LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Valsartan Jubilant
(valsartan)

SE/H/1355/01/DC

This module reflects the scientific discussion for the approval of Valsartan Jubilant. The procedure was finalised on 2014-09-22. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Valsartan Jubilant, 320 mg, film-coated tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Jubilant Pharmaceuticals nv, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and CY, DE, DK, IT, NL and UK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Diovan, 80 mg, capsules authorised in Germany since 1996, with Novartis Pharma GmbH as marketing authorisation holder.
The reference product used in the bioequivalence study is Diovan, 320 mg forte Filmtabletten from Germany with Novartis Pharma GmbH as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Valsartan film-coated tablet is presented in the form of tablets containing 320 mg of valsartan. The excipients are cellulose microcrystalline, crospovidone, silica dental type, lactose anhydrous, magnesium stearate, hypromellose, titanium dioxide, macrogol and iron oxide yellow. The tablets are packed in aluminium/aluminium blisters and PVC/PE/PVDC blisters.

II.2 Drug Substance

Valsartan has a monograph in the Ph Eur.
Valsartan is a white or almost white hygroscopic powder which is practically insoluble in water. 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 film-coated tablets are formulated using excipients described in the current Ph Eur, except for iron oxide which is controlled according to acceptable in house specification. All raw materials used in the product are of vegetable origin or has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance, such as poor aqueous solubility, hygroscopic properties and polymorphism.

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, with no special storage precautions (aluminium/alumimium blister) or when stored below 30 °C (PVC/PE/PVDC blister).

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

Valsartan has an oral bioavailability of 23%. Following an oral dose of valsartan maximal plasma concentrations occur at approximately 2–4 hours. Food decreases exposure (as measured by AUC) to valsartan by about 40% and peak plasma concentration (C_{max}) by about 50%, although from about 8 h post dosing plasma valsartan concentrations are similar for the fed and fasted groups. This reduction in AUC is not, however, accompanied by a clinically significant reduction in the therapeutic effect, and valsartan can therefore be given either with or without food according to the SPC of the originator. The pharmacokinetics of valsartan is linear in the therapeutic dose range. The half-life of valsartan is 6 hours.

Bioequivalence was evaluated in one single-dose, replicated crossover study conducted in 36 healthy volunteers, comparing Valsartan, 320 mg, film-coated tablets with Diovan, 320 mg, film-coated tablets under fasting conditions. The study was conducted at Jubilant Clinsys Limited, Noida, UP, India between 16th January and 3rd March 2013. Blood samples were collected pre-dose and up to 72 hours post-dose. The study design is considered acceptable. Plasma concentrations of valsartan were determined with a validated LC/MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

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 Valsartan 160 mg film-coated tablets SE/H/951/01-03/DC (content) and Valsartan/Hydrochlorothiazide Jubilant 80 mg/12.5 mg, 160 mg/12.5 mg, 160mg/25 mg, 320 mg/12.5 mg, 320 mg/25 mg, film-coated tablets PT/H/0607/001-005/DC (layout). The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Valsartan Jubilant, 320 mg, film-coated tablet is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Valsartan Jubilant, 320 mg, film-coated tablet was successfully finalised on 2014-09-22.

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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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