IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Cetirizine dihydrochloride Haleon 1 mg/ml oral solution
Cetirizine dihydrochloride
PA0678/162/001

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 1 mg/ml oral solution, Cetirizine dihydrochloride Haleon 1 mg/ml oral solution and Cetirizine Haleon 10mg Film Coated Tablets from Haleon Ireland Limited on 30th January 2025 for the following indication:
Cetirizine 10 mg film-coated tablets are indicated in adults and paediatric patients 6 years and above:
- for the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis.
- for the relief of symptoms of chronic idiopathic urticaria

Cetirizine 1mg/ml oral solution is indicated in adults and paediatric patients 2 years and above:
- for the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis.
- for the relief of symptoms of chronic idiopathic urticaria

This is a generic application, according to article 10.(1) of Directive 2001/83/EC as amended, with IE as the RMS and following countries as CMS - BE, DK, FI, IS, LU, NL, NO and SE (Cetirizine Haleon 10mg Film Coated Tablets IE/H/1342/002/DC), CMS- BE, LU, NO and SE (Cetirizine Hydrochloride 1 mg/ml oral solution IE/H/1341/001/DC) and DK, FI, IS and NL (Cetirizine dihydrochloride Haleon 1 mg/ml oral solution IE/H/1342/001/DC).

The applicant's products, Cetirizine Hydrochloride 10 mg Film-coated Tablet is a generic version of the reference product Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets (MAH: UCB Pharma) authorized in Ireland since 8th August 1988 and Cetirizine Hydrochloride 1 mg/ml oral solution is a generic version of the reference product Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets (MAH: UCB Pharma) authorized in Ireland since 26th March 1993.

The prescription status of the products in Ireland is as follows:

Cetirizine dihydrochloride Haleon 1 mg/ml oral solution (IE/H/1342/001/DC)
Not subject to medical prescription.
Supply through pharmacies only and promotion to the public for pack sizes of 200 ml or less.
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The Summary of Product Characteristics for (SmPC) these medicinal products are available on the HPRA's website at www.hpra.ie.

Name of the product	Cetirizine dihydrochloride Haleon 1 mg/ml oral solution
Name(s) of the active substance(s) (INN)	Cetirizine dihydrochloride
Pharmacotherapeutic classification (ATC code)	R06AE07
Pharmaceutical form and strength(s)	1mg/ml Oral Solution
Marketing Authorisation Number(s) in Ireland	PA678/162/001
Marketing Authorisation Holder	Haleon Ireland Limited
MRP/DCP No.	IE/H/1342/001/DC
Reference Member State	IE
Concerned Member State	BE, LU, NO and SE (Cetirizine Hydrochloride 1 mg/ml oral solution IE/H/1341/001/DC)

II. QUALITY ASPECTS

II.1. Introduction

Cetirizine dihydrochloride Haleon 1 mg/ml oral solution

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

Composition of the medicinal product:
Cetirizine dihydrochloride Haleon 1 mg/ml oral solution - One ml of solution contains 1 mg of 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 Specifications are based on the pharmacopoeial monographs for liquid preparations for oral use Cetirizine dihydrochloride Haleon 1 mg/ml oral solution), and the tests and control limits are considered appropriate for these type of products.

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 products 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 Cetirizine 1 mg/ml oral solution, Cetirizine dihydrochloride Haleon 1 mg/ml oral solution and Cetirizine Haleon 10mg Film Coated Tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Zirket 1 mg/ml oral solution on the European market. No new nonclinical data have been submitted. 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

As cetirizine 10 mg film-coated tablets and 1 mg/ml oral solution are generic products, they will not lead to an increased exposure to the environment. Additional studies on environmental risk are not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of cetirizine are well known. As cetirizine is a widely used, well-known active substance, the applicant has not provided additional nonclinical studies, and further studies are not required. The nonclinical overview on the nonclinical pharmacology, pharmacokinetics and toxicology provided is adequate. Nonclinical sections of the SmPC are in with the originator.

IV. CLINICAL ASPECTS

IV.1 Introduction

Cetirizine dihydrochloride 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 and Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets marketed by UCB Pharma.

For the film-coated tablets, a BCS biowaiver was requested, and the applicant submitted satisfactory justification. An univocal classification of cetirizine in relation to its permeability is not possible. There is no information on the bioavailability of cetirizine in the SmPC of the reference product. As a consequence, cetirizine should be considered as a drug substance with low permeability. The Applicant has clarified that the composition of the reference product is now the same across Europe. There are no differences in the qualitative composition of the test and reference core tablets. Comparative release profiles between three batches of the test and reference product have been provided in dissolution media having pH in the range of 1.2-6.8. More than 85% of cetirizine was released in 15 minutes in all case, showing that the dissolution profiles from test and reference product are similar over the physiological pH range.

The content of the SmPC for Cetirizine dihydrochloride Haleon 1 mg/ml oral solution approved during the decentralised procedure is in accordance with that accepted for the reference products Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets and Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets marketed by UCB Pharma

IV.2 Pharmacokinetics

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.

Renal impairment: The pharmacokinetics of the drug was similar in patients with mild impairment (creatinine clearance higher than 40 ml/min) and healthy volunteers. Patients with moderate renal impairment had a 3-fold increase in half-life and 70 % decrease in clearance compared to healthy volunteers.
Patients on hemodialysis (creatinine clearance less than 7 ml/min) given a single oral 10 mg dose of cetirizine had a 3-fold increase in half-life and a 70 % decrease in clearance compared to normals.
Cetirizine was poorly cleared by haemodialysis. Dosing adjustment is necessary in patients with moderate or severe renal impairment (see section 4.2).

Hepatic impairment: Patients with chronic liver diseases (hepatocellular, cholestatic, and biliary cirrhosis) given 10 or 20 mg of cetirizine as a single dose had a 50 % increase in half-life along with a 40 % decrease in clearance compared to healthy subjects.
Dosing adjustment is only necessary in patients with hepatic impairment if concomitant renal impairment is present.

Elderly: Following a single 10 mg oral dose, half-life increased by about 50 % and clearance decreased by 40 % in 16 elderly subjects compared to the normal subjects. The decrease in cetirizine clearance in these elderly volunteers appeared to be related to their decreased renal function.

Paediatric population: The half-life of cetirizine was about 6 hours in children of 6-12 years and 5 hours in children 2-6 years. In infants and toddlers aged 6 to 24 months, it is reduced to 3.1 hours.

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

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

Risk Management Plan

The MAH has submitted a risk management plan, 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 1 mg/ml oral solution, Cetirizine dihydrochloride Haleon 1 mg/ml oral solution and Cetirizine Haleon 10mg Film Coated Tablets.

Summary table of safety concerns in approved RMP:

Important identified risks	None
Important potential risks	None
Missing information	None

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.

Summary of the RMP
The submitted Risk Management Plan, version 0.4 signed 24 November 2025 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

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

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 Haleon 1 mg/ml oral solution from Haleon Ireland Limited are generic forms of Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets.

Zirtek Allergy (Cetirizine Hydrochloride) 10 mg Tablets is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

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 dihydrochloride Haleon 1 mg/ml oral solution from Haleon Ireland Limited demonstrated adequate evidence of efficacy for the approved indication(s) as well as a satisfactory risk/benefit profile and therefore granted marketing authorisations.

VI. REVISION DATE

11.12.2030