LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Amitriptylin Abcur
(amitriptyline hydrochloride)

SE/H/1643/01-03/MR

This module reflects the scientific discussion for the approval of Amitriptylin Abcur. The procedure was finalised at 2014-05-22. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Amitriptylin Abcur, 10 mg and 25 mg, film-coated tablet, is a generic application made according to Article 10(1) and Amitriptylin Abcur, 50 mg, film-coated tablet is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Abcur AB applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Saroten, 10 mg and 25 mg, film-coated tablet authorised in Sweden since 1963, with H. Lundbeck A/S as marketing authorisation holder. The applicant has applied for a full biowaiver claiming that amitriptylin is a BCS class I substance.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Amitriptylin Abcur is presented in the form of tablets containing 11.32 mg, 28.30 mg, and 56.60 mg of amitriptyline hydrochloride which corresponds to 10 mg, 25 mg, and 50 mg of amitriptyline. The excipients are lactose monohydrate, maize starch, povidone, talc, polyvinyl alcohol, macrogol, titanium dioxide, and iron oxide. The tablets are packed in PVC/Al blister or in a HDPE container with a PP screw cap.

The applicant has applied for a full biowaiver claiming that amitriptylin is a BCS class I substance. The pharmaceutical criteria for such a biowaiver are fulfilled. A BCS class I biowaiver is acceptable from a pharmaceutical point of view.

II.2 Drug Substance

Amitriptyline hydrochloride has a monograph in the Ph Eur.

Amitriptyline hydrochloride is a white or almost white powder or colourless crystals, which is/are freely soluble in water, in ethanol (96%) and in methylene chloride. The structure of amitriptyline hydrochloride 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

Amitriptyline Abcur, tablets are formulated using excipients described in the current Ph Eur. All raw materials used in the product, except lactose monohydrate, are of synthetic or vegetable origin. For lactose monohydrate was 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. For the products in the HDPE container no special storage precaution is needed. The products in blister package should be stored not above 30 °C and in the outer carton to protect from light.

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 applicant has applied for a full biowaiver claiming that amitriptylin is a BCS class I substance.

From a pharmacokinetic point of view, a BCS-class I based biowaiver is acceptable for an immediate release drug product if the drug substance has proven to exhibit complete absorption and the excipients that might affect bioavailability are quantitatively and qualitatively the same. It should also be confirmed that the substance is not a narrow therapeutic index drug.

The applicant has provided relevant overview/summary documents as background.

The excipients are considered acceptable. Further, in clinical studies (e.g. Mellström et al) it has been demonstrated that the fraction absorbed (fa) of amitriptyline is higher than 85 %. Further, it is agreed that the therapeutic window is not considered narrow in that sense that narrowed acceptance ranges would be necessary in bioequivalence studies performed with amitriptyline.

From a pharmacokinetic perspective, the requirements for being classified as a BCS class I substance are fulfilled.

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 risk/benefit ratio is considered positive and Amitriptylin Abcur, 10 mg and 25 mg, film-coated tablet is recommended for approval.

VI. APPROVAL

Amitriptylin Abcur, 10 mg and 25 mg, film-coated tablet was approved in the national procedure on 2014-05-22.

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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
SE/H/1643/01-03/MR	Initial Mutual Recognition Procedure	Yes	2017-02-14	Approval	N/A

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