IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

AMIDAFLUID 1 mg/ml, eye drops, solution
Propamidine isetionate
PA23520/001/001

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 Amidafluid 1mg/ml, eye drops, solution (propamidine isethionate) from Horus Pharma, on 23rd April 2025 indicated for:

the topical treatment of milder bacterial external ocular infections in adults such as
• milder forms of bacterial conjunctivitis caused by susceptible microorganisms (see section 4.4 and 5.1).
• milder forms of infectious blepharitis caused by susceptible microorganisms (see section 4.4 and 5.1).

This application for a marketing authorisation was submitted in accordance with Article 10(3) of Directive 2001/83/EC and is referred to as a 'hybrid' application. With Ireland as the Reference Member State in this decentralised procedure, Horus Pharma applied for a marketing authorisation for Amidafluid 1mg/ml, eye drops, solution in Ireland, Belgium, Denmark, Spain, Finland, France, Luxembourg, Netherlands, Norway and Sweden.

The authorisation was extended to additional CMS Italy, Portugal and Romania on 31st March 2026 in procedure IE/H/1297/001/E/001.

The reference product was Brolene 0.1% w/v Eye Drops Solution, MAH: Clonmel Healthcare Ltd.

The legal status for this marketing authorisation is subject to medical 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	Amidafluid 1mg/ml Eye drops, solution
Name(s) of the active substance(s) (INN)	Propamidine isethionate
Pharmacotherapeutic classification (ATC code)	S01AX15
Pharmaceutical form and strength(s)	0.1 Eye drops, solution
Marketing Authorisation Number(s) in Ireland (PA)	PA23520/001/001
Marketing Authorisation Holder	Horus Pharma
MRP/DCP No.	IE/H/1297/001/DC
Reference Member State	IE
Concerned Member State	BE, DK, ES, FI, FR, IT, LU, NL, NO, PT, RO, SE,

II. QUALITY ASPECTS

II.1. Introduction

This application is for Amidafluid 1mg/ml Eye drops, solution.

II.2 Drug substance

The active substance is propamide isetionate, an established active substance, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP). The Active Substance Master File (ASMF) procedure is followed.

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 finished product contains 1 mg/ml of propamidine isethionate.

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/ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances*)

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 eye preparations, 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 Amidafluid 1 mg/ml eye drops, solution.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Amidafluid 1mg/ml, eye drops, solution on the European market. No new preclinical data have been submitted. This is acceptable for this type of application.

The pharmacodynamic, pharmacokinetic and toxicological properties of propamidine isethionate are well known.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

Since Amidafluid 1mg/ml, eye drops, solutionis intended for generic substitution, this will not lead to an increased exposure to the environment. Additional studies on environmental risk assessment are therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of propamidine isethionate are well known. As propamidine isethionate is a widely used, well-known active substance, the applicant has not provided additional studies, and further studies are not required. A nonclinical overview based on literature review was provided and is acceptable. Non-clinical findings are adequately represented in the appropriate sections of the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

Propamidine isethionate 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 Brolene 0.1% w/v Eye Drops Solution, marketed by Clonmel Healthcare Ltd.

A biowaiver was applied for by the applicant. This biowaiver application was justified by the applicant as the medicinal product is essentially similar to the reference medicinal product, Brolene® 0.1% w/v Eye Drops Solution, which is manufactured by Clonmel Healthcare Ltd and has been nationally authorised in Ireland since 1983. The product contains the same active ingredients as the reference product, in the same concentrations and in the same physical and dosage form. In line with Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents (CPMP/239/95) and Guideline on the investigation of bioequivalence, (CPMP/EWP/QWP/1401/98 Rev.1/Corr**), the criteria for a biowaiver are met.

IV.2 Pharmacokinetics

Pharmacokinetics were not studied. Propamidine isetionate Horus Pharma 1 mg/ml is intended for topical ophthalmic application and systemic absorption of propamidine is expected to be negligible after topical administration to the eye.

