LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Esomep
(esomeprazole magnesium trihydrate)

SE/H/885/01-02/DC

This module reflects the scientific discussion for the approval of Esomep. The procedure was finalised 2010-05-12. 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

AstraZeneca AB has applied for a marketing authorisation for Esomep, gastro-resistant tablets, 20 and 40 mg. This was an informed consent application submitted in accordance with Article 10c of Directive 2001/83/EC as amended, through the Decentralised Procedure. Esomep has the same composition and the same pharmaceutical form as Nexium, 20 and 40 mg gastro-resistant tablets, approved in Sweden since 10 March 2000 with the Marketing Authorisation Holder AstraZeneca AB. The product contains esomeprazole magnesium trihydrate as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

ESOMEP is presented in the form of gastro-resistant tablets containing 22.3 mg and 44.5 mg of Esomeprazole magnesium trihydrate which corresponds to 20 and 40 mg mg of the Esomeprazole. The excipients are of pharmacopeia grade. The gastro-resistant tablets are packed in blister and plastic bottle.

II.2 Drug Substance

Esomeprazole magnesium trihydrate has a monograph in the Ph Eur (01/2009:2372).

Esomeprazole magnesium trihydrate which is the (-)-enantiomer of the magnesium salt of Omeprazole. The specific rotation for Esomeprazole magnesium trihydrate is –139.6°. Esomeprazole is thermodynamically stable and only one crystal modification of Esomeprazole magnesium trihydrate has been found. The substance is crystalline as observed with powder X-ray diffraction. The solubility in water of is 1.5 mg/ml with a corresponding pH of about 10.0. The molecule contains one asymmetrically substituted sulphoxide moiety, which makes the molecule chiral. In Esomeprazole the sulphur atom has the S-configuration.

The structure of Esomeprazole magnesium trihydrate 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

The dosage form is a multi unit pellet system (MUPS) containing individually enteric-coated pellets. The tablet is designed to disintegrate in the stomach shortly after administration and disperse the pellets in the gastric contents. The tablets contain iron oxide yellow and reddish

brown (E172) as well as titanium oxide (E171) as colorants. All excipients comply with compendial specifications.

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 30 ºC.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Reference has been made to the original Nexium dossier and amendments by subsequent variations. No additional non-clinical studies have been provided or are considered necessary since a letter of consent from AstraZeneca AB, dated 3 August 2009, has been submitted, which authorizes use of the non-clinical documentation for Nexium in support of this application.

IV. CLINICAL ASPECTS

IV.1 Discussion on the clinical aspects

Reference has been made to the original Nexium dossier and amendments by subsequent variations. No additional clinical studies have been provided or are considered necessary since a letter of consent from AstraZeneca AB, dated 3 August 2009, has been submitted, which authorizes use of the clinical documentation for Nexium in support of this application.

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 Nexium, SE/H/211/01-03/II/64. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and the application for Esomep, gastro-resistant tablets, 20 and 40 mg is recommended for approval.

The applicant has made a commitment to harmonize the SmPC for Esomep with the Nexium SmPC after the completion of the ongoing renewal for Nexium.

VI. APPROVAL

The Decentralised procedure for Esomep, gastro-resistant tablets, 20 and 40 mg was successfully finalised 2010-05-12.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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)

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