IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Famotidine 20 mg film-coated tablets
Famotidine
PA1142/043/001

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 Famotidine 20mg film-coated tablets from Amdipharm Limited on 6th July 2026 for the prevention of recurrent duodenal ulcers, duodenal ulcer, benign gastric ulcer, Zollinger-Ellison syndrome and symptomatic treatment of mild reflux oesophagitis.

This national marketing authorisation application was submitted in accordance with article 10(1) of Directive 2001/83/EC as amended (generic application).

Famotidine 20mg and 40mg Film-coated tablets are 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	Famotidine 20 mg film-coated tablets
Name(s) of the active substance(s) (INN)	Famotidine
Pharmacotherapeutic classification (ATC Code)	A02BA03
Pharmaceutical form and strength(s)	20mg film coated tablets
Marketing Authorisation Number(s) in Ireland (PA)	PA1142/043/001
Marketing Authorisation Holder	Amdipharm Limited Unit 17 Northwood House Northwood Crescent Northwood Dublin 9 D09 V504 Ireland

II. QUALITY ASPECTS

II.1. Introduction

This application is for Famotidine 20mg and 40mg film-coated tablets

II.2 Drug substance

The active substance is famotidine 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

Composition of the medicinal product

Famotidine 20 mg film-coated tablets contains 20 mg of the active substance famotidine.
Famotidine 40 mg film-coated tablets contain 40 mg of the active substance famotidine

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)

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 film-coated 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 sites 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 Famotidine 20 mg and 40 mg film-coated tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

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

III.2 Ecotoxicity/environmental risk assessment

Since Famotidine is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.3 Discussion on the non-clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of Famotidine are well known. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology provided is adequate. As Famotidine is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Non-clinical findings are adequately represented in the appropriate sections of the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

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

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Pepdine 20 mg/40 mg comprime pellicule Film-coated tablets.

For this generic application, the applicant has submitted one bioequivalence study in which the pharmacokinetic profile of the test product Famotidine 40 mg film-coated tablets is compared with the pharmacokinetic profile of the reference product.

An open label, single-dose, randomised, two-way, crossover bioequivalence study was carried out. Famotidine 40 mg film-coated tablet was compared to the reference product.

Based on the pharmacokinetic parameters of active substance the reference tablet and test tablet Famotidine 40 mg tablet are bioequivalent with extent to the rate and extent of absorption and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

The 20 mg strength film-coated tablets are dose proportional with the 40 mg strength film-coated tablets. The pharmacokinetics of the active substance are linear. The results of the bioequivalence study performed with the 40 mg strength therefore apply to the other strengths. For the 20 mg strength the conditions of a biowaiver as outlined in the relevant CHMP Note for Guidance are fulfilled.

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

IV.2 Pharmacokinetics

Famotidine kinetics are linear.
Famotidine is quickly resorbed after oral administration.
Oral bioavailability is about 40 %.

Peak plasma concentrations are achieved 1-3.5 hours after administration. Peak plasma concentrations are approximately 0.04 to 0.06 µg/ml after administration of 20 mg of famotidine and 0.075 to 0.1 µg/ml after administration of 40 mg of famotidine. Repeated administration does not lead to an accumulation of the active ingredient. Famotidine absorption is not influenced by concomitant food intake.

Famotidine is found in the cerebrospinal fluid only to a limited extent. The fluid/plasma ratio 4 hours after administering 40 mg of famotidine was a mean of 0.1.

Famotidine is excreted in maternal milk. 6 hours after oral administration, a milk/plasma concentration ratio of 1.78 was reached. The elimination half-life in the plasma is 2.6 to 4 hours.

Up to 30-35 % of the active ingredient is metabolised in the liver; a sulfoxide metabolite is formed.

24 hours after oral administration, 25-30 % of the active ingredient is excreted via the urine unchanged; after intravenous administration, 65-70 % is excreted unchanged in urine. Renal clearance is 250-450 ml/min, which indicates tubular secretion. A slight amount can be eliminated as sulfoxide.

Renal insufficiency:
As renal function declines, renal and total clearance of famotidine decrease without there being an increase in non-renal elimination. The elimination half-life after intravenous injection of a single dose of 20 or 10 mg of famotidine is increased to 4.5-9 hours in moderate renal insufficiency (creatinine clearance 60-30 ml/min), to 10-12 hours in severe renal insufficiency (creatinine clearance < 30 ml/min) and to 18-27 hours in patients with terminal renal insufficiency or anuria. The amount of unchanged famotidine excreted with the urine is reduced to 60 % in patients with moderate renal insufficiency. In cases of severe renal insufficiency it is only 25 %.

Depending on the dialysis procedure (haemofiltration, 5-hour haemodialysis or continuous haemofiltration), dialysis patients have an elimination half-life of 7-14 hours after intravenous administration of 20 mg of famotidine; after oral administration of 20 mg of famotidine, it is 22.5 hours.

Liver function impairment:

The pharmacokinetics of famotidine are unchanged in patients with liver function impairment.

Kinetics among older patients:
Pharmacokinetic studies on older patients showed no signs of any clinically significant age-related changes; however, age-related impairment of renal function should be considered when determining the dosage.

IV.3 Pharmacodynamics

No additional studies investigating the pharmacodynamic effects of Famotidine 20 mg and 40 mg film-coated tablets were conducted which is acceptable for this generic application.

For further information see the SmPCs Section 5.1.

IV.4 Clinical Efficacy

No new applicant generated efficacy studies were submitted with this application.

IV.5 Clinical Safety

No new Applicant-generated safety studies or bibliographical data were submitted in this application.

During the pivotal bioequivalence study, both the test and reference products were well tolerated by the subjects. There were no deaths, serious adverse events (SAEs) or adverse events (AEs) reported in this study.

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.

The submitted Risk Management Plan, version 1.1 signed 15 Nov 2024 is considered acceptable.

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

This national marketing authorisation application was submitted in accordance with article 10(1) of Directive 2001/83/EC as amended (generic application).

One bioequivalence study was submitted in which the pharmacokinetic profile of the test product Famotidine 40 mg film-coated tablets is compared with the pharmacokinetic profile of the reference product.

All data of which are within the accepted ranges and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

With respect to the grant of a biowaiver for Famotidine 20 mg film-coated tablets, the bioequivalence guideline requirements were found to have been met.

Famotidine is a well-known active substance with established efficacy and tolerability. The safety results reported in the bioequivalence study were found to be consistent with the known safety profile of famotidine and no other safety studies were submitted in support of this study which is acceptable.

V. OVERALL CONCLUSIONS

Famotidine 20 mg and 40 mg film-coated tablets are a generic form of Pepdine 20mg/40 mg comprime pellicule film-coated tablets . Famotidine 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 HPRA, on the basis of the data submitted considered that Famotidine 20 mg and 40 mg film-coated tablets demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
New National	CRN00DM9M	SmPC, IPAR and PIL	6th July 2026	5th July 2031