LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Alimemazin Evolan
(alimemazine tartrate)

Asp no: 2017-1003

This module reflects the scientific discussion for the approval of Alimemazin Evolan. The procedure was finalised on 2018-08-08. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Alimemazin Evolan, 40 mg/ml, oral drops, solution, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Evolan Pharma AB 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 Theralen, 40 mg/ml, oral drops, solution, authorised in SE since 1963, with Sanofi AB as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

II. QUALITY ASPECTS

II.1 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.

II.2 Medicinal 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. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

No bioequivalence study has been submitted since the applied product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as the reference product. The qualitative composition of Alimemazin Evolan and Theralen is the same with the exception of buffers, flavours and antioxidants. The test product contains sodium citrate (buffering agent), sodium metabisulfite (antioxidant) and ascorbic acid (antioxidant) which are not present in the reference formulation. Further, the reference product contains spearmint flavour which is not present in the test product. The small amounts of these excipients are considered to be non-relevant from a bioavailability perspective. With regards to other excipients, the quantitative composition of the test product is considered to be very similar to the composition of the reference product. Taken together, the composition of Alimemazin Evolan 40 mg/ml oral drops is considered sufficiently similar to Theralen 40 mg/ml oral drops and the lack of bioequivalence studies acceptable.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

IV.3 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 Alimemazin Evolan.

Safety specification

Part II Module SVIII - Summary of the safety concerns

Table 1. Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Epilepsy and seizures • Cardiovascular diseases/QT prolongation • Increased risk of adverse reactions in elderly and patients with dementia
Important potential risks	• Interaction with other medicinal products • Pregnancy, lactation and fertility
Missing information	• None

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

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

Summary of the RMP
The submitted Risk Management Plan, version 1.0 signed 07 Sep 2017 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 MPA;
- 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.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the user test carried out on the product Alimemazin Evolan, 20 mg capsules, regarding the content and to the user test carried out on the product Natriumklorid Evolan 500 mg capsules regarding the layout.
The user test of the Alimemazin Evolan, 20 mg capsules leaflet was assessed and accepted in the national procedure 5.4.1-2017-19382. The user test of the leaflet for Natriumklorid Evolan 500 mg capsules was assessed and accepted in the national procedure 5.4.1-2014-5246.
The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Alimemazin Evolan, is found adequate. There are no objections to approval of product name, from a non-clinical and clinical point of view. The product information is acceptable.
The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

Alimemazin Evolan, 40 mg/ml, oral drops, solution was approved in the national procedure on 2018-08-08.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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