IPAR

Public Assessment Report for a Medicinal Product for Human Use

Scientific discussion

Zirtek Allergy Relief 10mg film-coated tablets
CETIRIZINE DIHYDROCHLORIDE
PA0891/008/005

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.

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Zirtek Allergy Relief 10mg Film Coated Tablets, from UCB (Pharma) Ireland Limited on 27th of March 2015 for relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis and the relief of symptoms of chronic idiopathic urticaria in adults and paediatric patients 6 years and above.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that UCB (Pharma) Ireland Limited the marketing authorisation holder for Zirtek 10 Milligram Film Coated Tablet PA0891/008/002, an authorised medicinal product in Europe, has cross referred to this dossier to obtain an authorisation for Zirtek Allergy Relief 10mg Film Coated Tablets PA0891/008/005. Zirtek Allergy Relief 10mg Film Coated Tablets PA0891/008/005 has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Zirtek 10 Milligram Film Coated Tablet PA0891/008/002.

This product is subject to prescription in pack sizes exceeding 7 tablets. It is not subject to medical prescription in pack sizes not exceeding 7 tablets. It is for supply through pharmacies only and can be promoted to the public in pack sizes not exceeding 7 tablets. (See VII Updates).

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	Zirtek Allergy Relief 10mg film-coated tablets
Name(s) of the active substance(s) (INN)	CETIRIZINE DIHYDROCHLORIDE
Pharmacotherapeutic classification (ATC code)	R06AE07
Pharmaceutical form and strength(s)	10mg film-coated tablets
Marketing Authorisation Number(s) in Ireland (PA)	PA0891/008/005
Marketing Authorisation Holder	UCB (Pharma) Ireland Limited

II QUALITY ASPECTS

II.1. Introduction

This application is for Zirtek Allergy Relief 10 mg film-coated tablets.

II.2 Drug substance

The active substance is cetirizine dihydrochloride, 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

Each film-coated tablet contains 10 mg 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 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 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(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.

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 Zirtek Allergy Relief 10mg film-coated tablets.

III NON-CLINICAL ASPECTS

III.1 Introduction

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

See clinical section.

III.3 Pharmacokinetics

See clinical section

III.4 Toxicology

Not applicable as this is an informed consent application.

III.5 Ecotoxicity/environmental risk assessment

Not applicable as this is an informed consent application.

III.6 Discussion on the non-clinical aspects

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

IV CLINICAL ASPECTS

Cetirizine is a well known active substance with established efficacy and tolerability.
This active substance is the same as that present in Zirtek 10 Milligram Film Coated Tablet UCB (Pharma) Ireland Limited PA0891/008/002 (MRP IE/H/209/1-3). The content of the SmPC and PIL approved during the national procedure is in accordance with that accepted for the reference product, Zirtek 10 Milligram Film Coated Tablet PA0891/008/002 (MRP IE/H/209/1-3) UCB (Pharma) Ireland Limited .

IV.2 Pharmacokinetics

Following oral administration of cetirizine the steady-state peak plasma concentrations is approximately 300 ng/ml and is achieved within 1.0 ± 0.5 h. No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days. The distribution of pharmacokinetic parameters such as peak plasma concentration (Cmax) and area under curve (AUC), is unimodal in human volunteers.
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.
The apparent volume of distribution is 0.50 l/kg. Plasma protein binding of cetirizine is 93 ± 0.3%. Cetirizine does not undergo extensive first pass metabolism. About two third of the dose are excreted unchanged in urine. The terminal half-life is approximately 10 hours. Cetirizine exhibits linear kinetics over the range of 5 to 60 mg.

IV.3 Pharmacodynamics

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H1 - receptors. In vitro receptor binding studies have shown no measurable affinity for other than 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 atopia subjects submitted to allergan challenge. Studies in healthy volunteers show that cetirizine, at doses of 5 and 10 mg strongly inhibits the wheal and flare reactions induced by very high concentrations of histamine into the skin, but the correlation with efficacy is not established.
In a 35-day study in children aged 5 to 12, no tolerance to the antihistaminic effect (suppression of wheal and flare) of cetirizine was found. When a treatment with cetirizine is stopped after repeated administration, the skin recovers its normal reactivity to histamine within 3 days.

In a six-week, placebo-controlled study of 186 patients with allergic rhinitis and concomitant mild to moderate asthma, cetirizine 10 mg once daily improved rhinitis symptoms and did not alter pulmonary function. This study supports the safety of administering cetirizine to allergic patients with mild to moderate asthma.
In a placebo-controlled study, cetirizine given at the high daily dose of 60 mg for seven days did not cause statistically significant prolongation of QT interval.

IV.4 Clinical Efficacy and Safety

As this is an informed consent application no new clinical efficacy or safety data has been submitted. Efficacy and safety is expected to be similar to the reference product Zirtek 10 Milligram Film Coated Tablet PA0891/008/002 (MRP IE/H/209/1-3) UCB (Pharma) Ireland Limited

The marketing authorisation holder (MAH) submitted a summary of the Pharmacovigilance System, including confirmation of the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

Risk Management Plan (usual pharmacovigilance requirements +/- additional requirements)

The schedule for Periodic Safety Update Reports (PSUR) submission should be addressed

IV.6 Discussion on the clinical aspects

Cetirizine is a well known substance and has been widely marketed. As this is an informed consent application no new efficacy or safety data have been submitted. Efficacy and safety is expected to be similar to the reference product Zirtek 10 Milligram Film Coated Tablet PA0891/008/002 (MRP IE/H/209/1-3) UCB (Pharma) Ireland Limited.
The product information SmPC and patient leaflet are identical to the reference product.

V OVERALL CONCLUSIONS

The quality of this product is acceptable and no new non clinical or clinical safety concerns have been identified. The applicant's product Zirtek Allergy Relief 10mg film-coated tablets PA 0891/008/005 is identical to the reference product, Zirtek 10 Milligram Film Coated Tablet PA0891/008/002.
The benefit risk is therefore considered to be positive.
Therefore a marketing authorisation has been granted.

VI REVISION DATE

31st March 2015

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
Variation to change the legal status to permit supply as a non prescription medicine of a maximum pack size of 30 tablets (SWITCH)	2010 - National Variation Type II (60 day) crn 2154976	SmPC and PIL	24/11/2014	31/3/2015