LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Amlodipin Accord
(amlodipine besilate)

SE/H/842/01-02/MR

This module reflects the scientific discussion for the approval of Amlodipin Accord 5 mg and 10 mg tablets. The procedure was finalised at 2011-07-14. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Accord Healthcare Limited has applied for a marketing authorisation for Amlodipin Accord, 5 mg and 10 mg tablets claiming essential similarity to Norvasc 5 mg and 10 mg tablets marketed in Sweden by Pfizer AB. The product contains amlodipine besilate as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Norvasc 10 mg tablets marketed by Pfizer AB in the Netherlands.

II. QUALITY ASPECTS

II.1 Introduction

Amlodipin Accord is presented in the form of tablets containing amlodipine besilate equivalent to 5 mg and 10 mg of amlodipine respectively. The excipients are microcrystalline cellulose, sodium starch glycolate, disodium hydrogen citrate, croscarmellose sodium, crospovidone and magnesium stearate. The tablets are packed in PVC/PVdC//aluminium blister packs.

II.2 Drug Substance

Amlodipine besilate has a monograph in the Ph. Eur. and the CEP procedure is applied. It is a white or almost white powder, freely soluble in methanol, sparingly soluble in ethanol, slightly soluble in water and 2-propanol.

The structure of amlodipine besilate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on 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

Amlodipin Accord 5 mg and 10 mg tablets are formulated using excipients described in the current Ph. Eur., except for disodium hydrogen citrate which is controlled according to the current ed. of BP. None of the excipients are of human or animal origin.

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, 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

Results from one bioequivalence study of the 10 mg tablet (study AMLO/2003/114) were included in the original application. In 2007 the applicant submitted an additional bioequivalence study of the 10 mg tablet (study CPU/AMLO/06/014) after changing the manufacturing site.

Study AMLO/2003/114: A single-dose two-way crossover bioequivalence study with the 10 mg tablet was performed, March until April 2004 at Synchron Research Services PVT. LTD, Ahmedabad, India. The study was conducted under fasting conditions in a total of 28 healthy volunteers. Amlodipine in plasma was determined using a validated LC-MS-MS method. The 90% confidence interval for AUC and C_{max} was within the acceptance criteria of 0.80-1.25. The two formulations are considered bioequivalent.

Study CPU/AMLO/06/014: This was a single-dose two-way crossover study with the 10 mg tablet, performed between October and November 2006 at Jubilant Clinsys Ltd., Noida, India. The study was conducted under fasting conditions in a total of 28 healthy volunteers. Amlodipine in plasma was determined using a validated LC-MS-MS method at Bioanalytical Operations, Jubilant clinsys Ltd., Noida, India. The 90% confidence interval for AUC and C_{max} was within the acceptance criteria of 0.80-1.25. The two formulations are considered bioequivalent.

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 Amlodipin Alternova 5 mg and 10 mg tablets, MRP number SE/H/755/01-02/MR.
The bridging report submitted by the applicant has been found acceptable.

Bioequivalence has been demonstrated. The results of the conducted bioequivalence study 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 applicant commited to submit a variation to harmonise the SmPC according to the outcome of the article 30 referral for the originator product Norvasc (amlodipine) which was still ongoing at time of day 90 of the MRP.

The risk/benefit ratio is considered positive and Amlodipin Accord, tablet, 5 mg and 10 mg, is recommended for approval.

VI. APPROVAL

The Mutual recognition procedure for Amlodipin Accord, 5 mg and 10 mg, tablet was successfully finalised on 2011-07-14.

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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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