IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Cetirizine dihydrochloride Pinewood 10 mg film-coated Tablets
Cetirizine dihydrochloride
PA0281/252/001

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 Cetirizine dihydrochloride Pinewood 10mg Film-coated tablet, from Pinewood Laboratories Ltd on 3rd of June 2022.

This is a generic product and the legal basis for this application is article 10 (1) of Directive 2001/83/EC as amended.

HPRA was RMS in this decentralised procedure and Malta was a CMS.

This medicinal product has been approved with the following indications in adults and children from age 6 years:

-the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis.
-for the relief of symptoms of chronic idiopathic urticaria.

This medicinal product is subject to prescription, which may be renewed.

The Summary of Product Characteristics for (SmPC) and Patient Information Leaflet for this medicinal product is available on the HPRA's website.

Name of the product	Cetirizine dihydrochloride Pinewood 10mg Film-coated tablet
Name(s) of the active substance(s) (INN)	Cetirizine dihydrochloride
Pharmacotherapeutic classification (ATC code)	R06AE07
Pharmaceutical form and strength(s)	10mg Film-coated tablet
Marketing Authorisation Number(s) in Ireland (PA)	PA0281/252/001
Marketing Authorisation Holder	Pinewood Laboratories Ltd
MRP/DCP No.	IE/H/1176/001/DC
Reference Member State	IE
Concerned Member State	MT

II. QUALITY ASPECTS

II.1. Introduction

This application is for Cetirizine dihydrochloride Pinewood 10 mg Film-coated Tablet

II.2 Drug substance

The active substance is cetirizine dihydrochloride, an established active substance described in the EuropeanPharmacopoeia, 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

Each film-coated tablet contains 10mg cetirizine dihydrochloride.

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 establishedpharmaceutical 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 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.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Zirtek® Allergy (Cetirizine Hydrochloride) 10 mg Tablets (MAH: UCB Pharma) authorized in Portugal since 11 August 1989. No new preclinical data have been submitted.

The pharmacodynamic, pharmacokinetic and toxicological properties of cetirizine are well known. As cetirizine is a widely used, well-known active substances, and this is a generic application, the applicant has not provided additional nonclinical studies and further studies are not required. The overview provided based on literature review is thus appropriate.

III.5 Ecotoxicity/environmental risk assessment

Since Cetirizine dihydrochloride Pinewood 10 mg Film-coated Tablet is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary. The applicant has submitted a justification for the absence of an ERA, in accordance with the guideline (CHMP/SWP/4447/00), which is acceptable.

III.6 Discussion on the non-clinical aspects

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

IV. CLINICAL ASPECTS

IV.1 Introduction

Cetirizine 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, Zirtek® Allergy (Cetirizine Hydrochloride) 10 mg Tablets (MAH: UCB Pharma).

For this generic application, the applicant has submitted one bioequivalence study in which the pharmacokinetic profile of the test product Cetirizine dihydrochloride Pinewood 10 mg Film-coated Tablet was compared with the pharmacokinetic profile of the reference product, Zirtek® Allergy (Cetirizine Hydrochloride) 10 mg Tablets (MAH: UCB Pharma).

A randomized, two treatment, two period, two sequence, single dose, two way crossover, bioequivalence study in healthy adult male subjects was carried out under under fasting conditions. Cetirizine dihydrochloride Pinewood 10 mg Film-coated Tablet was compared with the pharmacokinetic profile of the reference product, Zirtek® Allergy (Cetirizine Hydrochloride) 10 mg Tablets (MAH: UCB Pharma).

Based on the pharmacokinetic parameters of cetirizine, Zirtek® Allergy (Cetirizine Hydrochloride) 10 mg marketed by UCB Pharma and Cetirizine dihydrochloride Pinewood 10 mg Film-coated Tablet, the test product are bioequivalent with extent to the rate and extent of absorption and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

IV.2 Pharmacokinetics

The pharmacokinetic profile of cetirizine is well characterised.

Absorption:
The steady - state peak plasma concentrations is approximately 300 ng/ml and is achieved within 1.0 ± 0.5 h. The distribution of pharmacokinetic parameters such as peak plasma concentration (Cmax) and area under curve (AUC), is unimodal.
The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased. The extent of bioavailability is similar when cetirizine is given as solutions, capsules or tablets.

Distribution:
The apparent volume of distribution is 0.50 l/kg. Plasma protein binding of cetirizine is 93 ± 0.3 %. Cetirizine does not modify the protein binding of warfarin.

Biotransformation:
Cetirizine does not undergo extensive first pass metabolism.

Elimination:
The terminal half-life is approximately 10 hours and no accumulation is observed for cetirizine following daily doses of 10 mg for 10 days. About two third of the dose are excreted unchanged in urine.

Linearity/Non-linearity:
Cetirizine exhibits linear kinetics over the range of 5 to 60 mg.

Additional information on the PK characteristics of cetirizine in renal impairment, hepatic impairment, elderly and paediatrics is provided in the product information.

IV.3 Pharmacodynamics

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H1-receptors. In addition to its anti-H1 effect, cetirizine was shown to display anti-allergic activities: at a dose of 10 mg once or twice daily, it inhibits the late phase recruitment of eosinophils, in the skin and conjunctiva of atopic subjects submitted to allergen challenge.

IV.4 Clinical Efficacy

No clinical efficacy data are provided as this is a generic application.

IV.5 Clinical Safety

Safety review of the bioequivalence study provided did not raise any new or significant safety concerns.

As this is a generic application, no other clinical safety data are required.

A Risk Management Plan, version 3.1, dated 17 November 2021 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 Cetirizine Pinewood 10mg 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 approval concerns a generic application, there are no new efficacy or safety studies required as the applicant can refer to the data of the reference medical products. Instead, the demonstration of bioequivalence is pivotal to the assessment and has already been described.

V. OVERALL CONCLUSIONS

Cetirizine dihydrochloride Pinewood 10mg Film-coated tablet is a generic form of Zirtek® Allergy 10 mg Tablet (UCB Pharma), which 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 Cetirizine Pinewood 10mg 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

13.05.2027