LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Azelainsyra Evolan
(azelaic acid)

This module reflects the scientific discussion for the approval of Azelainsyra Evolan. The procedure was finalised at 2026-04-14. For information on changes after this date please refer to the module 'Steps taken after the finalisation of the initial procedure - Summary'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se

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 Azelainsyra Evolan, 150 mg/g, Gel.

The active substance is azelaic acid. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

The active substance in Azelainsyra Evolan is azelaic acid. Azelaic acid is a saturated, straight-chained dicarboxylic acid.

The proposed therapeutic indication is:
För lindring av mild till måttlig acne vulgaris i ansiktet med papler och pustler.
För topikal behandling av papulopustulös rosacea,

Azelainsyra Evolan should be applied to the affected skin areas twice a day. Approximately 0.5 g = 2.5 cm of gel is sufficient for the entire facial area.

An antimicrobial action and a direct influence on follicular hyperkeratosis are assumed to be the basis for the therapeutic efficacy of azelaic acid in acne. Clinically, a significant reduction of the colonization density of Propionibacterium acnes and a significant reduction in the fraction of free fatty acids in the skin surface lipids are observed.

While the pathophysiology of rosacea is not completely understood, there is increasing consensus that inflammation involving the elevation of several pro- inflammatory effector molecules such as kallikrein-5 and cathelicidin as well as reactive oxygen species (ROS), is a central process of this disease. Azelaic acid has been demonstrated to modulate the inflammatory response in normal human keratinocytes by: a) activating the peroxisome proliferator-activated receptor γ (PPARγ); b) inhibiting the trans-activation of nuclear factor-kB (NF-kB); c) inhibiting the production of pro-inflammatory cytokines and d) inhibiting the release of ROS from neutrophils, as well as direct scavenging effects on existing ROS.

The safety and efficacy of Azelainsyra Evolan for the treatment of acne vulgaris in children below the age of 12 years have not been established.

The safety and efficacy of Azelainsyra Evolan for the treatment of papulopustular rosacea in children below the age of 18 years have not been established.

II.2 General comments on the submitted dossier

The application for Azelainsyra Evolan, 150 mg/g, Gel, 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 Finacea, 150 mg/g, Gel authorised in SE since 2002, with LEO Pharma A/S 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 acceptable statements/declarations are provided from the manufacturer 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
Pharmacodynamic, pharmacokinetic and toxicological properties of azelaic acid are well known. As azelaic acid is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Azelaic acid 150 mg/g gel is not expected to result in a significant risk to the environment.

III.3 Clinical aspects

Pharmacokinetics
No pharmacokinetic bioequivalence studies have been conducted with the applied product Azelainsyra Evolan 150 mg/g gel compared to the reference product Finacea 150 mg/g gel.

All the relevant clinical information provided in the Clinical overview is literature-based. Azelaic acid is a naturally occurring compound present in many foods (wheat, rye, and barley) and is also formed endogenously. Endogenous plasma concentration and daily urinary excretion of azelaic acid are highly dependent on dietary intake. Azelaic acid can be detected in the serum and urine of humans after topical application, although percutaneous absorption is low with current formulations designed for local activity.

Absence of bioequivalence studies is acceptable since Azelainsyra Evolan is regarded as a simple formulation and pharmaceutical equivalence has been demonstrated.

Pharmacodynamics/Clinical efficacy/Clinical safety
Azelaic acid is a well-known active substance and the chosen excipients are well-established. No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Absence of clinical studies is acceptable since Azelainsyra Evolan is regarded as a simple formulation and pharmaceutical equivalence has been demonstrated.

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 Azelainsyra Evolan.

Part II Safety specification
Summary of safety concerns from RMP Part II: Module SVIII.

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 June 5, 2024, 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 generic product, Azelainsyra Evolan, is found adequate.

There are no objections to approval of Azelainsyra 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

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to

- Finacea 15% gel AT/H/0124/001/MR, regarding content and
- Dokusatnatrium/Sorbitol Evolan 1 mg/ml + 250 mg/ml rectal solution, 5.4.1-2023-099010 regarding layout.

The bridging report submitted by the applicant has been found acceptable.

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
-	-	-	-	-	-