LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Valsartan Jubilant
# (valsartan)

# SE/H/951/01-03/DC

**This module reflects the scientific discussion for the approval of Valsartan Jubilant. The procedure was finalised at 2011-03-08. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

Jubilant Pharmaceuticals nv has applied for a marketing authorisation for Valsartan Jubilant, film-coated tablets, 40 mg, 80 mg and 160 mg claiming essential similarity to Diovan, capsules, 80 mg marketed in the EU by Novartis Pharma GmbH. The product contains valsartan as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Diovan, film-coated tablets marketed by Novartis Pharma GmbH in Germany.

# II. QUALITY ASPECTS

## II.1 Introduction

Valsartan Jubilant is presented in the form of film-coated tablets containing 40, 80 or 160 mg ofvalsartan. The excipients are microcrystalline cellulose, crospovidone, silica dental type, magnesium stearate, anhydrous lactose, hypromellose, titanium dioxide, macrogol, yellow iron oxide (40-80-160 mg) and red iron oxide (80 mg). The tablets are packed in Al-blister consisting of Al/OPA/Al/PVC.

## II.2 Drug Substance

Valsartan has a monograph in the Ph Eur.
Valsartan is a white to almost white powder which is practically insoluble in water. The structure of valsartan has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and 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.

## II.3 Medicinal Product

Valsartan Jubilant film-coated tablet is formulated using excipients described in the current Ph Eur, except for iron oxides which are controlled according to acceptable in house specifications. All raw materials used in the product are of vegetable origin or has been declared to be without risk of TSE/BSE contamination.
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, with no special storage precautions.

# 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

To support the application, the applicant has submitted one single-dose bioequivalence study in the fasting state with the strength 160 mg, performed at Clinsys Clinical Research Limited, Noida, Uttar Pradesh, India. The study was a randomised, open label, two-treatment, four-period, two-sequence single-dose replicate crossover study conducted in 44 (37 completed) healthy volunteers under fasting conditions. Plasma concentrations of valsartan were determined with a validated LC/MS/MS method. The 90% CI for the test/reference ratio for $AUC_{0-t}$ for valsartan were within the conventional acceptance range of 80-125%. A wider acceptance range for $C_{max}$ of 75-133 % was prospectively defined in the study protocol, and the replicated design study demonstrated that the intra-individual variability for $C_{max}$ for the reference product was greater than 30 % (33.89 %). Thus the widened confidence interval for $C_{max}$ is considered justified. The 90% confidence interval for the test/reference ratio of the population geometric means for $C_{max}$ was within the widened range 75-133%. Thus, bioequivalence has been demonstrated for the 160 mg strength.

The pharmacokinetics of valsartan is linear within the therapeutic dose range.

## 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 English.
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.

The results of the conducted bioequivalence study can be extrapolated to other strengths since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Valsartan Jubilant, film-coated tablets, 40 mg, 80 mg and 160 mg is recommended for approval.

# VI. APPROVAL

The Decentralised procedure for Valsartan Jubilant, film-coated tablets, 40 mg, 80 mg and 160 mg was successfully finalised on 2011-03-08.

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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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