LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Zolmitriptan Jubilant (zolmitriptan)

SE/H/984/01-02/DC

This module reflects the scientific discussion for the approval of Zolmitriptan Jubilant. The procedure was finalised on 10 March 2011. 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

Jubilant Pharmaceuticals nv has applied for a marketing authorisation for Zolmitriptan Jubilant, film-coated tablet, 2,5 mg and 5 mg claiming essential similarity to Zomig, 2,5 mg and 5 mg, film-coated tablet marketed in Sweden by AstraZeneca AB. The product contains zolmitriptan as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bioequivalence study is AscoTop, 5 mg, film-coated tablet marketed by AstraZeneca GmbH in Germany.

II. QUALITY ASPECTS

II.1 Introduction

Zolmitriptan Jubilant is presented in the form of film coated tablets containing 2.5 or 5 mg of zolmitriptan. The excipients are Lactose, anhydrous, Microcrystalline cellulose, Sodium starch glycolate (Type A), Magnesium stearate, Hypromellose (E464), Titanium dioxide (E171), Macrogol and Iron oxide red (E172). The tablets are packed in aluminium blisters.

II.2 Drug Substance

Zolmitriptan does not have a monograph in the Ph Eur.

Zolmitriptan is a off-white to cream coloured crystalline powder which is freely soluble in methanol. The aqueous solubility is slightly soluble at pHs 2-3 and very slightly soluble at pHs 4-7. The structure of “drug substance” has been adequately proven and its physico-chemical properties sufficiently described. Zolmitriptan has one asymmetric carbon and the drug substance used is the S-configuration. 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

Zolmitriptan Jubilant, film-coated tablet, 2,5 mg and 5 mg is formulated using excipients described in the current Ph Eur, except for Opadry coating which is controlled according to acceptable in house specifications. 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 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.

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

Zolmitriptan is rapidly and well absorbed, and has an oral bioavailability of approximately 40%. Following an oral dose 75 % of maximal plasma concentrations occur at approximately 1 hour. There is no food interaction for the originator product, and therefore no restriction with respect to food in the labelling. When given as a single oral dose in healthy volunteers, AUC and C_{max} showed approximate dose proportionality within the dose range 2.5 to 50 mg. Zolmitriptan is cleared principally by hepatic metabolism, and one of the metabolites (N-desmethyl-zolmitriptan) is pharmacologically active and is likely to contribute to the therapeutic activity. The mean elimination half life is around 3 h.

The applicant has submitted one bioequivalence study (ZOLM/09/076), in which Zolmitriptan 5 mg film-coated tablets are compared with the reference product AscoTop, 5 mg, film-coated tablets following a single dose under fasting conditions. The study has been performed by Clinsys Clinical Research Limited, in Uttar Pradesh, India. Bioequivalence has been adequately shown for the 5 mg strength.

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 Zolmitriptan Jubilant 2.5 mg and 5 mg orodispersible tablets, accepted in procedure SE/H/984/03-04/DC. The bridging report submitted by the applicant has been found 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 Zolmitriptan Jubilant, 2,5 mg and 5 mg, film-coated tablet, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Zolmitriptan Jubilant, 2,5 mg and 5 mg, film-coated tablet, was successfully finalised on 10 March 2011.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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)

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