LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Methotrexate Orion
(methotrexate)

SE/H/1422/01/DC

This module reflects the scientific discussion for the approval of Methotrexate Orion. The procedure was finalised at 2015-03-10. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Methotrexate Orion, 25 mg/ml, solution for injection in pre-filled syringe, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Orion Corporation applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI and NO as concerned member states (CMS).

The European reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Lantarel FS, 25 mg/ml, solution for injection in pre-filled syringe, authorised in DE since 1991, with Wyeth Pharma GmbH, as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Methotrexate Orion is presented in the form of a solution for injection in pre-filled syringes containing 25 mg/mL of methotrexate. The excipients are sodium chloride, sodium hydroxide and water. The solution for injection is filled in syringes of glass.

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. Relevant information on chirality is presented. 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

Methotrexate Orion, solution for injection in pre-filled syringes is formulated using excipients described in the current Ph. Eur. All raw materials used in the product have 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.

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

No bioequivalence study has been submitted. The applied product is intended for parenteral use (subcutaneous and intramuscular). According to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) no bioequivalence studies are required, if the test product is of the same type of solution (aqueous or oily), contains the same concentration of the same active substance and the same excipients in similar amounts as the medicinal product currently approved.

The applied product contains the same active substance in the same concentration as the reference product and the same excipients as the reference product. Even though the reference product contains methotrexate dinatrium, this is assessed as not affecting the bioavailability. Thus, the absence of a bioequivalence study is 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.

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

Content:
Methorexate 2.5 mg/ml solution for injection.

The user test of the Methorexate 2.5 mg/ml solution for injection leaflet was assessed and accepted in national procedure in UK (PL22856/0015-17/0001 and approved by the MHRA in November 2007.

Layout
Venlafaxin Orion 37,5 mg, 75 mg and 150 mg.

The user test of the Venlafaxin Orion 37,5 mg, 75 mg and 150 mg leaflet was assessed and accepted in DC procedure: DE/H/1320/01-03/DC in 2008.

The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Methotrexate Orion, 25 mg/ml, solution for injection in pre-filled syringe, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Methotrexate Orion, 25 mg/ml, solution for injection in pre-filled syringe, was successfully finalised on 2015-03-10.

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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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