IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Ibuprofen 200mg Film-coated tablets
Ibuprofen
PA23341/002/001

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 Ibuprofen 200mg, 400mg & 600mg Film-coated Tablets, from Hualan Pharmaceuticals Limited, on the 12th of December 2025 indicated for:

Ibuprofen 200 mg film-coated tablets:

For short term symptomatic treatment of mild to moderate pain and fever.

Ibuprofen 400 mg film-coated tablets:

Adults and adolescents from 12 years of age (≥40 kg)
Symptomatic treatment of pain and inflammation in arthritic diseases (e.g. rheumatoid arthritis), degenerative arthritic conditions (e.g. osteoarthritis), and in painful swelling and inflammation after soft tissue injuries.
Symptomatic treatment of mild to moderate pain and fever.

Ibuprofen 600 mg film-coated tablets:

Adults and adolescents from 15 years of age (≥50 kg)
Symptomatic treatment of pain and inflammation in arthritic diseases (e.g. rheumatoid arthritis), degenerative arthritic conditions (e.g. osteoarthritis), and in painful swelling and inflammation after soft tissue injuries

This decentralised marketing authorisation application was submitted in accordance with article 10(1) of Directive 2001/83/EC as amended (generic application). The reference member state is Ireland and the concerned member state is Belgium, Germany, Denmark, Spain, Netherlands and Sweden.

The European reference medicinal product is Brufen Forte 600 mg film-coated tablets by Viatris Healthcare SA NV registered in Belgium since July 1984.

Ibuprofen 200 mg Film-coated tablets are not subject to medical prescription,
Ibuprofen 400 mg and 600 mg Film-coated tablet 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	Ibuprofen 200mg Film-coated tablets
Name(s) of the active substance(s) (INN)	Ibuprofen
Pharmacotherapeutic classification (ATC Code)	M01AE01
Pharmaceutical form and strength(s)	200mg Film-coated tablets
Marketing Authorisation Number(s) in Ireland (PA)	PA23341/002/001
Marketing Authorisation Holder	Hualan Pharmaceuticals Limited 16/17 College Green Dublin 2 Dublin D02 V078 Ireland
MRP/DCP No.	IE/H/1326/001/DC
Reference Member State	IE
Concerned Member State(s)	BE DE DK ES NL SE

II. QUALITY ASPECTS

II.1. Introduction

This application is for Ibuprofen 200mg, 400mg and 600mg Film-coated Tablets.

II.2 Drug substance

The active substance is ibuprofen 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 pharmacopeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Ibuprofen, colloidal anhydrous silica, microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, sodium lauryl sulfate, magnesium stearate, hypromellose, talc.

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 pharmacopeial monograph for the dosage form 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 site 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 200mg, 400mg and 600mg Film-coated Tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is the same as that present in Brufen Forte on the European market since 1984. No new preclinical data have been submitted. This is acceptable for this type of application. The pharmacodynamic, pharmacokinetic and toxicological properties of Ibuprofen are well known.

III.2 Ecotoxicity/environmental risk assessment

Ibuprofen poses a known risk to the aquatic environment. Additional studies on environmental risk assessment for Ibuprofen 200mg, 400mg & 600mg Film-coated Tablets are not deemed necessary. The risk is adequately indicated in section 5.3 and 6.6 of SmPC.

III.3 Discussion on the non-clinical aspects

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

Ibuprofen 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 Brufen Forte marketed by Viatris Healthcare SA NV.

For this generic application, the applicant has submitted one bioequivalence study in which the pharmacokinetic profile of the test product ibuprofen is compared with the pharmacokinetic profile of the reference product Brufen Forte.

A single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study was carried out. Ibuprofen 600 mg Film-coated tablet was compared to the reference product Brufen Forte 600mg Film-coated tablet, Viatris Healthcare SA NV. Based on the pharmacokinetic parameters of active substance, the reference tablet Brufen Forte 600 mg Film-coated tablet marketed by Viatris Healthcare SA NV and test tablet Ibuprofen 600 mg film-coated 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.

