LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Dexametason Abcur
Dexamethasone

SE/H/1260/01-02/DC

This module reflects the scientific discussion for the approval of Dexametson Abcur. The procedure was finalised at 2013-03-21. 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 Dexametason Abcur, 1 and 4 mg tablets is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Abcur AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI, IS and NO concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Fortecortin 4 mg tablets authorised in Germany since 1997, with Merck Pharma GmbH as marketing authorisation holder.

The reference product used in the bioequivalence study is Fortecortin 4 mg tablet licensed in Germany.

II. QUALITY ASPECTS

II.1 Introduction

Dexametason Abcur is presented in the form of tablets containing 1 or 4 mg of dexamethasone. The excipients are lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate and talc. The tablets are packed in PVC/Al blisters.

II.2 Drug Substance

Dexamethasone has a monograph in the Ph Eur.

Dexamethasone is a practically white, crystalline powder which is practically insoluble in water; sparingly soluble in acetone, alcohol, dioxane, and methanol; slightly soluble in chloroform and very slightly soluble in ether. The structure of dexamethasone has been adequately proven and its physico-chemical properties sufficiently described. The route of synthesis has been adequately described.

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

Dexametason Abcur tablets are formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable origin or 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.

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, with no special storage precautions.

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

Bioequivalence was evaluated in one pivotal bioequivalence study. In Study CPA 416-12/GA12-01 bioequivalence between Dexametason Abcur 4 mg tablets and Fortecortin 4 mg tablets was evaluated. The study was a single-dose, two-way crossover study conducted in 26 healthy volunteers under fasting conditions. Blood samples were collected pre-dose and up to 24 hours post-dose. The study design is considered acceptable. Plasma concentrations of dexamethasone were determined with an adequately validated LC/MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Given that dexamethasone exhibit non-linear pharmacokinetics with a less than dose-proportional increase in AUC with increasing doses, an additional bioequivalence study with the lowest strength of 1 mg would have been appropriate. However, given that the 1 mg strength is not available for the reference product this request is not possible to comply with. As all biowaiver criteria for additional strengths (i.e. same manufacturing process, proportional composition, comparable dissolution profiles) are fulfilled, no further studies with the 1 mg tablet are requested and a biowaiver for this strength 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
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 Finnish.
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 results of the conducted bioequivalence study with the 4 mg strength can be extrapolated to other strength of 1 mg since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

VI. APPROVAL

Decentralised procedure for Dexametason Abcur, 1 and 4 mg tablets was successfully finalised on 2013-03-21.

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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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