information leaflet and label give clear instructions to the patient not to use any other psoriasis treatment, other than an emollient (moisturiser), while using Dovonex Psoriasis Ointment.

Incorrect use – frequently and to a very wide extent

From data available, there is no evidence that the prescription product (Dovonex Ointment) is known to be frequently and to a very wide extent used incorrectly. Calcipotriol is not considered to be a compound associated with abuse or addiction potential and there is no known illicit use of topical calcipotriol. Incorrect use of the pharmacy product Dovonex Psoriasis Ointment, frequently and to a very wide extent would therefore not be expected, nor would abuse of the product.

Activity and/or adverse reactions require further investigation

This product has been used as a prescription product since 1991 and the activity and adverse reactions are well established. Therefore, this criterion does not apply.

Is normally prescribed as an injection

This product is for application to the skin only, so this criterion does not apply.

5. Further details on the application

Risk Management Plan
The application contains a risk management plan (RMP). RMPs are documents that contain information on a medicine's safety profile and one or more of the following:

- how any risks identified in the safety profile will be prevented or minimised in patients
- plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine
- risk factors for side effects
- measuring the effectiveness of measures taken to prevent or minimise risks.

The RMP for this product has identified the main risks associated with the product and proposes how these will be managed in the product information (SmPC, labelling and patient information leaflet) and through the pharmacy training materials.

Label and leaflet
The patient information leaflet and label are provided in Annex 2 and 3.

Summary of Product Characteristics
The Summary of Product Characteristics is provided in Annex 4. This document is a description of Dovonex Psoriasis' properties and the conditions attached to its use. It is used as a reference by healthcare professionals.

6. What do you think?

- Dovonex Psoriasis 50 microgram/g Ointment is used to treat mild to moderate plaque psoriasis which has been previously diagnosed by a doctor, in adults aged 18 years of age and over.
- Calcipotriol is only at the moment available on prescription (as Dovonex Ointment).
- We propose to make it available in pharmacies.
- The Commission on Human Medicines has advised that this product can be available as a Pharmacy medicine.
- We want to know what you think about this change.

Please tell us your views – please use the form on the next page in Annex 1. Please respond by 20 April 2017.

Response document for MHRA public consultation on the proposal to make Dovonex Psoriasis Ointment available in Pharmacies
Ref: ARM95

ANNEX 1

Your details

Name:

Position (if applicable):

Organisation (if applicable):

Email:

1. Do you consider that Dovonex Psoriasis Ointment should be available as a Pharmacy medicine?

Yes ☐ No ☐ Not sure ☐

Please provide any comments or evidence to support your response:

2. Do you have any specific comments on the leaflet or the label provided in the public reclassification report for Dovonex Psoriasis Ointment?

3. Do you have any other comments on the reclassification?

4. The MHRA may publish consultation responses. Do you want your response to remain confidential?

Yes ☐ Partially* ☐ No ☐

*If partially, please indicate which parts you wish to remain confidential. In line with the Freedom of Information Act 2000, if we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances. Responses to consultation will not normally be released under FOI until the regulatory process is complete.

Responses can be continued onto a separate page if required. This form should be returned by email (reclassification@mhra.gsi.gov.uk) to arrive by **20 April 2017.** Contributions received after that date cannot be included in the exercise.

Package leaflet: Information for the patient

Dovonex® Psoriasis 50 microgram/g ointment

calcipotriol

What is in this leaflet

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
Always use this medicine exactly as described in this leaflet or as your pharmacist has told you.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- In this leaflet Dovonex® Psoriasis 50 microgram/g ointment will be called Dovonex Psoriasis.
- **You must talk to your doctor if you do not see any improvement in your psoriasis after 4 weeks.**

1. What Dovonex® Psoriasis is and what it is used for

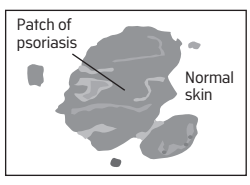
Dovonex Psoriasis contains the active substance calcipotriol. This medicine belongs to a group of medicines called anti-psoriatics. It is a type of vitamin D. Vitamin D controls how the cells in your skin grow.

