LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Etoposide Accord (etoposide)

SE/H/1330/01/DC

This module reflects the scientific discussion for the approval of Etoposide Accord. The procedure was finalised at 2014-04-29. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Etoposide Accord, concentrate for solution for infusion, 20 mg/ml, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Accord Healthcare AB, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, BE, BG, CY, CZ, DE, DK, EE, ES, FI, HU, IE, IS, IT, LT, LV, MT, NL, NO, PL, PT, RO, SI, SK and UK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Vepesid, koncentrat till infusionsvätska, lösning, 20 mg/ml, authorised in SE in 1982, with Bristol-Myers Squibb AB as marketing authorisation holder. The MA was withdrawn in 2009.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Etoposide Accord is presented in the form of a concentrate for solution for infusion containing 20 mg of etoposide per millilitre. The concentrate is filled in clear glass vials (5 ml or 12.5 ml) with Teflon faced rubber stoppers and aluminium seals. Etoposide Accord must be diluted in sodium chloride solution (0.9% w/v) or dextrose solution (5% w/v) prior to use.

II.2 Drug Substance

The drug substance etoposide is a derivate of podophyllotoxin. Etoposide is described in a monograph published in the European Pharmacopeia (Ph. Eur.). The substance is a white or almost white, slightly hygroscopic crystalline powder which is practically insoluble in water, sparingly soluble in methanol, slightly soluble in alcohol and in methylene chloride.

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

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Etoposide Accord, concentrate for solution for infusion is formulated using excipients described in the current Ph. Eur. The excipients are citric acid anhydrous, benzyl alcohol, polysorbate 80, polyethylene glycol 300 and ethanol anhydrous. None of the excipients are of human or animal origin.

The pharmaceutical development work has been described. The function of each excipient has been explained and the manufacturing process justified. The container closure system is considered suitable for this dosage form.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

The tests and limits in the release and shelf-life specifications are considered appropriate to control the quality of the finished product in relation to its intended purpose. The analytical procedures have been validated.

Stability studies under ICH conditions have been performed and the data presented support the shelf-life claimed in section 6.3 of the SPC. Satisfactory chemical and physical in-use stability has also been demonstrated for dilutions prepared in accordance with the instructions given in the SPC.

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

Micelles are formed when the drug product is diluted prior to administration. Based on the references submitted by the applicant it is however considered highly unlikely that polysorbate 80, in the concentrations used in the proposed formulation, would play a role from a pharmacokinetic and clinical perspective. The absence of bioequivalence studies is therefore considered justified.

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.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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.

The risk/benefit ratio is considered positive and Etoposide Accord, 20 mg/ml, concentrate for solution for infusion is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Etoposide Accord, 20 mg/ml, concentrate for solution for infusion was successfully finalised on 2014-04-29.

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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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