IV.3 Pharmacodynamics

Propamidine is a member of the aromatic diamidine group of compounds which possess bacteriostatic properties against a wide range of organisms. These diamidines exert antibacterial action against pyrogenic cocci, antibiotic resistant staphylococci and some gram-negative bacilli. The activity of the diamidines is retained in the presence of organic matter such as tissue fluids, pus, and semen.

Mechanism of action
The exact mechanism of action of diamidines remains partially unknown, but some effects were described such as inhibition of oxygen uptake and catabolic (oxidative) metabolism of bacteria, and induction of leakage of amino acids by effects on cell membrane. Such effects are actually consistent with their structure of cationic surface-active agents. Damage to the cell surface

of some Gram-negative bacteria such as P. aeruginosa and Enterobacter cloacae has been also described. Propamidine isetionate is effective in both Gram-positive and Gram-negative bacteria.

IV.4 Clinical Efficacy

Considering the local administration route and the local activity of this ophthalmic product, bioequivalence cannot be demonstrated through bioequivalence studies. As a result, the application was submitted as a hybrid application. A biowaiver was applied for by the applicant on the basis that qualitative-quantitative composition of the applied for product has comparable physical-chemical properties to that of the reference product Brolene, and as such, pharmaceutical equivalence between the two products has been established. In line with Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents (CPMP/239/95) and Guideline on the investigation of bioequivalence, (CPMP/EWP/QWP/1401/98 Rev.1/Corr**), the criteria for a biowaiver are met.

In addition, the applicant provided bibliographic data on the efficacy of the active substance.

The data provided supports of the use of Amidafluid 1mg/ml Eye drops, solution for the claimed indications.

No company efficacy studies have been submitted and this is acceptable in keeping with the legal basis of this application.

IV.5 Clinical Safety

Propamidine isethionate has been available in the EU for 40 years with the first national authorisation of the active in Ireland in 1983. Therefore, propamidine isetionate has an established clinical safety profile. The applicant provided a satisfactory overview on the safety of the active substance.

The SmPC captures the known relevant safety information.

No new clinical studies were completed which is acceptable for an abridged/hybrid application.

Risk Management Plan
The MAH has submitted a risk management plan, 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 Amidafluid 1mg/ml, eye drops, solution(propamidine isetionate).

Safety specification

Important identified risks	• None
Important potential risks	• None
Missing information	• None

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Periodic Safety Update Report (PSUR)
With regard to PSUR submission, the MAH should take the following into account:

- 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.
- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

IV.6 Discussion on the clinical aspects

Amidafluid 1mg/ml, eye drops, solution has proven chemical-pharmaceutical quality and is a hybrid form of a suitable approved reference product: Brolene 0.1% w/v Eye Drops Solution. A biowaiver was applied for by the applicant. This biowaiver application was justified by the applicant as the medicinal product is essentially similar to the reference medicinal product. In line with Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents (CPMP/239/95) and Guideline on the investigation of bioequivalence, (CPMP/EWP/QWP/1401/98 Rev.1/Corr**), the criteria for a biowaiver are met. No clinical studies or bioequivalence/bioavailability studies are considered necessary.

The clinical pharmacology of ocular propamidine isethionate is well established; as such, the applicant has supplied bibliographic data to support the evaluation of the pharmacological profile of the active ingredient. These references were sufficient in the context of this application to support the granting of a marketing authorisation for this product for the claimed indications.

V. OVERALL CONCLUSIONS

Amidafluid 1mg/ml, eye drops, solution is a hybrid form of Brolene 0.1% w/v Eye Drops Solution. Brolene 0.1% w/v Eye Drops Solution is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The content of the SmPC approved during the decentralised procedure is in accordance with that accepted for the reference product Brolene 0.1% w/v Eye Drops Solution, marketed by Clonmel Healthcare Ltd.

A biowaiver was applied for by the applicant. In line with Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents (CPMP/239/95) and Guideline on the investigation of bioequivalence, (CPMP/EWP/QWP/1401/98 Rev.1/Corr**), the criteria for a biowaiver are met.

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 Amidafluid 1mg/ml, eye drops, solution was the same as the reference product and therefore granted a marketing authorisation.

VI. REVISION DATE

23.04.2030