This medicine is used in adults to treat:
Mild or moderate plaque psoriasis (psoriasis vulgaris) which has been previously diagnosed by a doctor. Psoriasis is mild or moderate when it affects an area of skin no bigger than the skin surface on one of your arms.

If the cells in your skin grow too much you may get psoriasis. Psoriasis is a condition where your skin develops raised red patches and silver coloured scaly patches. The scaly patches are dead cells that would normally fall off your skin without you noticing.

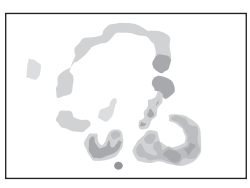
Dovonex Psoriasis works by reducing the amount of cells your skin makes. This means your skin symptoms will reduce too.

These diagrams explain how your skin may improve when you use this medicine.



Your skin before treatment.

After about two weeks you may see a change in your skin. The scaly or flaky patches usually clear up first. They will feel smoother.



The redness of the skin will start to clear up next. It may clear up in the centre first.

2. What you need to know before you use Dovonex® Psoriasis

Do not use this medicine:
- If you are allergic to calcipotriol or any of the other ingredients of this medicine (listed in section 6)
- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby
- If you have been told by a doctor that you have high or low levels of a substance called calcium in your body.

Warnings and precautions

You should see your doctor once a year for a routine check of your psoriasis.

Talk to your doctor before using this medicine:
- If your psoriasis is much worse or different to when your doctor last saw it
- If you have specific types of psoriasis covering large areas of the body (guttate or erythrodermic/exfoliative) or psoriasis with pus-filled bumps (pustular). Ask your doctor if you are unsure
- If your joints swell or are painful or if you have problems with your nails
- If you have liver or kidney problems
- If you are already having ultraviolet (UV) light treatment.

Stop using this medicine and talk to your doctor:
- If your psoriasis becomes worse at any time, or is no better after using the medicine every day for 4 weeks
- If you need to use more than 60 grams (1 tube) of ointment per week.

You can use Dovonex Psoriasis for up to 12 weeks. If you feel your psoriasis has improved a lot or has completely cleared up, you may stop using this medicine at any time within 12 weeks. You may start to use this medicine again if your psoriasis comes back after clearing up.

You must see your doctor if you feel that your psoriasis has not cleared up by up to 50% after using this medicine for 12 weeks.

Excess calcium in the blood
This medicine can cause increases in calcium levels in the body so it is important that you do not use more than the recommended dose. You should apply Dovonex Psoriasis once a day and you must not use more than 60 grams (1 tube) of ointment per week.

Signs of an increased blood calcium level can include:
- Passing water (urine) more frequently or in greater quantities than usual
- Increased thirst
- Dry or metallic taste in the mouth
- Stomach upsets (including pain, feeling sick, nausea, vomiting and constipation)
- Feeling weak or having pains in the muscles or bones
- Tiredness and confusion.

If you get any of these symptoms, stop using this medicine and tell your doctor straight away.

You are not likely to get too much calcium in your blood if you use this medicine as outlined in this leaflet or as your pharmacist has told you.

Do not use this medicine:
- on your face, as it may irritate the skin on your face or accidentally get in your eyes
- on your scalp, as in this area psoriasis is difficult to treat and special treatments may be needed
- on your genitals or in skin folds such as armpits or under the breasts, as you may be more likely to get skin side effects in these areas.

Do not cover your skin with any dressings or bandages when you have applied this medicine.

You should avoid sunbathing or using sunbeds while you are using this medicine.

Children and adolescents
Do not use this medicine on children and adolescents aged less than 18 years old as supervision by a doctor is needed in these age groups. Dovonex Psoriasis is only suitable for use in adults over 18 years old.

Other medicines and Dovonex Psoriasis
Tell your pharmacist if you are taking or have recently taken or might take any other medicines. This includes any medicines which you have bought without a prescription or herbal medicines.

You should not use any other psoriasis treatment other than a moisturiser (emollient) while you are using this medicine.

