LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Misafar
(telmisartan)

SE/H/1231/01-02/DC

This module reflects the scientific discussion for the approval of Misafar. The procedure was finalised at 2012-11-29. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Specifar S.A. has applied for a marketing authorisation for Misafar, tablets, 40 mg and 80 mg claiming essential similarity to Micardis, tablets, 40 mg and 80 mg marketed in the EU by Boehringer Ingelheim International GmbH. The product contains telmisartan as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Micardis, 80 mg, tablets, from Germany, marketed by Boehringer Ingelheim Limited.

II. QUALITY ASPECTS

II.1 Introduction

The drug product is presented in the form of tablets containing 40 mg or 80 mg of telmisartan. The excipients are sodium hydroxide, povidone, meglumine, mannitol, crospovidone, talc and magnesium stearate. The tablets are packed in two possible aluminium blister packs (peelable or push-through).

II.2 Drug Substance

Telmisartan has a monograph in the Ph Eur. The drug substance is a white or slightly yellowish, crystalline powder which is practically insoluble in water. The structure of telmisartan 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

The drug product is a tablet and formulated using excipients described in the current Ph Eur. 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, 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

Bioequivalence was evaluated in one single-dose, two-treatment, four-period, two-sequence single-dose fully replicated crossover study conducted in 48 healthy volunteers, comparing Telmisartan, 80 mg, tablet with Micardis, 80 mg, tablet under fasting conditions. The study was conducted at Vimta Labs Ltd., India between 11 May and 24 June 2011. Blood samples were collected pre-dose and up to 48 hours post-dose. The sampling period was relatively short compared to telmisartan half-life, but given the short time to Cmax (0.5-1h), the absorption is expected to be completed after 48 hours, and the absorption phase sufficiently covered with the chosen sampling period. Further supportive data including the results from an additional statistical analysis in which subjects with a too large extrapolated AUC was removed was also provided. Plasma concentrations of telmisartan were determined with an adequately 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%; bioequivalence was demonstrated.

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
RMS is of the opinion that when the generic application refers to a centrally authorised reference product a full user test is not required since the leaflet is harmonised with the originator. This is the case for Telmisartan, referring to Micardis, thus, we did not require a full user test of the PL text.

A user consultation with target patient groups on the **layout** of the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Valsartan / HCTZ tablets, DE/H/2779/001-003/DC, and Valsartan Capsules, UK/H/3958/001-003/DC. The applicant states that the layout will be comparable regarding design, size and font size. The bridging of layout was considered satisfactorily.

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 Misafar, 40 mg and 80 mg, tablets is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Misafar, 40 mg and 80 mg, tablets was successfully finalised on 2012-11-29.

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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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