LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Ondansetron Orifarm
(ondansetron)

SE/H/835/01-02/DC

This module reflects the scientific discussion for the approval of Ondansetron Orifarm. The procedure was finalised 2009-11-17. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

Orifarm Generics A/S has applied for a marketing authorisation for Ondansetron Orifarm, 4 and 8 mg orodispersible tablets claiming essential similarity to Zofran munlöslig, 4 and 8 mg orodispersible tablets marketed in Sweden by GlaxoSmithKline AB. The product contains ondansetron as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Zofran Zydis 8 mg liofilizado oral marketed by GlaxoSmithKline in Spain.

II. QUALITY ASPECTS

II.1 Introduction

Ondansetron Orifarm is presented in the form of orodispersible tablets containing 4 or 8 mg of ondansetron. The excipients are mannitol, sorbitol, crospovidone, colloidal silicon dioxide, microcrystalline cellulose, aspartame, strawberry flavouring, sodium stearyl fumarate and magnesium stearate. The orodispersible tablets are packed in aluminium/aluminium blisters.

II.2 Drug Substance

Ondansetron (base) does not have a monograph in the Ph Eur. However, there is a Ph Eur monograph for ondansetron hydrochloride dihydrate.

Ondansetron is a white to off-white powder which is soluble in chloroform and acetic acid. The structure of ondansetron 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 and reagents.

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

Ondansetron Orifarm orodispersible tablets is formulated using excipients described in the current Ph Eur, except for strawberry flavouring which is controlled according to acceptable in-house specifications. 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 with the reference product was evaluated in one single-dose bioequivalence study on the 8 mg tablet. The applicant has requested a biowaiver for the lower 4 mg strength. Given that ondansetron AUC shows a dose-linear relationship up to 8 mg, this is acceptable from a pharmacokinetic point of view..

The study was a randomized, single-dose, 2-period, 2-sequence, crossover bioequivalence study in 28 healthy male and female subjects conducted under fasting conditions at Algorithme Pharma Inc, Monteral, Quebec, Canada between 2005/09/08 and 2005/09/17. No GCP issues have been identified. Ondansetron in plasma was determined using a validated HPLC method with MS detection at Algorithme Pharma Inc laboratory for bioanalysis.

The 90% confidence interval of ondansetron AUC0-t, AUC0-inf and Cmax were within the pre-defined acceptance range of 80-125%. Bioequivalence has been sufficiently shown.

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 testing of the package leaflet has been performed and is acceptable.

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 Ondansetron Orifarm, 4 and 8 mg orodispersible tablets is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Ondansetron Orifarm, 4 and 8 mg, orodispersible tablets was successfully finalised on 17 November 2009.

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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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