LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Valsartan/Hydrochlorothiazide Sandoz
(Valsartan and Hydrochlorothiazide)

SE/H/922/01-05/DC

This module reflects the scientific discussion for the approval of Valsartan/Hydrochlorothiazide Sandoz. The procedure was finalised at 2010-04-28. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Sandoz A/S, Denmark has applied for a marketing authorisation for Valsartan/Hydrochlorothiazide Sandoz, film-coated tablets, 80/12,5 mg, 160/12,5 mg, 160/25 mg, 320/12,5 mg and 320/25 mg claiming essential similarity to Co-Tareg, film-coated tablets, 80/12,5 mg marketed the EU by Novartis Pharma SAS. The product contains valsartan and hydrochlorothiazide as active substances. For approved indications see the Summary of Product Characteristics. No bioequivalence studies have been performed.

II. QUALITY ASPECTS

II.1 Introduction

Valsartan/Hydrochlorothiazide Sandoz is presented in the form of film-coated tablets containing 80 mg, 160 mg or 320 mg of valsartan and 12.5 mg or 25 mg of hydrochlorotiazide. The excipients are microcrystalline cellulose, crospovidone, magnesium stearate, colloidal anhydrous silica, hypromellose, macrogol, talc, titanium dioxide, red iron oxide, yellow iron oxide, black iron oxide. The tablets are packed in PVC/PVDC-Al blister, PVC/PE/PVDC-Al blister or PA/Al/PVC-Al blister.

II.2 Drug Substance

Valsartan has a monograph in the Ph Eur. The substance is a white powder which is freely soluble in ethanol. The structure of valsartan has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on chirality is presented. 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.

Hydrochlorotiazide has a monograph in the Ph Eur. The substance is a white crystalline powder which is very slightly soluble in water. The structure of hydrochlorothiazide 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

Valsartan/Hydrochlorothiazide Sandoz, film-coated tablet, 80 mg/12.5 mg, 160 mg/12.5 mg, 160 mg/25 mg, 320 mg/12.5 mg and 320 mg/25 mg is formulated using excipients described in the current Ph Eur, except for iron oxides which are controlled according to NF. All raw materials used in the product are of vegetable 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 30°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

No bioequivalence studies have been performed. The applicant states that the products applied for are identical to the corresponding formulations of the originator.

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

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Diovan Comp SE/H/0565/001-005/R/001. The PL of Diovan Comp has been changed during the recent referral procedure, and the new proposed PL for SE/H/922, 923, 924, 932/01-05/DC is in line with the referral PL for Diovan Comp. The layout in accordance with the HEXAL AG,

DE/H/769/DC, DE/H/859-860/DC, DE/H/717-719/MR, NL/H/355/01-03 and DE/H/1226-1227/001-003.
The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Valsartan/Hydrochlorothiazide Sandoz, film-coated tablets, 80/12,5 mg, 160/12,5 mg, 160/25 mg, 320/12,5 mg and 320/25 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Valsartan/Hydrochlorothiazide Sandoz, film-coated tablets, 80/12,5 mg, 160/12,5 mg, 160/25 mg, 320/12,5 mg and 320/25 mg was successfully finalised on 2010-04-28.

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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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