LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Acetylsalicylsyra Evolan
(acetylsalicylic acid)

SE/H/2698/001/DC

This module reflects the scientific discussion for the approval of Acetylsalicylsyra Evolan. The procedure was finalised at 2025-12-04. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Acetylsalicylsyra Evolan, 75 mg, Film-coated tablet.

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

II. EXECUTIVE SUMMARY

II.1 About the product

Acetylsalicylic acid (ASA, aspirin) is a non-steroidal anti-inflammatory drug (NSAID) and has a well-characterised antiplatelet effect. The action of ASA on platelet COX is permanent, lasting for the life of the platelet (7 to 10 days). Via the effect on COX, ASA also has an inhibitory action on prostacyclin biosynthesis.
The tablets applied for are intended for use in secondary prevention and acute myocardial infarction and in line with other approved products. The doses proposed are also in line with approved products.

II.2 General comments on the submitted dossier

The application for Acetylsalisylsyra Evolan, 75 mg, Film-coated tablet, is a Generic Art. 10(1) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK as the sole concerned member state (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Trombyl, 75 mg, tablet, authorised in SE since 1991, with Pfizer AB as marketing authorisation holder.

European Reference Product (ERP)
A European Reference Product is used in CMS DK: Trombyl, 75 mg, tablet, authorised in SE since 1991, with Pfizer AB as marketing authorisation holder.

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

The RMS 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 Community, the RMS 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 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 acetylsalicylic acid are well known. As active substance 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)
A satisfactory environmental risk assessment has been provided and there is no need for additional studies.

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

III.3 Clinical aspects

Pharmacokinetics
No studies have been conducted. The Applicant claims that acetylsalicylic acid belongs to BCS class I and that bioequivalence studies can be waived.

<u>Pharmacokinetic properties of the active substance</u>
Absorption: After oral administration, acetylsalicylic acid is rapidly absorbed from the gastrointestinal

tract.

Elimination: Acetylsalicylic acid is rapidly metabolised to salicylic acid, with a half-life of 15-30 minutes. Salicylic acid is subsequently predominantly converted into glycine and glucuronic acid conjugates. Elimination kinetics of salicylic acid is dose-dependent, because the metabolism is limited by liver enzyme capacity. Thus, elimination half-time varies and is 2-3 hours after low doses (75 mg – 160 mg).

BCS-based biowaiver

The application is based on a Biopharmaceutical Classification System (BCS) based biowaiver and no bioequivalence study has been submitted. The applicant claims that acetylsalicylic acid is BCS class I substance.

According to the ICH M9 guideline on biopharmaceutics classification system-based biowaivers (EMA/CHMP/ICH/493213/2018), a BCS class I-based biowaiver is applicable for an immediate release product if the drug substance is not considered to have a narrow therapeutic index and has been proven to exhibit high solubility and high permeability (BCS class I). Also, *in vitro* dissolution characteristics of the test and the reference product should be either very rapid or similarly rapid and the excipients that might affect bioavailability should be qualitatively the same and quantitatively similar.

Background/Applicant's justification

It can be concluded that the drug substance has been proven to exhibit high solubility and complete absorption (BCS class I). None of the excipients included in the drug product are known to influence bioavailability and the difference in excipients is acceptable for a BCS class I-biowaiver. ASA is not considered to be a narrow therapeutic index drug.

Discussion and overall conclusion

Acetylsalicylic acid is not considered to have a narrow therapeutic index in the sense that narrowed acceptance ranges would be necessary in bioequivalence studies performed with Acetylsalicylic acid.

It can be concluded that the drug substance has been proven to exhibit high solubility. For details, see section III.1 Quality aspects.

It can be concluded that the extent of absorption is above 85% and thus, acetylsalicylic acid can be classified as a BCS class I substance.

None of the excipients included in the drug product are known to influence bioavailability. The difference in excipients is acceptable for a BCS class I-biowaiver.

Acceptable in vitro dissolution data has been submitted. For details, see section III Quality aspects.

In conclusion, the justification for a BCS (Biopharmaceutics Classification System) based biowaiver can be accepted.

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted, which is acceptable.

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 RMS 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 Acetylsalisylsyra Evolan.

Part II Safety specification
The MAH has submitted the version 0.1 RMP dated 5 Nov 2024 and proposed the following summary safety concerns: None important identified risk, important potential risks or missing information.

Assessor's comments: The Applicant has proposed no safety concerns which is accepted. This is in line with the CMDh conclusion stated in the "List of safety concerns per approved Risk Management Plan (RMP) of active substances per product".

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 5 Nov 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.

Common renewal date
The common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the generic product, Acetylsalisylsyra Evolan, is found adequate. There are no objections to approval of Acetylsalisylsyra 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 in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

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 PlL 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
-	-	-	-	-	-