LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Injexate
(methotrexate)

SE/H/1431/01/DC

This module reflects the scientific discussion for the approval of Injexate. The procedure was finalised on 2015-10-01. 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 Injexate, 50 mg/ml, solution for injection in pre-filled syringe, is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Accord Healthcare Limited applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, BE, BG, CY, CZ, DE, DK, FI, FR, HU, IE, IT, LT, NL, NO, PL, 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 Metoject, 10 mg/ml, solution for injection, pre-filled syringe, authorised in SE since 2002, with medac Gesellschaft für klinische Spezialpräparate mbH 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

No bioequivalence studies have been submitted in this application.

The applied product is an aqueous solution intended for subcutaneous administration and contains the same excipients as the reference product. The dosages (7.5mg-30mg) in the pre-filled syringes for the applied product are no new dosages since these are already approved for either Metoject 10mg/ml or Metoject 50mg/ml or both. The volume for injection in the pre-filled syringes for the applied product is the same as in the prefilled syringes for Metoject 50mg/ml solution for injection. Thus the absences of bioequivalence studies are considered 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 Injexate.

Safety specification

The Summary of safety concern as presented by the Applicant adequately reflects the risk profile for the product.

Summary of safety concerns

Important identified risks	• Medication error / dose related toxicity (1) • Hepatic impairment / hepatotoxicity (1) • Renal impairment (1) • Immunosuppression / Immunotoxicity (1) • Gastrointestinal toxicity (1) • Pulmonary toxicity (1) • Hematotoxicity (1) • Administration during pregnancy and lactation (1) • Neurotoxicity (1) • Skin and subcutaneous tissue disorders (1)
Important potential risks	• Infertility (1) • Accidental exposure / contact with skin (1) • Use in elderly patients (1)
Missing information	• Use in children under 3 years of age (1)

Pharmacovigilance plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is considered acceptable based on the well-known safety profile of methotrexate.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is considered acceptable based on the well-known safety profile of methotrexate.

RMS recommendation

The RMP is approved.

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 Metoject 50 mg/ml solution for injection, pre-filled syringe SE/H/643/01/DC regarding content and to

Esomeprazole Sodium 40 mg/ml Powder for solution for injection/Infusion UK/H/5566/01/DC regarding layout. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Injexate, 50 mg/ml, solution for injection in pre-filled syringe 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

The Decentralised procedure for Injexate, 50 mg/ml, solution for injection in pre-filled syringe was positively finalised on 2015-10-01.

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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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
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Internet: www.mpa.se E-mail: registrator@mpa.se