

Public Assessment Report

Scientific discussion

Omeprazol Actavis (Omeprazole)

SE/H/754/01-03/MR

This module reflects the scientific discussion for the approval of Omeprazol Actavis. The procedure was finalised at 2009-11-19. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Actavis Nordic A/S has applied for a marketing authorisation for Omeprazol Actavis, hard gastro-resistant capsules, 10 mg, 20 mg and 40 mg claiming essential similarity to Losec MUPS, hard gastro-resistant capsules, 10 mg, 20 mg and 40 mg marketed in Sweden by AstraZeneca AB. The product contains omeprazole as active substance. For approved indications see the Summary of Product Characteristics. The reference products used in the bio-equivalence studies are Mopral 10 mg hard gastro-resistant capsule by AstraZeneca, France and Mopral 20 mg hard gastro-resistant capsule by Astra España, Spain.

II. QUALITY ASPECTS

II.1 Introduction

Omeprazol Actavis is presented in the form of hard gastro-resistant capsules containing 10 mg, 20 mg and 40 mg of omeprazole. The excipients are sugar spheres (sucrose, maize starch, water), methacrylic acid-ethyl acrylate co-polymer (1:1) dispersion, hypromellose, talc, mannitol, macrogol 6000, titanium dioxide (E171), polysorbate 80, dinatrium phosphate, anhydrous, sodium lauryl sulphate, gelatine, water, titanium dioxide (E171), quinoline yellow (E104) (10 mg and 20 mg capsules only) and indigo carmine (E132) (40 mg capsule only). The capsules are packed in OPA-ALU-PVC/ALU blisters or HDPE capsule containers with PP lid (containing silica gel as desiccant).

II.2 Drug Substance

Omeprazole has a monograph in the Ph Eur.

Omeprazole is a white to off-white crystalline powder which is freely soluble in ethanol and methanol and very slightly soluble in water. The structure of omeprazole has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on e.g. 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

Omeprazol Actavis, hard gastro-resistant capsules, 10 mg, 20 mg and 40 mg is formulated using excipients described in the current Ph Eur, except for quinoline yellow and indigo carmine which is/are controlled according to acceptable in house specifications. 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 (EMA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance, such as poor aqueous solubility 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 in the original container.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refers to a product approved based on a full application with regard to non-clinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

The pharmacokinetic documentation for Omeprazol Actavis comprised one bioequivalence study with both single and multiple dose administration in the fasted state and one single dose bioequivalence study performed under fed conditions. The studies were conducted with the 20 mg strength. The absence of studies with the other capsule strengths is considered acceptable from a pharmacokinetic point of view, as the dose-dependency in the pharmacokinetics of omeprazole is fairly moderate.

The first study was a single and multiple dose 3-way crossover bioequivalence study under fasting conditions, with Mopral® capsules (Astra España, Spain) and Losec® capsules (Astra pharmaceuticals Pty Ltd, Australia) as reference products.

The other study was single dose 2-way crossover bioequivalence study, with Mopral® capsules (Astra, France) as reference product. The study medications were administered with a continental breakfast with a high fat content, since high-calorie constituents, such as croissants, butter and whole milk, were administered. Thus, although the meal was not of the “standard FDA breakfast” type, the meal is considered to fulfil the requirements of a high-fat meal

The study designs were adequate and the clinical and analytical sites have been judged to be GCP and GLP compliant.

Bioequivalence was demonstrated between the test and reference formulations during fasting (single and multiple dose) and fed (single dose) conditions, since the 90% confidence interval limits were within the 80-125% range for C_{max} , AUC_{0-t} and AUC_{0-inf} for all comparisons.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refers 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 and is acceptable.

The results of the conducted bioequivalence studies can be extrapolated to 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 Omeprazol Actavis, hard gastro-resistant capsules, 10 mg, 20 mg and 40 mg is recommended for approval.

The applicant has committed to submit a variation to harmonise the SPC, PL and labelling to the reference product Losec when the Commission Decision for Losec has been submitted.

VI. APPROVAL

The Mutual recognition/Decentralised procedure for Omeprazol Actavis, hard gastro-resistant capsules, 10 mg, 20 mg and 40 mg was successfully finalised on 2009-11-19.

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)