LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Lamotrigin Medartuum
Lamotrigine

SE/H/728/01-04/MR

This module reflects the scientific discussion for the approval of Lamotrigin Medartuum. The procedure was finalised at 2007-10-05. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Medartuum Medical AB has applied for a marketing authorisation for Lamotrigin Medartuum tablets 25 mg, 50 mg, 100 mg and 200 mg claiming essential similarity to Lamictal® 25 mg, 50 mg, 100 mg and 200 mg tablets marketed in Sweden by GlaxoSmithKline. The product contains lamotrigine as active substance and is indicated for the treatment of epilepsy as monotherapy or in combination with other antiepileptic drugs. The reference product used in the bio-equivalence study is Lamictal 200 mg tablets marketed by GlaxoSmithKline in Greece.

II. QUALITY ASPECTS

II.1 Introduction

Lamotrigin Medartuum is presented in the form of tablets containing 25 mg, 50 mg, 100 mg or 200 mg lamotrigine. The excipients are lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, yellow iron oxide, povidone and magnesium stearate. The tablets are packed in PVC–Al blisters.

II.2 Drug Substance

Lamotrigine does not have a monograph in the European Pharmacopoeia, but a draft monograph has been published in PharmEuropa. When this monograph has been adopted, the drug substance should conform to it. Information on lamotrigine has been supplied in the form of an ASMF from the active substance manufacturer (Biogena, Cyprus).

Lamotrigine is a white to off white powder which is practically insoluble in water, slightly soluble in methanol and DMSO, sparingly soluble in isopropanol and acetone, soluble in DMF. The structure of lamotrigine has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and 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

Lamotrigin Medartuum tablets 25 mg, 50 mg, 100 mg and 200 mg are formulated using excipients described in the current Ph Eur, except for yellow iron oxide which conforms to the current USP. All raw materials used in the product 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, such as poor aqueous solubility.

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

One bioequivalence study was submitted for the 200 mg strength. The absence of studies with other tablet strengths is considered acceptable from a pharmacokinetic point of view, as the pharmacokinetics is linear up to 450 mg. The study did not evaluate the influence of food on the pharmacokinetics. This is considered appropriate since the reference product did not show any food effect. Bioequivalence was shown with respect to the rate and extent of absorption.

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 testing of the package leaflet has been performed.

The results of the conducted bioequivalence study can be extrapolated to the other strengths since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Lamotrigin Medartuum tablets 25 mg, 50 mg, 100 mg and 200 mg is recommended for approval.

VI. APPROVAL

The Mutual recognition procedure for Lamotrigin Medartuum tablets 25 mg, 50 mg, 100 mg and 200 mg was successfully finalised on 2007-10-05.

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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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