LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Metotrexat Accord
(methotrexate)

SE/H/1205/02/DC

This module reflects the scientific discussion for the approval of Metotrexat Accord. The procedure was finalised at 2014-07-09. 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

The application for Metotrexat Accord, 100 mg/ml, concentrate for solution for infusion, is a generic application made according to Article 10(1) of Directive 2001/83/EC. This generic application is an extension to Metotrexat Accord, 25 mg/ml, solution for injection. The applicant, Accord Healthcare Limited, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, BE, CY, CZ, DE, DK, ES, FI, FR, HU, IE, LT, MT, NL, NO, PT, 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 Methotrexate Pfizer, 100 mg/ml, concentrate for solution for infusion, authorised in Sweden since 1991, with Pfizer AB as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Metotrexat Accord is presented in the form of a concentrate for solution for infusion containing 100 mg/ml of methotrexate. The excipients are sodium hydroxide and water for injection. The concentrate is filled in glass vials closed with butyl rubber stoppers.

II.2 Drug Substance

Methotrexate has a monograph in the Ph Eur.

Methotrexate is a yellow to orange, crystalline 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 concentrate for solution for infusion is formulated using excipients described in the current Ph Eur. No excipients of human or animal origin are used.

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 30 °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

The applied product is to be administered as an aqueous intravenous solution containing the same active substance as the currently authorised product. None of the excipients are known to interact with the drug substance, and the same excipients are used as in the reference product. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1).

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

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 product Metotrexat Accord 25 mg/ml, solution for injection. The user test of the Metotrexat Accord 25 mg/ml leaflet was first assessed and accepted in the national 1B-variation Dnr 2121:20111-82243, it was also included and accepted in the procedure SE/H/1205/01/MR. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Metotrexat Accord, 100 mg/ml, concentrate for solution for infusion, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Metotrexat Accord, 100 mg/ml, concentrate for solution for infusion, was successfully finalised on 2014-07-09.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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)

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