IPAR

Public Assessment Report for a Medicinal Product for Human Use

Scientific discussion

Dovonex Psoriasis 50 microgram/g ointment
CALCIPOTRIOL, ANHYDROUS
PA0046/064/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Dovonex Psoriasis 50 microgram/g Ointment, from Leo Laboratories Limited on 08th April 2016 for the topical treatment in adults of mild to moderate plaque psoriasis which has been previously diagnosed by a doctor.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Dovonex 50 microgram/g Ointment, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Dovonex Psoriasis 50 microgram/g Ointment. Dovonex Psoriasis 50 microgram/g Ointment has the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form as Dovonex 50 microgram/g Ointment.

Dovonex Psoriasis 50 microgram/g Ointment is available from pharmacies and is not subject to medical prescription.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie

Name of the product	Dovonex Psoriasis 50 microgram/g ointment
Name(s) of the active substance(s) (INN)	CALCIPOTRIOL, ANHYDROUS
Pharmacotherapeutic classification (ATC code)	D05AX02
Pharmaceutical form and strength(s)	50 microgram/g
Marketing Authorisation Number(s) in Ireland (PA)	PA0046/064/001
Marketing Authorisation Holder	Leo Laboratories Limited

II QUALITY ASPECTS

II.1. Introduction

This application is for Dovonex Psoriasis 50 microgram/g Ointment.

II.2 Drug substance

The application was submitted as an 'informed consent' application. This means that the Marketing Authorisation Holder for Dovonex 50 microgram/g Ointment, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Dovonex Psoriasis 50 microgram/g Ointment. Therefore, the quality aspects of the drug substance in Dovonex Psoriasis 50 microgram/g Ointment are the same as those for the authorised medicinal product Dovonex 50 microgram/g Ointment.

II.3 Medicinal product

The application was submitted as an 'informed consent' application. This means that the Marketing Authorisation Holder for Dovonex 50 microgram/g Ointment, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Dovonex Psoriasis 50 microgram/g Ointment. Therefore, the quality aspects of the medicinal product Dovonex Psoriasis 50 microgram/g Ointment are the same as those for the authorised medicinal product Dovonex 50 microgram/g Ointment.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

Dovonex Psoriasis 50 microgram/g Ointment has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as the authorised medicinal product Dovonex 50 microgram/g Ointment.

III NON-CLINICAL ASPECTS

This active substance is the same as that present in Dovonex 50 microgram/g Ointment on the Irish market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

IV CLINICAL ASPECTS

IV.1 Introduction

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Dovonex 50 microgram/g Ointment, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Dovonex Psoriasis 50 microgram/g Ointment. Dovonex Psoriasis 50 microgram/g Ointment has the same qualitative and quantitative composition in terms of active substances (calcipotriol) and the same pharmaceutical form as Dovonex 50 microgram/g Ointment.

Calcipotriol is a well-known active substance in Europe with established favourable efficacy and tolerability. Dovonex 50 micrograms/g Ointment was first authorised in Ireland in 1991.

The method of sale and supply for Dovonex Psoriasis 50 micrograms/g Ointment differs to that of Dovonex 50 micrograms/g Ointment. Dovonex Psoriasis 50 micrograms/g Ointment is not subject to medical prescription and is available through pharmacies, whereas the reference product is prescription-controlled.

Assessment of this application was carried out in line with the principles detailed in the European Commission's "Guideline on changing the classification for the supply of a medicinal product for human use" and the HPRA's "Guide to the reclassification (Switching) of legal supply status of human medicinal products". Following this assessment, the HPRA concluded that Dovonex Psoriasis 50 micrograms/g Ointment is suitable for pharmacy only sale, without the need for medical prescription.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Dovonex 50 micrograms/g Ointment, marketed by Leo Laboratories Limited. Changes have been introduced to the SmPC and Patient Information Leaflet to reflect the fact that Dovonex Psoriasis 50 microgram/g Ointment may be supplied through pharmacies and is not subject to medical prescription.

