LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Metotrexat Accord
(methotrexate)

SE/H/1205/01/MR

This module reflects the scientific discussion for the approval of Metotrexat Accord. The procedure was finalised at 2012-05-22. For information on changes after this date please refer to the module 'Update'.

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.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

Accord Healthcare Limited UK has applied for a marketing authorisation for Metotrexat Accord, 25 mg/ml injektions-/ infusionsvätska, lösning claiming essential similarity to Methotrexate Wyeth, 25 mg/ml, solution for injection authorised in Sweden since 1985, with Pfizer AB as marketing authorisation holder. The product contains methotrexate as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Metotrexat Accord is presented in the form of a solution for injection. The excipients are hydrochloric acid, sodium chloride, sodium hydroxide and water for injection. The product is packed in glass vials.

II.2 Drug Substance

Methotrexate has a monograph in the Ph Eur.

Methotrexate is a yellow or orange, crystalline, hygroscopic powder which is practically insoluble in water. The structure of methotrexate has been adequately proven and its physico-chemical properties sufficiently described. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active 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

Metotrexat Accord 25 mg/ml solution for injection is formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable origin/has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance, such as poor aqueous solubility and stability.

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 specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored below 25°C.

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

As the product is to be administered as an aqueous intravenous solution, no difference in absorption rate or bioavailability between the two products is expected. Thus, no bioequivalence study is required.

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 Metotrexat Accord, 25 mg/ml solution for injection is recommended for approval.

VI. APPROVAL

Metotrexat Accord, 25 mg/ml solution for injection was approved in the national procedure 2008-02-08.

The Mutual recognition procedure for Metotrexat Accord, 25 mg/ml solution for injection was successfully finalised 2012-05-22.

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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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