Do not take calcium supplements or any other medicines that contain calcium while using this medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, do not use this medicine and talk to your doctor.

Driving and using machines
This medicine should not have any effect on your ability to drive or use machines. Check with your pharmacist if you develop any side effects that may interfere with your ability to drive, operate machinery or take part in any other activity where they may put you or others at risk.

Important information about some of the ingredients of Dovonex Psoriasis
This medicine contains:
- Propylene glycol. This is a skin moisturiser. It may irritate your skin.

Please ask your pharmacist if you are worried about any of the ingredients in this medicine.

3. How to use Dovonex® Psoriasis

Always use this medicine exactly as described in this leaflet. You should check with your pharmacist if you are not sure.

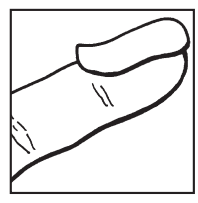
How to apply Dovonex Psoriasis
This medicine is only for use on your skin. Do not swallow it. Do not put it inside your body. You should only use the ointment to treat a total area of skin no bigger than the skin surface on one of your arms (around 10% of your body surface area).

Do not use this medicine:
- on your face, as it may irritate the skin on your face or accidentally get in your eyes
- on your scalp, as in this area psoriasis is difficult to treat and special treatments may be needed
- on your genitals or in skin folds such as armpits or under the breasts, as you may be more likely to get skin side effects in these areas.

Remove the cap. Check the seal is not broken before you first use the ointment. You will need to break the seal by using the point in the back of the cap.

Always wash your hands before using this medicine.

Apply the ointment to the skin which has the psoriasis. You can squeeze your medicine on to your skin directly, or you can squeeze it on to your finger first if you wish, to measure how much ointment to use. Squeeze the ointment along your finger from the tip to the first joint as shown in the diagram. This is called a fingertip unit.



As a guide, around 6 fingertip units will sufficiently cover an area equal in size to one entire arm (not including your hand). If you need to use a little more or a little less do not worry. Then rub it in gently to cover the psoriasis.

Always wash your hands after using Dovonex Psoriasis, unless you are treating your hands. This will stop any medicine accidentally spreading to other parts of your body. Do not worry if you accidentally get any ointment on your normal skin, but wash it off if it spreads too far.

Do not cover your skin with any dressings or bandages when you have applied this medicine.
Do not shower or bath immediately after applying the ointment.

You should try to keep your skin well moisturised, particularly after a bath or shower. If you use a moisturiser, wait for it to soak in before you use your medicine.

How much Dovonex Psoriasis to use

Adults:
Apply Dovonex Psoriasis to the affected area once daily.
You can use this medicine for up to 12 weeks.
Do not use more than 60 grams (1 tube) each week.
If your psoriasis becomes worse at any time or it is no better after using the medicine every day for 4 weeks, stop using this medicine and see your doctor.
You must see your doctor if you feel that your psoriasis has not improved by up to 50% after using this medicine for 12 weeks.

If you use more Dovonex Psoriasis than you should
Tell your doctor or pharmacist straight away and take this leaflet with you. If you use more of this medicine than you should, you may get too much calcium in your blood and your doctor may need to do a blood test to check for this. Your doctor may tell you to stop using this medicine until your calcium level goes back to normal.

If you forget to use Dovonex Psoriasis
If you forget to use your medicine, use it as soon as you remember. Then continue to use your medicine at the usual time.

Do not use a double dose to make up for a forgotten dose.

If you have any further questions about using this medicine, please ask your pharmacist.

4. Possible side effects
Like all medicines, Dovonex Psoriasis can cause side effects, although not everybody gets them.

Important side effects to look out for:

You must get urgent medical help if you have any of the following symptoms. You may be having an allergic reaction:
- You have difficulty breathing
- Your face, including around your eyes, swells
- Your skin develops a severe rash, particularly if the skin is blistering or bleeding.