For multiple strengths, a comment on dose proportionality may be required, as follows:

The 200 mg and 400 mg film-coated tablets are dose proportional with the 600 mg film-coated tablets. The pharmacokinetics of the active substance are linear in the range of 200 mg to 800 mg. The results of the bioequivalence study performed with the 600 mg film-coated tablets therefore apply to the other strengths. For the 200 mg and 400 mg strength the conditions of a biowaiver as outlined in the relevant CHMP Note for Guidance are fulfilled.

The content of the SmPCs approved during the decentralised procedure is in accordance with that accepted for the EU reference product.

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

IV.2 Pharmacokinetics

No additional studies investigating the pharmacokinetic effects of Ibuprofen 200 mg, 400 mg and 600 mg film-coated tablets were conducted which is acceptable for this generic application.

Absorption
Ibuprofen is rapidly absorbed from the gastrointestinal tract with a bioavailability of 80-90%. Peak serum concentrations occur one to two hours after administration. If administered with food, peak serum concentrations are lower and achieved more slowly than when taken on an empty stomach Food does not affect markedly total bioavailability.

Distribution
Ibuprofen is extensively bound to plasma proteins (99%). Ibuprofen has a small volume of distribution being about 0.12-0.2 L/kg in adults.

Biotransformation
Ibuprofen is rapidly metabolized in the liver through cytochrome P450, preferentially CYP2C9, to two primary inactive metabolites, 2-hydroxyibuprofen and 3-carboxyibuprofen. Following oral ingestion of the drug, slightly less than 90% of an oral dose of ibuprofen can be accounted for in the urine as oxidative metabolites and their glucuronic conjugates. Very little ibuprofen is excreted unchanged in the urine.

Elimination
Excretion by the kidney is both rapid and complete. The elimination half-life is approximately two hours. The excretion of ibuprofen is virtually complete 24 hours after the last dose.

Special populations

Elderly
Given that no renal impairment exists, there are only small, clinically insignificant differences in the pharmacokinetic profile and urinary excretion between young and elderly.

Renal impairment
For patients with mild renal impairment, increased unbound (S)-ibuprofen, higher AUC values for (S)-ibuprofen and increased enantiomeric AUC(S/R) ratios as compared with healthy controls have been reported.

In end-stage renal disease patients receiving dialysis, the mean free fraction of ibuprofen was about 3% compared with about 1% in healthy volunteers. Severe impairment of renal function may result in accumulation of ibuprofen metabolites. The significance of this effect is unknown. The metabolites can be removed by haemodialysis (see sections 4.2, 4.3 and 4.4).

Hepatic impairment
Alcoholic liver disease with mild to moderate hepatic impairment did not result in substantially altered pharmacokinetic parameters.
In cirrhotic patients with moderate hepatic impairment (Child Pugh's score 6-10) treated with racemic ibuprofen, an average 2-fold prolongation of the half-life was observed and the enantiomeric AUC ratio (S.R) was significantly lower compared to healthy controls, suggesting an impairment of metabolic inversion of (R)-ibuprofen to the active (S)-enantiomer.

IV.3 Pharmacodynamics

No additional studies investigating the pharmacodynamic effects of Ibuprofen 200 mg, 400 mg and 600 mg film-coated 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.

Risk Management Plan

A Risk Management Plan, version 0.1, dated 21 September 2023 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 Ibuprofen 200mg, 400mg & 600mg film-coated tablets It is concluded that routine pharmacovigilance and risk minimisation measures are sufficient.

Summary table of safety concerns as approved in RMP:

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

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

This decentralised 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 Ibuprofen 600 mg film-coated tablets is compared with the pharmacokinetic profile of the reference product Brufen Forte 600 mg film-coated tablets, Viatris Healthcare SA NV.

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 Ibuprofen 200mg and 400 mg tablets, the bioequivalence guideline requirements were found to have been met.

Ibuprofen is a well-known active substance with established efficacy and tolerability. The EU reference product for this application, Brufen Forte marketed by Viatris Healthcare SA NV has been on the market in IE since 1984. The safety results reported in the bioequivalence study were found to be consistent with the known safety profile of ibuprofen and no other safety studies were submitted in support of this study which is acceptable.

V. OVERALL CONCLUSIONS

Ibuprofen 200 mg, 400 mg and 600 mg film-coated tablets are a generic form of Brufen Forte. Ibuprofen 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 Ibuprofen 200 mg, 400 mg and 600 mg film-coated tablets demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.