LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Cetimax
(cetirizine dihydrochloride)

SE/H/816/01/DC

This module reflects the scientific discussion for the approval of Cetimax. The procedure was finalised at 29 September 2010. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Vitabalans Oy has applied for a marketing authorisation for Cetimax, film-coated tablet, 10 mg claiming essential similarity to Zyrlex, film-coated tablets, 10 mg marketed in Sweden by USB Nordic A/S. The product contains cetirizine as active substance. For approved indications see the Summary of Product Characteristics.

The reference product used in the bioequivalence study is Zyrtec, tablet, 10 mg marketed by UCB Pharma Oy in Finland.

II. QUALITY ASPECTS

II.1 Introduction

Cetimax is presented in the form of tablets containing 10 mg of cetirizine dihydrochloride. The excipients are microcrystalline cellulose, pregelatinised starch, croscarmellose sodium, colloidal anhydrous silica, magnesium stearate, polydextrose, hypromellose, titanium dioxide and macrogol. The tablets are packed in PVC/PVdC/Al blisters.

II.2 Drug Substance

Cetirizine dihydrochloride has a monograph in the Ph Eur.

Cetirizine dihydrochloride is a white or almost white powder which is freely soluble in water, practically insoluble in acetone and in methylene chloride. The structure of cetirizine dihydrochloride has been adequately proven and its physico-chemical properties sufficiently described. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active substance specification includes relevant tests and the limits for impurities/degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Cetimax film-coated tablet is formulated using excipients described in the current Ph Eur, except for the coating agent which is controlled according to acceptable in house specifications. All raw materials used in the product are of vegetable or synthetic origin.

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored below 25 °C.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

Following an oral dose of cetirizine, maximal plasma concentrations are reached within 0.25 to 3 hours. The extent of absorption was not reduced with food for the originator product but the rate of absorption decreased. However, there is no restriction with respect to food in the labelling. Following an oral dose, cetirizine is excreted mainly (2/3 of the dose) in the urine as unchanged drug. The terminal half-life is approximately 10 hours. Cetirizine displays linear pharmacokinetics over 5 to 60 mg.

To support the application, the applicant has submitted as report one bioequivalence study (V-805) where Cetimax 10 mg tablets were compared with Zyrtec®10 mg tablets under fasting conditions. Bioequivalence was demonstrated, see results below.

Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range)

Treatment	AUC_{0-t} ng/ml/h	$AUC_{0-\infty}$ ng/ml/h	C_{max} ng/ml	t_{max} h
Test	**1940.9 ± 450.49**	**2020.4 ± 64.616**	**247.96 ± 64.616**	**0.75 0.25-3.00**
Reference	**1901.6 ± 445.05**	**1992.1 ± 465.56**	**258.64 ± 65.623**	**0.75 0.50-2.00**
90% CI	**0.990-1.054**	**0.992-1.061**	**0.889-1.028**	**-**

AUC_{0-t}	area under the plasma concentration-time curve from time zero to t hours
$AUC_{0-\infty}$	area under the plasma concentration-time curve from time zero to infinity
C_{max}	maximum plasma concentration
t_{max}	time for maximum plasma concentration

**calculated based on ln-transformed values*

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation
The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was the Czech language.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

Follow-up measures:

Area[1]	**Description**
Quality	*Drug product: Intermediate stability studies need to be performed when the accelerated studies show results outside the specification according to "ICH Guideline on stability testing: Stability testing of existing active substances and related finished products" The applicant commits to start the intermediate stability studies as soon as possible and no later than 6 months after the receipt of the Day 120 DAR.*

1. Areas: Quality, Non-clinical, Clinical, Pharmacovigilance

The risk/benefit ratio is considered positive and Cetimax, film-coated tablet, 10 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Cetimax, 10 mg, film-coated tablet was successfully finalised on 29 September 2010.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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