

IPAR



Publicly Available Assessment Report for a Veterinary Medicinal Product

Demyrin 2 mg/g eye ointment

PRODUCT SUMMARY

EU Procedure Number	IE/V/0428/001
Name, Strength, Pharmaceutical Form	Demyrin 2 mg/g eye ointment
Active Substances(s)	Ciclosporin
Applicant	Elanco Europe Ltd Lilly House, Priestley Road Basingstoke Hampshire RG24 9NL United Kingdom
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Dogs
Indication For Use	For the treatment of Keratoconjunctivitis sicca (KCS, 'dry eye'). For the treatment of chronic superficial keratitis ('pannus').
ATC Code	QS01XA90
Legal basis of original application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure	29/03/2017 (UK) 19/05/2017 (IE)
Concerned Member States for original procedure	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Spain, Sweden. Added via RMS change: UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of

commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. 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 product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference product is Optimune, marketed in the UK since June 1994. The applicant claimed exemption from the requirement for bioequivalence studies in accordance with the principles of exemption 7.1.d of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2). Whilst acknowledging that although this guideline does not relate to topically applied products, the applicant provided references to two guidelines for human products which adhere to a similar justification support the application. This was considered acceptable. The quantity of the proposed product to be delivered to the eye of the animal is identical to that of the reference product. Additionally, the formulations are identical. The product is intended for use in dogs, for the treatment of keratoconjunctivitis sicca (KCS, 'dry eye') and chronic superficial keratitis ('pannus').

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC.[\[1\]](#) The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [\[2\]](#) of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

[\[1\]](#) SPC – Summary of product Characteristics.

[\[2\]](#) Efficacy – The production of a desired or intended result.

II. QUALITY ASPECTS

II.A. Composition

The product contains 2.0 mg/g ciclosporin and the excipients petrolatum and lanolin alcohol, refined maize oil and white soft paraffin.

The container/closure system consists of an aluminium tube lacquered with epoxy-phenol containing 3.5 g of product, with an LDPE nozzle. The cap is a tamper-evident HDPE screw fit cap. The particulars of the containers and controls

performed are provided and conform to the regulation. The choice of the formulation and the absence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of: mixing of soft paraffin and petrolatum, the active substance is dissolved in maize oil, all components are then mixed, sterilisation is then performed, followed by homogenisation and filling and packaging of the product.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is ciclosporin, an established active substance described in the European Pharmacopoeia (Ph. Eur). The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

Excipients described in the Ph. Eur are white soft paraffin and refined maize oil. Suitable certificates of analysis were provided. Petrolatum and lanolin alcohol are not monographed in a pharmacopoeia, but cited in the specification provided by the applicant. Specifications for the packaging have been suitably justified, and where appropriate, material is in accordance with the Ph. Eur.

II.C.4. Substances of Biological Origin

An appropriate EMA TSE declaration was provided. Lanolin from living sheep sourced in Australia or New Zealand which produce products for human consumption are not expected to present a risk associated with TSE.[\[1\]](#)

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product include those for: appearance, drop point, identification of the active substance, assay ciclosporin, impurities, minimum fill and sterility.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. Satisfactory data were also received for the finished product.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.

Shelf-life after first opening the immediate packaging: 28 days.

This veterinary medicinal product does not require any special storage conditions.

[1] TSE – Transmissible spongiform encephalopathy.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Due to the nature of the application, warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users or the environment. No pharmacological or toxicological data were required for this section.

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product, and are similar to those of the reference product. The following applicant's user recommendations are appropriate:

- Avoid contact with the skin and particularly any transfer of product from hands to your mouth or eyes. If any contact with fingers occurs, wash hands immediately.
- Wash hands after use

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The product will only be used in non-food animals and as a result environmental exposure will be low. The environmental assessment is appropriately described only in relation to Phase I. A Phase II ERA was not required.

IV. CLINICAL ASSESSMENT

Due to the nature of the application, no preclinical or clinical studies were required. However, in order to satisfy the requirement that the reference product and proposed product are identical with regard to delivery to the eye of the target species, dogs, a study on the comparative viscosity of the proposed product was required. Three batches of the proposed product were compared to four batches of the reference product. Viscosity was seen to be comparable. No further efficacy data were required.

V. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics the benefit/risk profile of the products is favourable.