LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Oxybutynin Accord
oxybutynin hydrochloride

SE/H/1062/01-02/DC

This module reflects the scientific discussion for the approval of Oxybutynin Accord. Please note that the marketing authorisation was first approved with the name "Oxybutynin Accord" and therefore this name is used throughout the document. The procedure was finalised at 2012-03-22. 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

Accord Healthcare has applied for a marketing authorisation for “Oxybutynin Intas 2,5 and 5 mg tablets claiming essential similarity to “Ditropan 5mg tablets marketed in Sweden by Sanofia-aventis AB. The product contains oxybutynin hydrochloride as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is “Ditropan 5 mg, tablets marketed by Sanofi-aventis AB in the UK.

II. QUALITY ASPECTS

II.1 Introduction

Oxybutynin Intas is presented in the form of tablets containing 2.5 and 5 mg of Oxybutynin hydrochloride. The excipients are powdered cellulose, lactose monohydrate, talc and magnesium stearate. The tablets are packed in PVC/PVdC-Aluminium foil blisters.

II.2 Drug Substance

The drug substance, Oxybutynin hydrochloride, is described in the European Pharmacopoeia. The manufacturer and supplier of the active substance has obtained a Certificate of Suitability from EDQM.

Oxybutynin hydrochloride is a white or almost white, crystalline powder which is freely soluble in water and ethanol, soluble in acetone, practically insoluble in cyclohexane. The structure of oxybutynin hydrochloride has been adequately proven and its physico-chemical properties sufficiently described.

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. Reference is made to the Ph Eur Certificate of Suitability. The certificate states at 12 months re-test period.

II.3 Medicinal Product

Oxybutynin Intas tablets are formulated using excipients described in the current Ph Eur, except for Cellactose 80 which is a 75:25 mixture of lactose monohydrate (Ph Eur) and powdered cellulose (Ph Eur). The components of Cellactose 80 are separately controlled in accordance with Ph Eur monographs on cellulose, powdered and lactose monohydrate. The only raw material of animal origin (calf rennet and milk) used in the product is lactose monohydrate. The supplier of lactose certifies that the milk is sourced from healthy animals in the same conditions as milk collected for human consumption (EMEA/410/01 rev 2) and that the lactose is prepared without use of other ruminant materials than calf rennet. The supplier further certifies that the calf rennet is in accordance with public statement EMEA/571/02 of February 2002.

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, when stored below 30°C.

From a quality view, there are no objections to approval of Oxybutynin Intas.

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-way crossover study conducted in 34 healthy volunteers, comparing Oxybutynin 5 mg, tablets with Ditropan 5 mg, tablets under fasting conditions. The study was conducted at Lambda Therapeutic Research Ltd, Navi Mumbai, India between 27 January and 07 February 2010. Blood samples were collected pre-dose and up to 48 hours post-dose. The study design is considered acceptable. Plasma concentrations of oxybutynin and the major metabolite N-desethyloxybutynin were determined with an achiral 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% for both oxybytynin and N-desethyloxybutynin.

The results from the study on the 5 mg tablet can be extrapolated to the lower strength of 2.5 mg. Although the data on linearity is sparse, there are indications that the pharmacokinetics of oxybutynin is linear. Also, the highest most commonly used tablet strength was used in the bioequivalence study.

In conclusion: Bioequivalence has been 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

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.

VI. APPROVAL

Decentralised procedure for Oxybutynin Intas 2,5and 5 mg tablets were successfully finalised on 2012-03-22.

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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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