The applicant has provided a document "Reclassification Addendum to Risk Management Plan for Topical Calcipotriol Containing Products" version 1.

IV.2 Pharmacokinetics

In the PK studies submitted by the applicant, the transdermal absorption of calcipotriol has been shown to be in the range of 1-6% of the administered dose.

Following systemic exposure, calcipotriol appears to be rapidly and extensively metabolised.

IV.3 Pharmacodynamics

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.

IV.4 Clinical Efficacy

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application.

The content of the dossier assessed during the licensing procedure is in accordance with that accepted for the reference product Dovonex 50 micrograms/g Ointment, marketed by Leo Laboratories Limited.

To reflect the fact that this product will be supplied in pharmacies without need for a medical prescription, the authorised indication differs to that of the prescription-controlled reference product and is:

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%).

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

The applicant has provided justification for a once daily application for Dovonex Psoriasis 50 micrograms/g Ointment. Warnings relating to lack of effectiveness or deterioration of disease have been included in the SmPC and Patient Information Leaflet.

IV.5 Clinical Safety

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Dovonex 50 microgram/g Ointment, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Dovonex Psoriasis 50 microgram/g Ointment. Dovonex Psoriasis 50 microgram/g Ointment has the same qualitative and quantitative composition in terms of active substances (calcipotriol) and the same pharmaceutical form as Dovonex 50 microgram/g Ointment.

Calcipotriol is a well-known active substance in Europe with established acceptable tolerability. Dovonex 50 micrograms/g Ointment was first authorised in Ireland in 1991. The content of the dossier assessed during the licensing procedure is in accordance with that accepted for the reference product Dovonex 50 micrograms/g Ointment, marketed by Leo Laboratories Limited. The applicant has also provided a review of the available post-marketing safety data as part of this application.

The SmPC and Patient Information Leaflet have been updated to reflect that this product is available through pharmacies and is not subject to medical prescription. Specific warnings relating to duration of use, deterioration of disease, emergence of new symptoms, risk of hypercalcaemia, drug interactions, and undesirable effects have been included in the SmPC and Patient Information Leaflet.

Patients are advised to attend their doctor yearly for a review of their psoriasis. Patients should attend their doctor for review if they develop worsening symptoms, nail involvement or pain/swelling of their joints.

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

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

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.

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

Pharmacovigilance System

The marketing authorisation holder (MAH) submitted a summary of the Pharmacovigilance System, including confirmation of the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

The **Risk Management Plan** document "Reclassification Addendum to Risk Management Plan for Topical Calcipotriol Containing Products" outlines the following safety concerns:

Important identified risks:
Hypercalcaemia

Important Potential Risks:
Potential enhancement of UV radiation induced skin cancer

Important missing information:
None

The safety concerns will be addressed with routine pharmacovigilance activities.

Assessor comments on the Risk Management Plan:
The applicant is requested to revise the current RMP in line with the agreed information relating to indication and dosage in the agreed SmPC. The applicant is reminded that the RMP should be a stand-alone document in line with GVP Module V Risk Management Systems.

In accordance with Article 107c(7) of Directive 2001/83/EC as amended, the substance calcipotriol was published in the List of Union reference dates and frequency of submission of periodic safety update reports (PSURs) on the 1st of October 2012. For calcipotriol, PSURs must be submitted every 13 years, therefore the next PSUR submission for this medicinal product is due on the 28th of February 2026.

IV.6 Discussion on the clinical aspects

Dovonex 50 micrograms/g Ointment been marketed in Ireland since 1991. The efficacy and safety profile is well established. The HPRA, on the basis of the data submitted, considered that Dovonex Psoriasis 50 micrograms/g Ointment has the same qualitative and quantitative composition as Dovonex 50 micrograms/g Ointment.

V OVERALL CONCLUSIONS

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

On the basis of the data submitted, the HPRA considered that Dovonex Psoriasis 50 micrograms/g Ointment has the same qualitative and quantitative composition as the reference product, Dovonex 50 micrograms/g, which has proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile. A marketing authorisation is therefore granted.