IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Clopidogrel Azure 75 mg film-coated tablets
Clopidogrel Hydrogen Sulfate
PA22871/027/001

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.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Clopidogrel 75 mg film-coated tablets, from Azure Pharmaceuticals Limited, on 30th January 2026 in
Secondary prevention of atherothrombotic events

- Adult patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
- Adult patients suffering from acute coronary syndrome:

    - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA).
    - ST segment elevation acute myocardial infarction, in combination with ASA in patients undergoing percutaneous coronary intervention (including patients undergoing a stent placement) or medically treated patients eligible for thrombolytic/fibrinolytic therapy.*Patients with moderate to high-risk Transient Ischemic Attack (TIA) or minor Ischemic Stroke (IS)*Clopidogrel in combination with ASA is indicated in:

    - Adult patients with moderate to high-risk TIA (ABCD2[1] score ≥4) or minor IS (NIHSS[2] ≤3) within 24 hours of either the TIA or IS event. *Prevention of atherothrombotic and thromboembolic events in atrial fibrillation*In adult patients with atrial fibrillation who have at least one risk factor for vascular events, are not suitable for treatment with Vitamin K antagonists (VKA) and who have a low bleeding risk, clopidogrel is indicated in combination with ASA for the prevention of atherothrombotic and thromboembolic events, including stroke.

This application was submitted in accordance with Article 10(1) of Directive 2001/83/EC and is referred to as a 'generic' application. With Ireland as the Reference Member State (RMS) in this decentralised procedure, Azure Pharmaceuticals Limited applied for a marketing authorisation for Clopidogrel 75 mg film-coated tablets in Malta. The reference product was Plavix 75 mg film-coated tablets, MAH: Sanofi Winthrop Industrie.

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	Clopidogrel Azure 75 mg film-coated tablets
Name(s) of the active substance(s) (INN)	Clopidogrel Hydrogen Sulfate
Pharmacotherapeutic classification (ATC Code)	B01AC04
Pharmaceutical form and strength(s)	75 mg film-coated tablets
Marketing Authorisation Number(s) in Ireland (PA)	PA22871/027/001
Marketing Authorisation Holder	Azure Pharmaceuticals Ltd. 12 Hamilton Drive The Rock Road Blackrock Dundalk Co. Louth A91 T997 Ireland
MRP/DCP No.	IE/H/1185/001
Reference Member State	Ireland
Concerned Member State(s)	Malta

II. QUALITY ASPECTS

II.1. Introduction

This application is for Clopidogrel 75 mg film-coated tablets.

II.2 Drug substance

The active substance is clopidogrel hydrogen sulfate, an established active substance described in the European 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 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 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 tablets, 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 have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.7 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 EU legislation for use with foodstuffs requirements.

P.8 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 and Pharmaceutical 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 Clopidogrel 75 mg film-coated tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Plavix 75 mg film-coated tablets on the European market. No new preclinical data have been submitted. This is acceptable for this type of application.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

Since Clopidogrel 75mg Film-coated Tablets is a generic product, it will not lead to an increased exposure to the environment. Further environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of clopidogrel are well known. As clopidogrel is a widely used and well-known active substance the applicant has not provided additional studies, and further studies are not required. Overview based on literature review was provided and is acceptable for this type of generic application.

IV. CLINICAL ASPECTS

IV.1 Introduction

Clopidogrel is a well-known active substance with established efficacy and tolerability.

With the exception of data from one bioequivalence study (Study 0239-16), no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of this study is satisfactory.

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

IV.2 Pharmacokinetics

For this generic application, the applicant has submitted one bioequivalence study in which the pharmacokinetic profile of the test product Clopidogrel 75 mg film-coated tablets is compared with the pharmacokinetic profile of the reference product Plavix 75 mg film-coated tablets.

Study 0239-16 was a randomised, single-dose, two-treatment, two-sequence, four-period, fully replicate, crossover bioequivalence study comparing the test product (Clopidogrel 75 mg film-coated tablets) to the reference product (Plavix 75 mg film-coated tablets) in healthy adult human subjects under fasting conditions.

A summary of pharmacokinetic results is presented for Study 0239-16 below:

Treatment	**AUC_{0-t}** xg/ml/h	**C_{max}** xg/ml
Test	3074.935 ± 8437.8851	1754.785 ±5740.2681
Reference	3078.867 ± 8622.9004	1633.016 ± 5089.4638
***Ratio (90% CI)**	108.2 (100.33-116.79)	110.7 (101.12-121.10)

*ln-transformed values

Based on the pharmacokinetic parameters of clopidogrel, the test and reference product 75 mg formulations are considered bioequivalent with respect to the extent and rate of absorption under fasting conditions. The 90% confidence intervals calculated for AUC_{0-t} and C_{max} were inside the normal range of acceptability (80.00 – 125.00 %).

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

With the exception of the safety data submitted with the bioequivalence study, no new safety data were submitted with this application.

The safety data from the bioequivalence study showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from this study.

Risk Management Plan

A risk management plan was submitted, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Clopidogrel 75mg film-coated tablets.

Important identified risks	Major bleeding (including intracranial haemorrhage (ICH)
Important potential risks	None
Missing information	None

Routine pharmacovigilance activities and routine risk minimisation measures are considered appropriate to manage the risks of this product.

Periodic Safety Update Reports (PSURs) shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

V. OVERALL CONCLUSIONS

OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

Clopidogrel 75 mg film-coated tablets are generic forms of Plavix 75 mg film-coated tablets. Plavix is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile. Bioequivalence for Clopidogrel 75 mg has been shown to comply with 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 HPRA, on the basis of the data submitted considered that Clopidogrel 75 mg film-coated tablets demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation for Clopidogrel 75 mg film-coated tablets.

VI. REVISION DATE

30th January 2031