LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Prednisolon Evolan
(prednisolone)

This module reflects the scientific discussion for the approval of Prednisolon Evolan. The procedure was finalised at 2025-07-09. For information on changes after this date please refer to the module 'Update'.

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TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Prednisolon Evolan, 31,25 mg, Rectal solution.

The active substance is prednisolone, prednisolone sodium phosphate. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

Prednisolon Evolan, 31.25 mg, rectal solution, contains the active ingredient prednisolone sodium phosphate. Prednisolone is a synthetic glucocorticoid with an anti-inflammatory effect.

The product applied for is a locally applied and locally acting aqueous solution intended for the treatment of ulcerative proctosigmoiditis. The aim is to achieve locally high concentration of cortison and thereby induce an effect without reaching a high plasma level of cortison. Therebye systemic effects may be avoided.

II.2 General comments on the submitted dossier

The application for Prednisolon Evolan, 31,25 mg, Rectal solution, is a Hybrid Art. 10(3) application submitted according to Directive 2001/83/EC. The applicant applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Pred-Clysma 31,25 mg Rectal solution authorised in Sweden since 1963, with Bayer AB as marketing authorisation holder.

II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The MPA has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.
For manufacturing sites within the European Community, the MPA has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Drug substance
The structure of the drug substance has been adequately proven, and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described, and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

Drug Product
The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology
No new non-clinical studies on pharmacology, pharmacokinetics and toxicology have been submitted. As prednisolone is a widely used and well-known active substance this is considered to be acceptable. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Prednisolone is widely used in other products on the market and the use of Prednisolon Evolan is concluded not likely to significantly increase the total amount of prednisolone used in Sweden.
The lack of an environmental risk assessment is considered acceptable.

There are no objections to approval of Prednisolon Evolan from a non-clinical point of view.

III.3 Clinical aspects

Pharmacokinetics
The application for Prednisolon Evolan, 31.25 mg, rectal solution, is a hybrid Art. 10(3) application submitted according to Directive 2001/83/EC. No bioequivalence study has been submitted in this application. The applicant claims that Prednisolon Evolan, 31.25 mg, rectal solution, is essentially similar to Pred-Clysma, 31.25 mg, rectal solution, having the same active substance and in the same concentration. Furthermore, the applicant claims that Prednisolon Evolan, 31.25 mg, rectal solution, have the same qualitative and similar quantitative composition in excipients as Pred-Clysma, 31.25 mg, rectal solution. Therefore, published scientific literature is used to support this application instead of further clinical or non-clinical studies.

Discussion and overall conclusion
According to *Guideline on equivalence studies for the demonstration of therapeutic equivalence for locally applied, locally acting products in the gastrointestinal tract* (CPMP/EWP/239/95 Rev. 1, Corr.1*), if the test product is a solution at the time of administration and contains an active substance in the same concentration as an approved reference solution, studies supporting equivalent efficacy

and safety may be waived. The applied for product, which is a solution at the time of administration, contains the same active substance in the same concentration as the reference product. Furthermore, the differences in the excipient composition are acceptable since the pharmaceutical properties of the test product and reference product are similar. The absence of bioequivalence studies is acceptable

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies have been submitted. No data are required for an abridged application provided bioequivalence has been satisfactorily demonstrated or biowaiver has been accepted. A review of literature data has been provided as support.

Pharmacovigilance system

Proposed MAH: Evolan Pharma AB
The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the MPA considers the Summary acceptable.

Risk Management Plan
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Prednisolon Evolan.

Part II Safety specification

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Part III Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Part V Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Part VI Summary of the RMP
The Summary of the RMP is endorsed.

Conclusion RMP assessment
The submitted Risk Management Plan, version 0.1 signed 03-Jan-2023 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)

Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Renewal date
The renewal date will be 5 years after approval date.

IV. BENEFIT RISK ASSESSMENT

The quality of the hybrid product, Prednisolon Evolan, is found adequate. There are no objections to approval of Prednisolon Evolan, from a non-clinical and clinical point of view. The absence of bioequivalence studies is acceptable. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

N/A

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available on the Swedish MPA website.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available on the Swedish MPA website.

V.4.2 Assessment of User Testing

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PL was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-