

Public Assessment Report

Scientific discussion

Amlodipin Bluefish (Amlodipine besilate)

SE/H/783/01-02/MR

This module reflects the scientific discussion for the approval of Amlodipin Bluefish, 5 mg and 10 mg, tablets. The procedure was finalised at 2010-02-11. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Bluefish Pharmaceuticals AB has applied for a marketing authorisation for Amlodipin Bluefish 5 mg and 10 mg tablets claiming essential similarity to Norvasc 5 mg and 10 mg tablet 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 Istin 10 mg tablets marketed by Pfizer in UK.

II. QUALITY ASPECTS

II.1 Introduction

Amlodipin Bluefish is presented in the form of tablets containing 6.94 mg respective 13.87 mg of amlodipine besilate which corresponds to 5 mg respective 10 mg of amlodipine. The excipients are cellulose microcrystalline, calcium hydrogen phosphate, 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

Amlodipin Bluefish is 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, 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

The pharmacokinetic profiles of the test and the reference formulations were compared in a 2-way crossover single dose bioequivalence study. The study was performed during fasting conditions. A total of 22 subjects completed the study as per protocol and were included in the statistical analysis. The results were as follows:

	C_{max}	AUC_{0-t}	AUC_{0-∞}
Ratio test/ref	1.02	1.03	1.03
90% CI	0.926-1.10	0.958-1.10	0.964-1.11

Bioequivalence was demonstrated for C_{max} 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

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 Amlodipine Ratiopharm, NL/H/880/01-02/MR. The bridging report submitted by the applicant has been found acceptable.

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 Amlodipin Bluefish, 5 mg and 10 mg tablets are recommended for approval.

VI. APPROVAL

The Mutual recognition for Amlodipin Bluefish 5 mg and 10 mg tablets was successfully finalised on 2010-02-11.

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)