LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Injexate
(methotrexate)

SE/H/1431/02-11/DC

This module reflects the scientific discussion for the approval of Injexate. The procedure was finalised on 2017-03-02. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

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Accord Healthcare Limited has applied for a marketing authorisation for Injexate, 7,5mg, 10mg, 12,5mg, 15mg, 17,5mg, 20mg, 22,5mg, 25mg, 27,5mg, 30mg, solution for injection in pre-filled injector. The active substance methotrexate is the same as in Injexate, injection in pre-filled injector, marketed by Accord Healthcare Limited since 2015.

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article 10(3) of Directive 2001/83/EC.

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

No new data has been submitted by the applicant, which is considered acceptable.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

No bioequivalence study was submitted with 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 pre-filled syringes for Metoject 50mg/ml solution for injection. The formulation is the same as for the already approved product Injexate 50 mg/ml, solution for injection, pre-filled syringe (SE/H/1431/01/DC) which was approved without a bioequivalence study. Thus the absence of bioequivalence study is considered acceptable.

IV.2 Discussion on the clinical aspects

No new data on pharmacodynamics, clinical efficacy or clinical safety have been submitted by the applicant, which is considered acceptable.

IV.3 Risk Management Plans

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

Summary table of safety concerns as approved in the RMP

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 endorsed.

Risk minimisation measures

Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP

The RMP is approved.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Metojectpen 50 mg/ml solution for injection, prefilled pen. The user test of the Metojectpen leaflet was assessed and accepted in SE/H/643/01/DC. 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, 7,5mg, 10mg, 12,5mg, 15mg, 17,5mg, 20mg, 22,5mg, 25mg, 27,5mg, 30mg, solution for injection in pre-filled injector 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, 7,5mg, 10mg, 12,5mg, 15mg, 17,5mg, 20mg, 22,5mg, 25mg, 27,5mg, 30mg, solution for injection in pre-filled injector was positively finalised on 2017-03-02.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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