You should stop using this medicine and tell your doctor straight away if you spot any of the following signs which may be due to too much calcium in your blood or urine:
- You need to pass water (urine) more often
- You feel thirsty or have lost your appetite
- You have a dry mouth or a metallic taste in your mouth
- You feel weak or have pain in your muscles or bones
- You feel sick or have pain in your stomach (including nausea, vomiting and constipation)
- You feel tired, fatigued and confused.

Other possible side effects:

Common side effects (may affect up to 1 in 10 people)
- Worsening of your psoriasis
- Skin inflammation
- Redness of the skin
- Flaking skin
- Burning or stinging feeling
- Skin irritation
- Itching skin
- Pain in the area where the medicine is used.

Uncommon side effects (may affect up to 1 in 100 people)
- Infection in a hair follicle
- Rash, including red, itchy, scaly rash. Blisters may form. These may weep or become crusty
- Dry skin
- Changes in skin colour where the medicine is used.

Rare side effects (may affect up to 1 in 1000 people)
- Allergic reaction
- Too much calcium in the blood
- Increased sensitivity to sunlight
- Skin swelling or puffiness
- Itchy raised rash (hives)
- Skin conditions where there are oily glands. For example; on the face, centre of chest, or conditions such as dandruff
- Too much calcium in the urine.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Dovonex® Psoriasis
- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date on the tube and carton (EXP). The expiry date is the last day of that month.
- The tube should be discarded 6 months after first opening. Write the date you first opened the tube in the space provided on the carton.
- Do not store above 25°C.

Medicines should not be thrown away in waste water or in household waste. Please ask your pharmacist how to throw away any medicine you do not need anymore. If you do this you will help protect the environment.

6. Contents of the pack and other information
What Dovonex Psoriasis contains
- The active substance is calcipotriol. Dovonex Psoriasis contains 50 micrograms of calcipotriol in each gram of ointment.
- The other ingredients are disodium edetate, disodium phosphate dihydrate, all-*rac*-α-tocopherol, liquid paraffin, macrogol-(2)-stearyl ether, propylene glycol, purified water and white soft paraffin.

You can find important information about some of the ingredients in your medicine near the end of section 2 of this leaflet.

What Dovonex Psoriasis looks like and contents of the pack
This medicine is an off-white to yellowish-white translucent ointment.
It comes in aluminium tubes of 60 grams.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
LEO Laboratories Limited,
Hurley, Berkshire SL6 6RJ, UK.

Manufacturer:
LEO Laboratories Limited, Dublin 12, Ireland.

This leaflet was last revised in February 2017.

®Registered Trade Mark

FURTHER HELPFUL INFORMATION

People with psoriasis should see their doctor once a year for a regular check-up of their skin, their treatment and their general health. This is because psoriasis can affect other parts of the body as well as the skin. This is more likely if psoriasis is severe.

Moisturisers (emollients) are useful in treating psoriasis. Moisturisers can reduce skin dryness and itching. They can also reduce skin scaling and soften hard cracked areas, which may help treatments such as Dovonex Psoriasis to get into the skin.

You should use moisturisers instead of soap when washing or having a bath. Feel free to moisturise generously as often as you like, since this will help your skin symptoms.

It is a good idea to use a moisturiser before you treat your psoriasis, but allow about 30 minutes between moisturising and using Dovonex Psoriasis.

Please remember to keep Dovonex Psoriasis out of the reach of pets. If you suspect that your pet has eaten Dovonex Psoriasis or chewed the tube, please contact your vet as soon as possible as it may be harmful to your pet.

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LEO

No varnish

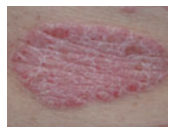
Dovonex®

PSORIASIS 50 microgram/g ointment

calcipotriol

- **Topical treatment for adults previously diagnosed with mild to moderate plaque psoriasis**
- **Patients with psoriasis should see their doctor once a year for review**

Dovonex®
PSORIASIS 50 mcg/g ointment
calcipotriol
60 g
YY-000000



WHAT IS PLAQUE PSORIASIS?

Plaque psoriasis is a condition where your skin develops raised red patches and silver coloured scaly patches.

