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:

1. Background about deciding where medicines are available
2. About Dovonex Psoriasis Ointment
3. Proposal to make Dovonex Psoriasis Ointment available as a Pharmacy medicine
4. How was the proposal assessed for Dovonex Psoriasis Ointment being available as a Pharmacy medicine?
5. Further details on the application
6. What do you think?

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

Dovonex® Psoriasis is a medicine used to treat mild to moderate plaque psoriasis (also known as psoriasis vulgaris) which is a skin disorder that causes your skin to grow in an unhealthy way and make scaly patches.  

This medicine is used in adults to treat mild to moderate plaque psoriasis (psoriasis vulgaris) which has been previously diagnosed by a doctor. Dovonex® Psoriasis is a steroid medicine which affects an area of skin larger than the size of the palm of your outstretched hand.  

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

In this leaflet, Dovonex® Psoriasis 50 microgram/g ointment will be called Dovonex Psoriasis.

Important information about some of the ingredients of this medicine.

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

This medicine is only for use on your skin. Do not use it on your face, as it may irritate the skin on your face. 

Driving and using machines

You should try to keep your skin well moisturised, as your skin is more sensitive while you are using Dovonex® Psoriasis. 

Other medicines and Dovonex® Psoriasis

You should 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 aged 18 years old and above.

Getting your psoriasis clearing up

If you feel your psoriasis has improved a lot or has cleared up, you may stop using this medicine. 

If your joints swell or are painful or if you have problems with your nails, talk to your doctor.

You should try to keep your skin well moisturised,

If you are pregnant or breast-feeding, think you may be pregnant or planning to have a baby, do not use this medicine.

Talk to your doctor before using this medicine:

You should try to keep your skin well moisturised,

If you have specific types of psoriasis covering large areas of your body (guttate or erythrodermic/exfoliative psoriasis) or if your psoriasis is much worse or different to when you were first diagnosed, you may be more likely to get side effects from using this medicine.

Do not use Dovonex® Psoriasis on areas of the body (e.g. the scalp, nostrils, under the breasts, as you may be more likely to get side effects from these areas).

If your skin is thin around your eyes, you may be more likely to get side effects on this area of your skin.

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

If you are already having ultraviolet (UV) light treatment.

Please ask your pharmacist if you need more information or if you do not understand any part of this leaflet.

If your psoriasis is much worse or different to when you were first diagnosed, you may be more likely to get side effects from using this medicine.

If your joints swell or are painful or if you have problems with your nails, talk to your doctor.

You should try to keep your skin well moisturised,

Do not use this medicine:

7. Package leaflet: Information for the patient

Package leaflet: Information for the patient

Dovonex® Psoriasis 50 microgram/g ointment

e-mail

Please return to:

ARTWORK

Dovonex® Psoriasis 50 microgram/g ointment

The diagrams explain how your skin may improve better after using the medicine every day for 4 weeks.

The medicine is a cream that is applied directly to your skin. If you need to use a little more or a little less do not use a different amount.

Use a little more or a little less.

This medicine is not for use on your face, as it may irritate the skin on your face.

This medicine is only for use on your skin. Do not use it on your face.

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3. How to use Dovonex® Psoriasis

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How much Dovonex Psoriasis to use

Adults

Apply Dovonex Psoriasis to the affected areas once daily. You can use this medicine for up to 12 weeks. Do not use more than one gram (10 tubes) weekly.

If you pass more Dovonex Psoriasis than you should

• Stop using the medicine straight away. Call a doctor straight away if you have swallowed or injected any of the medicine. Do not try to make anyone vomit. If you have injected the medicine into another part of the body, see your doctor straight away.

• If you have inserted Dovonex Psoriasis into the eyes or ears, wash that side of the face with plenty of water. If you have injected the medicine into the skin, see your doctor straight away.

Information on the safety of this medicine

www.mhra.gov.uk/yellowcard.

People should stop using Dovonex Psoriasis if they experience:

• Too much calcium in the urine.

• Skin conditions where there are oily glands. For example: on the face, centre of chest, or conditions affecting the skin in the axillary area, which may help treatments such as Dovonex Psoriasis to get into the skin.

• Changes in skin colour where the medicine is used.

Other possible side effects

• Too much calcium in the blood

• Allergic reaction

• Changes in skin colour where the medicine is used.

Do not use a double dose to make up for a forgotten dose. If you forget to use Dovonex Psoriasis, apply as usual the next day. Do not use double the usual dose to make up for a forgotten dose.

• The other ingredients are disodium edetate, disodium phosphate dibasic, disodium phosphate anhydrous, polysorbate 80, purified water and white soft paraffin.

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

What Dovonex Psoriasis looks like and contents of the pack

Dovonex Psoriasis contains 60 micrograms of calcipotriol in each gram of ointment. It comes in 60-gram tubes of 45 grams.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

LEO Laboratories Ltd, Willey, Berkshire SL6 6RJ, UK.

LEO Laboratories Limited, Dublin 12, Ireland.

