LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Vapress
(valsartan)

SE/H/1073/01-03/DC

This module reflects the scientific discussion for the approval of Vapress. The procedure was finalised at 2012-03-05. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Medochemie Ltd has applied for a marketing authorisation for Vapress film-coated tablets 40, 80 and 160 mg" claiming essential similarity to "Tareg, 40 mg, gélule, authorised in France since 1997 Novartis Pharma SAS. 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, 160 mg marketed by Novartis Pharma manufactured in Cyprus.

II. QUALITY ASPECTS

II.1 Introduction

Vapress is presented in the form of film-coated tablets containing 40 mg, 80 mg and 160 mg of valsartan. The excipients are microcrystalline cellulose, crospovidone, Povidone K 30, colloidal anhydrous silica, magnesium stearate, talc and quinoline yellow lake. The film-coated tablets are packed in blisters of PVC/PE/PVDC-Aluminium or PVC/PCTFE-Aluminium.

II.2 Drug Substance

Valsartan has a monograph in the Ph Eur.

Valsartan is a white to off-white hygroscopic powder which is practically insoluble in water, sparingly soluble in methylene chloride, freely soluble in anhydrous ethanol.
The structure of valsartan has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism 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 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 periods of 2, 3 and 5 years, respectively.

II.3 Medicinal Product

Vapress film-coated tablet is formulated using excipients described in the current Ph. Eur. or acceptable in house specification (quinoline yellow lake). All raw materials used in the product are of vegetable origin with exception of magnesium stearate, which is of animal origin. Magnesium stearate meets the criteria described in the current version of the monograph "Products with risk of transmitting agents of animal spongiform encephalopathies no 1483 of the Ph. Eur., current edition including supplements".

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 of 21 months, when stored below 30 °C in the original package.

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

Pharmacokinetics

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 50 healthy volunteers, comparing Vapress, 160 mg, tablets with Diovan, 160 mg, tablets under fasting conditions. The study was conducted at SC Kynetyx HT SRL, Romania between 16.09.2010 and 25.10.2010. Blood samples were collected pre-dose and up to 36 hours post-dose. The study design is considered acceptable. Plasma concentrations of valsartan were determined with an 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%. From a pharmacokinetic point of view, absence of studies with the additional strength(s) is acceptable, as the pharmacokinetics of valsartan is linear within the therapeutic dose range.

Based on the submitted bioequivalence study, Vapress, 160 mg, film-coated tablets is considered bioequivalent with Diovan, 160 mg, film-coated tablets.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Risk Management Plan
The safety profile of the reference product, valsartan, is well known. Routine pharmacovigilance will be sufficient, and an RMP is not required.

Periodic Safety Update Report (PSUR)
The applicant has applied for a PSUR submission scheme of 3 years upon approval. Valsartan is found on the PSUR Work sharing list published by the Heads of Medicines Agencies with

an EU Harmonised Birthday and related Data Lock Point (DLP). The applicant should follow yearly PSURs until 201304 and the DLP which is April 2012.

Pharmacovigilance system
The RMS considers that the Pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country

IV.1 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 Czech.
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 “Vapress film-coated tablets 40, 80 and 160 mg is recommended for approval.

VI. APPROVAL

Decentralised procedure for Vapress film-coated tablets 40, 80 and 160 mg was successfully finalised on 2012-03-05.

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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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