THIS MEDICINE IS SUITABLE IF:

- ☑ You are 18 years or older.
- ☑ A doctor has diagnosed plaque psoriasis in the past and your skin symptoms have not changed.
- ☑ Your psoriasis affects the skin on your body or limbs.

DO NOT USE THIS MEDICINE AND SEE YOUR DOCTOR IF YOU:

- ☒ Have an allergy to any ingredient listed on this pack.
- ☒ Are pregnant, or think you might be pregnant, or are planning to have a baby, or breast-feeding.
- ☒ Have a problem with how your body handles calcium.
- ☒ Have problems with your liver or kidneys.
- ☒ Have psoriasis on your face, genitals, scalp or skin folds.
- ☒ Have psoriasis affecting more than 10% of your body surface (about the area of skin on one arm).
- ☒ Have painful joints or nail problems.

Lot
EXP

LEO

Dovonex®
PSORIASIS 50 microgram/g ointment
calcipotriol

60 g

Read the package leaflet before use.
For application to the skin.

HOW TO USE THIS MEDICINE

- Wash your hands before and after use.
- Apply a layer of this ointment to the affected area once a day and rub in gently.
- A maximum weekly dose should not exceed 60 grams.

YOUR PSORIASIS SHOULD START TO IMPROVE WITHIN 4 WEEKS.

See your doctor:

- If no improvement is seen after 4 weeks of treatment.
- If your psoriasis changes or worsens.
- If you get any signs of an increased blood calcium level (see leaflet for further information).

IMPORTANT INFORMATION

Use this medicine on your skin only.
Contains propylene glycol. It may irritate your skin.
See leaflet for further information.
Keep out of the sight and reach of children.
Avoid excessive exposure to natural or artificial sunlight, e.g. sunbathing and sun beds, while you are using this medicine.
You should not use any other psoriasis treatment other than a moisturiser (emollient) while you are using this medicine.

Do not store above 25°C.

Contains:
calcipotriol 50 microgram/g

Other ingredients:
disodium edetate, disodium phosphate dihydrate, all-*rac*-α-tocopherol, liquid paraffin, macrogol-(2)-stearyl ether, propylene glycol, purified water, white soft paraffin.

