LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Amlodipine Vitabalans (amlodipine besilate)

SE/H/978/01-02/DC

This module reflects the scientific discussion for the approval of Amlodipine Vitabalans. The procedure was finalised at 16 March 2011. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Vitabalans Oy has applied for a marketing authorisation for Amlodipine Vitabalans, tablets, 5 mg and 10 mg claiming essential similarity to Norvasc, tablet, 5 mg and 10 mg, 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 bioequivalence study is Norvasc, tablets, 10 mg, marketed by Pfizer Oy in Finland.

II. QUALITY ASPECTS

II.1 Introduction

AmlodipinVitabalans is presented in the form of tablets containing 6.94 mg respective 13.88 mg of amlodipine besilate which corresponds to 5 mg respective 10 mg of amlodipine. The excipients are cellulose microcrystalline, silica colloidal anhydrous, sodium starch glycolate and magnesium stearate. The tablets are packed in PVC/PVdC-aluminium blisters.

II.2 Drug Substance

Amlodipine besilate has a monograph in the Ph Eur.

Amlodipine besilate is a white to almost white powder which is slightly soluble in water and 2-propanol, freely soluble in methanol and sparingly soluble in ethanol. The structure of amlodipine besilate 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

Amlodipine Vitablans tablets are formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable 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, when protected from light.

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 has been submitted for the 10 mg strength. The study was a randomised, two-treatment, two-period, two-sequence single-dose crossover study conducted in 18 healthy volunteers under fasting conditions. All subjects completed both study periods and were included in the pharmacokinetic analysis. Plasma concentrations of amlodipine were determined with a validated HPLC-MS method.

Bioequivalence was demonstrated for Cmax and AUC.

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
The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was Czech.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

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 risk/benefit ratio is considered positive and Amlodipine Vitabalans, 5 mg and 10 mg, tablets is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Amlodipine Vitabalans, 5 mg and 10 mg, tablet was successfully finalised on 16 March 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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