This leaflet was last revised in February 2017.

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FURTHER HELPFUL INFORMATION

People with psoriasis should have their doctor see a young person regularly, check 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.

Patients (particularly children) are suffering from this condition. Information on Dovonex Psoriasis can reduce skin dryness and itching. They can give your doctor more information on side effects, which will help treat these conditions. Patients may reduce the risk of hair loss by using Dovonex Psoriasis instead of the tube when washing or having a bath. Feel free to moisturise generously as often as you can, on any part of the body.

This can be a guide to a cosmetician before you treat your psoriasis, but allow about 10 minutes between moisturising and using Dovonex Psoriasis.

Please remember to keep Dovonex Psoriasis out of the reach of children. If you pass more Dovonex Psoriasis than you intended, do not use it again, and contact your pharmacist. If you pass more Dovonex Psoriasis than you intended, do not use it again, and contact your pharmacist.

Dovonex Psoriasis contains:

• The active substance is calcipotriol. Dovonex Psoriasis contains 60 micrograms of calcipotriol in each gram of ointment. It comes in 60-gram tubes of 45 grams.

• The other ingredients are disodium edetate, disodium phosphate dibasic, disodium phosphate anhydrous, polysorbate 80, purified water and white soft paraffin.

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

What Dovonex Psoriasis looks like and contents of the pack

Dovonex Psoriasis contains 60 micrograms of calcipotriol in each gram of ointment. It comes in 60-gram tubes of 45 grams.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

LEO Laboratories Ltd, Willey, Berkshire SL6 6RJ, UK.

LEO Laboratories Limited, Dublin 12, Ireland.

This leaflet was last revised in February 2017.

© Registered Trade Mark

FURTHER HELPFUL INFORMATION

People with psoriasis should have their doctor see a young person regularly, check 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.

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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.
- Your 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 problems with how your body handles calcium.
- Have problems with your liver or kidneys.
- Have plaque psoriasis on your face, genitals, scalp or skin folds.
- Have plaque psoriasis affecting more than 10% of your body surface (about the area of skin on one arm).
- Have painful joints or nail problems.

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Dovonex® PSORIASIS
50 microgram/g ointment
calcipotriol
Dovonex® PSORIASIS
50 microgram/g ointment
calcipotriol

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
PL 00043/0219

Discard the tube 6 months after first opening.
<table>
<thead>
<tr>
<th>Colour</th>
<th>Date</th>
<th>Sign.</th>
<th>Sign.</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% GB 000000</td>
<td>30/11/16</td>
<td>YY</td>
<td>YY</td>
<td>YY</td>
</tr>
</tbody>
</table>

**CRT 40 x 35 x 165 mm**

**Supplied / Place of production**

<table>
<thead>
<tr>
<th><strong>Dovonex ointment 60 g - OTC</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ireland</td>
</tr>
</tbody>
</table>

**Braille shown with PMS 231**

**Marburg medium**
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

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-r-c- α-tocopherol, liquid paraffin, macrogol-(2)-stearyl ether, propylene glycol, purified water, white soft paraffin.
See leaflet for further information.

PL 00043/0219
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.

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common ≥1/10</td>
<td></td>
</tr>
<tr>
<td>Common ≥1/100 to &lt;1/10</td>
<td></td>
</tr>
<tr>
<td>Uncommon ≥1/1,000 to &lt;1/100</td>
<td>Folliculitis</td>
</tr>
<tr>
<td>Rare ≥1/10,000 to &lt;1/1,000</td>
<td>Hypercalcaemia</td>
</tr>
<tr>
<td>Very rare &lt;1/10,000</td>
<td></td>
</tr>
<tr>
<td>Not known (cannot be estimated from the available data)</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common (≥1/100 to &lt; 1/10)</td>
<td>Psoriasis aggravated, Dermatitis, Erythema, Skin exfoliation, Skin burning sensation, Skin irritation, Pruritus</td>
</tr>
<tr>
<td>Uncommon (≥1/1,000 to &lt;1/100)</td>
<td>Rash*, Dry skin</td>
</tr>
<tr>
<td>Rare (≥1/10,000 to &lt;1/1,000)</td>
<td>Photosensitivity reaction, Skin oedema, Urticaria, Seborrhoeic dermatitis</td>
</tr>
</tbody>
</table>

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

### Renal and urinary disorders

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare (≥1/10,000 to &lt;1/1,000)</td>
<td>Hypercalciuria</td>
</tr>
</tbody>
</table>

### General disorders and administration site conditions

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common (≥1/100 to &lt;1/10)</td>
<td>Application site pain</td>
</tr>
<tr>
<td>Uncommon (≥1/1,000 to &lt;1/100)</td>
<td>Application site pigmentation changes</td>
</tr>
</tbody>
</table>

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](http://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: Antipsoriatrics 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<sub>3</sub>.

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<sup>2</sup>/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 AUTHOURISATION**
Date of first authorisation: dd-mmm-yyyy

10 **DATE OF REVISION OF THE TEXT**
Not applicable