LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Epranial
(esomeprazole)

SE/H/1032/01-02/DC

This module reflects the scientific discussion for the approval of Epranial. The procedure was finalised at 4 May 2011. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Ethypharm S.A. has applied for a marketing authorisation for Epranial, gastro-resistant tablet, 20 mg and 40 mg, claiming essential similarity to Nexium, gastro-resistant tablet, 20 mg and 40 mg, marketed in Sweden by AstraZeneca AB. The product contains esomeprazole as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bioequivalence studies is Inexium, gastro-resistant tablet, 20 mg and 40 mg marketed by AstraZeneca in France.

II. QUALITY ASPECTS

II.1 Introduction

Finished product is presented in the form of gastro-resistant tablet containing 20 mg and 40 mg of esomeprazole (as magnesium dihydrate) The excipients are of pharmaceutical grade. The gastro-resistant tablet are packed in/filled in aluminium blister or polyethylene bottle with polypropylene cap.

II.2 Drug Substance

Esomeprazole magnesium dihydrate does not have a monograph in the Ph Eur but there is a monograph for esomeprazole magnesium trihydrate.

Esomeprazole magnesium dihydrate is off-white to pale yellow coloured crystalline powder. The structure of esomeprazole magnesium dihydrate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism, 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

Esomeprazole 20 mg and 40 mg gastro-resistant tablet is formulated using excipients described in the current Ph Eur, except for film coating agents which are controlled according to acceptable in house specifications.

The product development has taken into consideration the physico-chemical characteristics of the active substance, such as aqueous solubility, hygroscopic properties, polymorphism and stability.

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 ºC.

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 has been shown for the 20 and 40 mg formulation under fasting conditions at single-dose conditions and for the 40 mg formulation also at multiple-dose conditions. Under fed conditions BE has not been shown between the test and originator products due to a smaller effect of food on Esomeprazole Ethypharm. It is well known that food reduces the exposure of esomeprazole but not to a clinically relevant extent and esomeprazole may be taken with or without food (see SPC of originator product). According to the document *Questions & Answers* EMEA/618604/2008 Rev 1, a difference in food-effect could be acceptable on a case-by-case basis. In this case a smaller reduction of exposure is not considered to be of any clinical efficacy or safety concern and no changes needs to be made in the dosing recommendations.

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 Esomeprazole Ethypharm 20mg and 40 mg gastro-resistant capsules, hard, DCP/MRP number IS/H/0149, 0150, 0155, 0156, 0157/01-02/DC. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Epranial, 20 mg and 40 mg, gastro-resistant tablet is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Epranial, 20 mg and 40 mg, gastro-resistant was successfully finalised on 4 May 2011.

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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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