LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Deferipron Evolan
(deferiprone)

Asp no: 2014-0271, 2014-0272

This module reflects the scientific discussion for the approval of Deferipron Evolan. The procedure was finalised on 2015-07-16. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Deferipron Evolan, 500 mg and 1000 mg, film-coated tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Evolan Pharma AB, applies through the Swedish National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Ferriprox, 500 mg and 1000 mg, film-coated tablet authorised in Union since 1999, with Apotex Europe B.V. 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 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

To support the application, the applicant has submitted one single-dose study with the 1000 mg strength in the fasting state.

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 36 healthy volunteers, comparing deferiprone, 1000 mg, film-coated tablet with Ferriprox, 1000 mg, film-coated tablet under fasting conditions. The study was conducted at Veeda Clinical Research Pvt. Ltd., Ahmedabad, India between 13th and 19th November 2014. Blood samples were collected pre-dose and up to 24 hours post-dose. The study design is considered acceptable. Plasma concentrations of deferiprone were determined with an adequately validated LC-MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%. From a pharmacokinetic point of view, absence of studies with the lower strength 500 mg is acceptable, as the pharmacokinetics of deferiprone is linear in the dose range 25 mg/kg to 50 mg/kg.

Based on the submitted bioequivalence study with the 1000 mg strength, Deferipron Evolan is considered bioequivalent with Ferriprox.

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 Deferipron Evolan.

Safety concerns:

Important identified risks	• Agranulocytosis • Neutropenia • Use in pregnancy • Arthropathy • Increased liver function test values • Skin disorders • Allergic reactions
Important potential risks	• Torsade de pointes
Important missing information	• Lactation toxicity • Off-label use • Long-term safety data • Risk in patients with hepatic impairment • Risk in patients with renal impairment • Risk in immunocompromised patients

Summary of the RMP
The RMP is approved.

V. USER CONSULTATION

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 PIL 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. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Deferipron Evolan, 500 mg and 1000 mg, film-coated tablet is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 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

Deferipron Evolan, 500 mg and 1000 mg, film-coated tablet was approved in the national procedure on 2015-07-16.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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