LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Donepezil Jubilant
(donepezil hydrochloride)

SE/H/1172/01-02/MR

This module reflects the scientific discussion for the approval of Donepezil Jubilant. The procedure was finalised on 2012-01-23. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Jubilant Pharmaceuticals NV, Belgium, has applied for a marketing authorisation for Donepezil Jubilant, 5 mg and 10 mg, film-coated tablets, claiming essential similarity to Aricept, 5 mg and 10 mg, film-coated tablets marketed in Sweden by Pfizer AB. The product contains donepezil hydrochloride as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Aricept, 5 mg, film-coated tablet marketed by Eisai GmbH/Pfizer GmbH in Germany.

II. QUALITY ASPECTS

II.1 Introduction

Donepezil Jubilant is presented in the form of tablets containing 5 mg or 10 mg of donepezil hydrochloride. The excipients are lactose monohydrate, cellulose microcrystalline, maize starch, hydroxypropyl cellulose (low substituted), magnesium stearate, hypromellose, macrogol, talc and titanium dioxide. The tablets are packed in blisters.

II.2 Drug Substance

Donepezil hydrochloride does not have a monograph in the Ph Eur. The drug substance is manufactured by Jubilant Life Sciences Limited (Nanjangud, India) and the manufacturer has an ASMF.

The drug substance is an off white to cream coloured powder with a pH dependent solubility in water. The structure of donepezil hydrochloride 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 a retest period of 4 years at long term conditions.

II.3 Medicinal Product

Donepezil Jubilant film-coated tablet is manufactured by Jubilant Life Sciences Limited, Roorkee, India. The tablets are formulated using excipients described in the current Ph Eur, except for low substituted Hydroxypropyl cellulose, which is controlled according to USP. All raw materials used in the product are of vegetable origin/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 drug product is manufactured using conventional methods and is packed in blisters.

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, 3 years with no special storage conditions.

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 bioequivalence study (Study DONE/07/050), in which Aricept film-coated tablets 5 mg were compared with Donepezil Jubilant film-coated tablets 5 mg following a single dose under fasting conditions. Bioequivalence for AUC and Cmax was demonstrated.

The results of study DONE/07/050 with 5 mg formulation can from a pharmacokinetic perspective be extrapolated to the other strength (10 mg), according to conditions specified in the Guideline on the Investigation of Bioequivalence.

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 Donepezil hydrochloride 5 mg and 10 mg film-coated tablets leaflet, which was assessed and accepted by MHRA in procedures PL 19156/0048-0001 and PL 19156/0048-0002. The bridging report submitted by the applicant has been found acceptable.

The results of the conducted bioequivalence study can be extrapolated to the other strength 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 Donepezil Jubilant, 5 mg and 10 mg, film-coated tablets, is recommended for approval.

VI. APPROVAL

The Mutual recognition procedure for Donepezil Jubilant, 5 mg and 10 mg, film-coated tablets, was successfully finalised on 2012-01-23.

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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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