IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Fexo 120 mg film-coated tablets
Fexofenadine hydrochloride
PA0074/096/001

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 Fexo 120 mg film-coated tablets from Rowa Pharmaceuticals Limited on 13th October 2023 indicated for:

Adults and children 12 years and older for the relief of symptoms associated with seasonal allergic rhinitis.

This national application for a marketing authorisation was submitted in accordance with Article 10(1) of Directive 2001/83/EC and is referred to as a generic application. The reference product is Telfast 120 mg film-coated Tablets (PA23180/003/002) from Opella Healthcare France SAS T/A Sanofi authorised in Ireland since 11/11/1997.

The product is subject to prescription.

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	Fexo 120 mg film-coated tablets
Name(s) of the active substance(s) (INN)	Fexofenadine hydrochloride
Pharmacotherapeutic classification (ATC code)	Fexofenadine- R06AX26
Pharmaceutical form and strength(s)	Film-coated tablet, 120 milligrams
Marketing Authorisation Number(s) in Ireland (PA)	PA0074/096/001
Marketing Authorisation Holder	Rowa Pharmaceuticals Limited
Case Reference Number	CRN00CV6S

II. QUALITY ASPECTS

II.1. Introduction

This application is for Fexo 120 mg film-coated tablets.

The product is a film-coated tablet, containing 120 mg of Fexofenadine hydrochloride, equivalent to 112 mg of Fexofenadine. All manufacturing operations are conducted in accordance with Good Manufacturing Practice.

II.2 Drug substance

The active substance Fexofenadine hydrochloride is an established active substance described in the European Pharmacopoeia (Ph. Eur.), which is manufactured in accordance with 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

Fexo 120 mg film-coated tablets contain the active substance Fexofenadine hydrochloride and the following other ingredients; microcrystalline cellulose, maize starch, magnesium stearate, croscarmellose sodium and povidone. The tablet coating is composed of hypromellose, macrogol, titanium dioxide (E171) and iron oxide (E172). All excipients are commonly used in pharmaceutical products.

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. The applicant demonstrated that the product is a stable product that is essentially similar to the reference product.

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 Ph. Eur. monograph for tablets and relevant ICH guidelines. 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 Fexo film-coated tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This product is a generic formulation of Telfast 120 mg film-coated Tablets 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.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

Since Fexo film-coated Tablets is a generic product, it 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

Pharmacodynamic, pharmacokinetic and toxicological properties of fexofenadine hydrochloride are well known. As fexofenadine hydrochloride is a widely used, well-known active substance, the applicant has not provided additional nonclinical studies and further studies are not required. A nonclinical overview based on literature review was provided and is acceptable for this type of generic application. Non-clinical sections of the SmPC are in line with the reference product which is acceptable.

IV. CLINICAL ASPECTS

IV.1 Introduction

Fexofenadine hydrochloride 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 of the reference product Telfast 120 mg film-coated Tablets marketed by Opella Healthcare France SAS T/A Sanofi (PA23180/003/002).

To support this generic application, the applicant submitted one bioequivalence study, in which the pharmacokinetic profile of the test product Fexofenadine hydrochloride 180 mg tablet is compared with the pharmacokinetic profile of the reference product Telfast 180 mg film-coated tablets, Aventis Pharma Ltd, UK.

This study was an open label, balanced, randomised, two treatment, two sequence, four-period (replicate design), single-dose crossover bioequivalence study of fexofenadine hydrochloride 180 mg tablets produced by Cipla Limited, India and Telfast® 180 mg tablets produced by Aventis Pharma ltd, UK in healthy, adult, male human subjects under fasting condition. The results demonstrated that the test and reference products are bioequivalent with extent to the rate and extent of absorption and fulfil the bioequivalence requirements outlined in the relevant CHMP Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98).

A justification for waiver of a study with the 120 mg strength was also provided in accordance with the bioaiver criteria as per the bioequivalence guideline.

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

IV.2 Pharmacokinetics

Absorption

Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with Tmax occurring at approximately 1-3 hours post dose. The mean Cmax value was approximately 427 ng/ml following the administration of a 120 mg dose once daily.

Distribution

Fexofenadine is 60- 70% to plasma protein bound.

Biotransformation and elimination

Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic) as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profile of fexofenadine follows a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of fexofenadine are linear for oral doses up to 120 mg BID. A dose of 240 mg BID produced slightly greater than proportional increase (8.8 %) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at these doses between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion, while up to 10% of ingested dose is excreted unchanged through the urine.

IV.3 Pharmacodynamics

Fexofenadine hydrochloride is a non-sedating H1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

IV.4 Clinical Efficacy

The efficacy of fexofenadine hydrochloride in the proposed indications is established in clinical use. No new clinical efficacy studies are provided and none are required.

IV.5 Clinical Safety

The overall safety profile of fexofenadine hydrochloride is established and generally known. No new safety studies are provided and none are required.

The safety information in the SmPC and Package Leaflet are in line with those of the reference product.

Risk Management Plan and PSUR Requirements

A Risk Management Plan, version 1.0, dated 18 July 2022 has been 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 fexofenadine hydrochloride 120mg film coated tablets. It is concluded that routine pharmacovigilance and risk minimisation measures are sufficient.

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.

IV.6 Discussion on the clinical aspects

As this is a generic application under Article 10(1) of Directive 2001/83/EC, additional non-clinical and clinical studies to demonstrate efficacy and safety are not required.
The product information is in line with the approved reference product, Telfast (PA23180/003/002).

V. OVERALL CONCLUSIONS

Fexo 120 mg film-coated tablets from Rowa Pharmaceuticals Limited is a generic form of Telfast 120 mg film-coated tablets, Opella Healthcare France SAS T/A Sanofi which is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Bioequivalence to the reference product has been shown following accordance with the CHMP guidance documents. A biowaiver has been submitted for the 120mg dose and is acceptable. 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, based on the data submitted, considered that Fexo 120 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

5 years from the finalisation of the procedure.

VII. UPDATES

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

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE

		AFFECTED		
New National	N/A	SmPC sections 1-9	13th October 2023	12th October 2028