IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Amlodipine 2.5 mg Tablets
Amlodipine besilate
PA23341/006/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Amlodipine 2.5, 5, 7.5 and 10 mg Tablets, from Hualan Pharmaceuticals Limited, on 11th September 2026 for hypertension, chronic stable angina pectoris and vasospastic (prinzmetal) angina.

This application for Amlodipine 5mg and 10mg Tablets is submitted under the legal basis of Article 10(1) Directive 2001/83/EC as amended and Amlodipine 2.5mg and 7.5mg Tablets are submitted under the legal basis of Article 10(3) Directive 2001/83/EC as amended.
The reference product was Istin 5mg and 10mg Tablets. MAH: Upjohn EESV.

The product is subject to prescription, which may be renewed.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www,hpra.ie

Name of the product	Amlodipine 2.5 mg Tablets
Name(s) of the active substance(s) (INN)	Amlodipine besilate
Pharmacotherapeutic classification (ATC code)	C08CA01
Pharmaceutical form and strength(s)	2.5mg Tablet
Marketing Authorisation Number(s) in Ireland	PA23341/006/001
Marketing Authorisation Holder	Hualan Pharmaceuticals Limited,
MRP/DCP No.	IE/H/1368/001/DC
Reference Member State	IE
Concerned Member State	DK, NL, SE

II. QUALITY ASPECTS

II.1. Introduction

This application is for Amlodipine 2.5 mg Tablets.

II.2 Drug substance

The active substance is amlodipine an established active substance described in the European/British Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is Amlodipine 2.5, 5, 7.5 and 10 mg Tablets is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ ICH guidelines, and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for the tablet dosage form, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur./EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Amlodipine 2.5, 5, 7.5 and 10 mg Tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Istin Tablets on the European market. As the pharmacodynamic, pharmacokinetic and toxicological properties of amlodipine besilate are well known, the applicant has not provided additional nonclinical studies, and further studies are not required. The overview provided based on literature review is thus appropriate.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

Amlodipine is not expected to pose a risk to the environment.

$PEC_{surfacewater}$ for amlodipine was calculated to be 0.05 mg/L using the default Fpen, which is above the action limit of 0.01 mg/L. A Phase II risk assessment was triggered. However, previous ERAs considered satisfactory by CHMP concluded that amlodipine is not expected to pose a risk to the environment.

A bioaccumulation potential for amlodipine is not indicated based on the log Kow which was below 4.5. A definitive PBT/vPvB assessment is not required.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of Amlodipine are well known since it has been marketed for several decades and resulting clinical experience is extensive. As Amlodipine besilate is a widely used, well-known active substance, the applicant has not provided additional nonclinical studies, and further studies are not required. The nonclinical overview on the nonclinical pharmacology, pharmacokinetics and toxicology provided is adequate.

IV. CLINICAL ASPECTS

IV.1 Introduction

This is a generic application submitted under article 10(1) and 10(3) of Directive 2001/83/EC.
Amlodipine is a well-known active substance with established efficacy and tolerability.

The content of the SmPC approved during the decentralised procedure is in accordance with that accepted for the reference product Istin 5 and 10 mg tablets marketed by MAH.

For this generic application, the applicant has submitted one bioequivalence study in which the pharmacokinetic profile of the test product Amlodipine 10mg tablets is compared with the pharmacokinetic profile of the reference product Norvasc 10 mg Tablets.

An Open Label, Balanced, Randomized, Two-Treatment, Two-Sequence, Two-Period, Single-Dose, Crossover Oral Bioequivalence Study in Healthy, Adult, Human Subjects Under Fasting Conditions.

Study 22-VIN-520

Treatment	**AUC_{0-t}** xg/ml/h	**$AUC_{0-\infty}$** xg/ml/h	**C_{max}** xg/ml	**t_{max}** h
Test	361.185 ± 80.2135	402.939± 100.3990	6.844 ± 1.1877	6.500 (3.00,14.00)
Reference	359.551 ± 80.2743	409.063 ± 103.7419	6.616 ± 103.7419	7.000 (5.00, 12.00)
***Ratio (90% CI)**	100.57% (96.26%-105.08%)	-	103.84% (97.92%-110.13%)	-

AUC_{0-t} Area under the plasma concentration curve from administration to last observed concentration at time t.
AUC_{0-72h} canbe reported instead of AUC_{0-t}, in studies with sampling period of 72 h, and where the concentration at 72 h is quantifiable. Only for immediate release products
$AUC_{0-\infty}$ Area under the plasma concentration curve extrapolated to infinite time.
$AUC_{0-\infty}$ does not need to be reported whenAUC_{0-72h} is reported instead of AUC_{0-t}
C_{max} Maximum plasma concentration
t_{max} **n**Time until Cmax is reached

Based on the pharmacokinetic parameters of active substance, the reference tablet Norvasc (amlodipine) 10 mg Tablets marketed by Pfizer and test tablet amlodipine) 10 mg Tablets are bioequivalent with extent to the rate and extent of absorption and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

Biowavier of strength
Similarity at all lower strengths is again stated by the applicant to been demonstrated against the higher strength the biobatch. A biowaiver, based on the criteria outlined in the Guideline on the investigation of bioequivalence, CPMP/EWP/QWP/1401/98 Rev. 1/Corr, has been proposed for 2.5mg, 5mg and 7.5 mg strengths of amlodipine tablets has been proposed.

2.5mg, 5mg and 7.5 mg strengths of amlodipine tablets are dose proportional with the 10 mg strength. The pharmacokinetics of the active substance are linear.

The results of the bioequivalence study performed with the 10 mg film-coated tablets therefore apply to the other strengths.

Compliance with GCP
The HPRA has been assured that GCP standards were followed in an appropriate manner in the studies conducted.

IV.2 Pharmacokinetics

No new Pharmacokinetics data were submitted and none are required for an application of this type.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted and none are required for an application of this type.

IV.4 Clinical Efficacy

No new efficacy data were submitted, and none are required for an application of this type.

IV.5 Clinical Safety

No new safety data were submitted, and none are required for an application of this type.
There were no reports of adverse events or deaths during the entire bioequivalence study.

Risk Management Plan (usual pharmacovigilance requirements +/- additional requirements)

The schedule for Periodic Safety Update Reports (PSUR) submission should be addressed

IV.6 Discussion on the clinical aspects

This application concerns a generic medicinal product Istin tablets. Istin tablets as an authorised medicinal product in Europe containing the active substance amlodipine since August 1989.

Bioequivalence with the reference medicinal product has been demonstrated. No clinically relevant differences in efficacy or safety are anticipated in the proposed indication. The benefit–risk balance is favourable.

V. OVERALL CONCLUSIONS

Amlodipine 2.5, 5, 7.5 and 10 mg Tablets is a generic form of Istin 5 and 10 mg tablets, Upjohn EESV (formerly Pfizer). Istin 5 and 10 mg tablets is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the CHMP guidance documents. The SmPC is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The applicant has demonstrated that the proposed leaflet(s) meets the criteria set out in Article 59(3) of Directive 2001/83/EC.

The HPRA, on the basis of the data submitted considered that Amlodipine 2.5, 5, 7.5 and 10 mg Tablets product was the same as the reference product and therefore granted marketing authorisation.

VI. REVISION DATE

17.02.2031