Date opened:_____

LEO Laboratories Limited
Hurley, Berkshire
SL6 6RJ, UK

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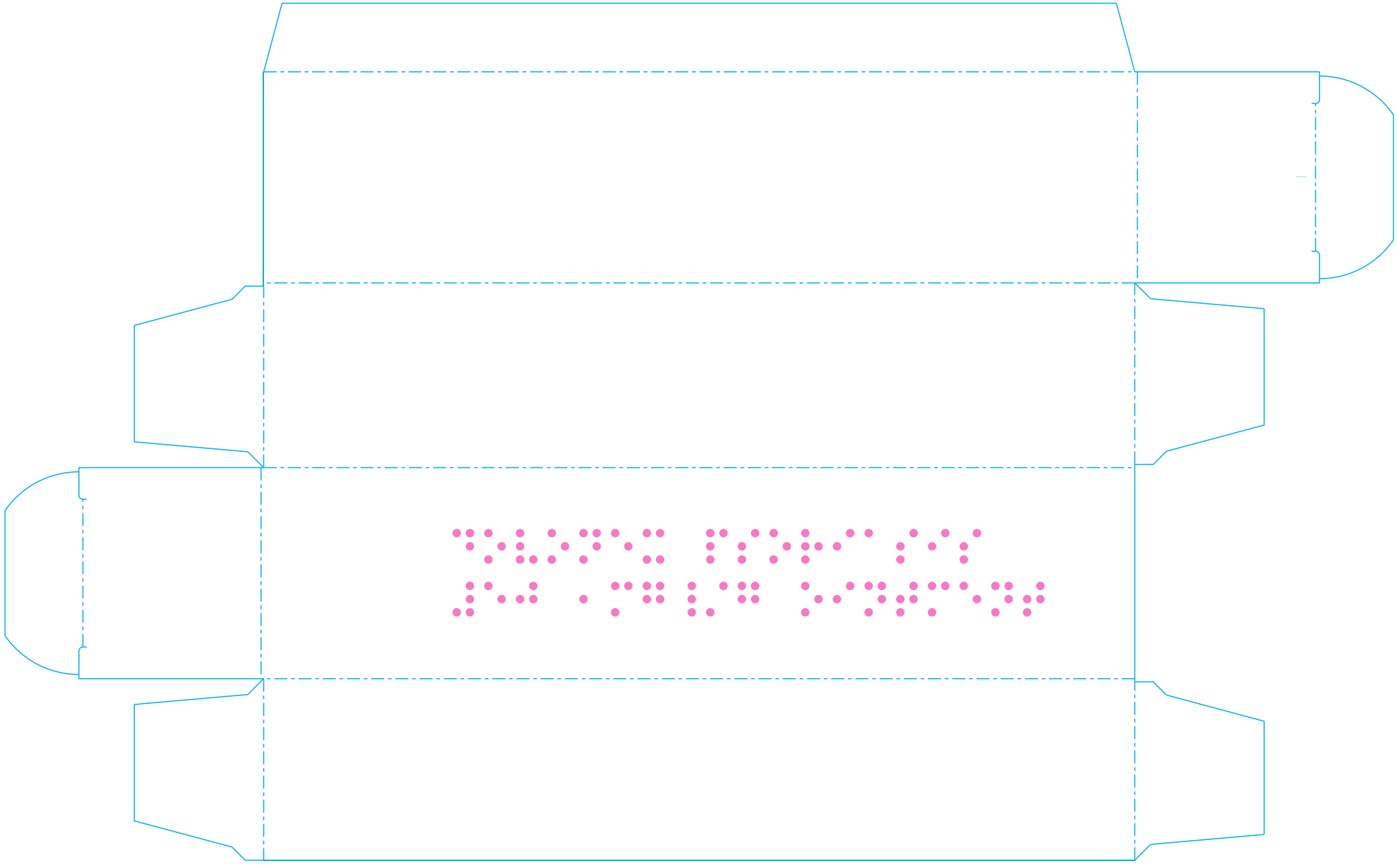
Discard the tube 6 months after first opening.

40 x 35 x 165
CIE03-03



Dovonex®

PSORIASIS 50 microgram/g ointment

calcipotriol

60 g

Topical treatment for adults previously diagnosed with mild to moderate plaque psoriasis

Contains: calcipotriol 50 microgram/g

Read the package leaflet before use.

For application to the skin.

IMPORTANT INFORMATION

Keep out of the sight and reach of children.

Do not store above 25°C.

Discard the tube 6 months after first opening.

LEO Laboratories Limited
Hurley, Berkshire SL6 6RJ, UK

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HOW TO USE THIS MEDICINE

- Wash hands before and after use.
- Apply a layer of ointment to the affected area once a day and rub in gently.
- A maximum weekly dose should not exceed 60 grams.

Other ingredients:
disodium edetate, disodium phosphate dihydrate, all-*rac*-α-tocopherol, liquid paraffin, macrogol-(2)-stearyl ether, propylene glycol, purified water, white soft paraffin.

See leaflet for further information.

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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 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 60 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 60 g of Dovonex Psoriasis 50 microgram/g ointment. The patient should be referred back to their doctor if they are using more than 60 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 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 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)

Approximately 25% of the patients treated with Dovonex Psoriasis 50 microgram/g ointment could experience an adverse reaction. These reactions are usually mild.

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
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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

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: 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

Data from a single study containing 5 evaluable patients with psoriasis treated with 0.3 - 1.7 g of a 50 micrograms/g tritium labelled calcipotriol ointment suggested that less than 1% of the dose was absorbed.

However, total recovery of the tritium label over a 96 hour period ranged from 6.7 to only 32.6%, figures maximised by uncorrected chemiluminescence. There were no data on 3H tissue distribution or excretion from the lungs.

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.

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/m^2/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

Purified water

White soft paraffin

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
Horizon
Honey Lane
Hurley
Berkshire
SL6 6RJ
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00043/0219

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: dd-mmm-yyyy

10 DATE OF REVISION OF THE TEXT

Not applicable