LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Fluoxetine Accord
(fluoxetine hydrochloride)

SE/H/753/01/DC

This module reflects the scientific discussion for the approval of Fluoxetine Accord. The procedure was finalised at 2010-03-22. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Accord Healthcare Limited has applied for a marketing authorisation for Fluoxetine Accord, 20 mg, hard capsules, claiming essential similarity to Prozac 20 mg capsules marketed in the EU by Eli Lilly. The product contains fluoxetine as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bioequivalence study is Prozac 20 mg hard capsules marketed by Eli Lilly in the UK.

II. QUALITY ASPECTS

II.1 Introduction

Fluoxetine Accord is presented in the form of hard capsules containing 22.4 mg of fluoxetine hydrochloride which corresponds to 20 mg fluoxetine. The excipients are

starch pregelatinised (maize)
silica colloidal anhydrous
magnesium stearate (E470b)
talc purified.

The capsule shell contains:
quinoline yellow (E104)
erythrosine (E127)
indigo carmine (El32)
titanium dioxide (E171)
gelatin.

The printing ink contains:
shellac glaze(E904)
iron oxide black (El72)
propylene glycol

The capsules are packed in/filled in PVC /Aluminium blisters.

II.2 Drug Substance

Fluoxetine hydrochloride has a monograph in the Ph Eur.

Fluoxetine hydrochloride is freely soluble in methanol, sparingly soluble in water and in methylene chloride. The structure of fluoxetine hydrochloride has been adequately proven and its physico-chemical properties sufficiently described. The substance does not exhibit polymorphism or isomerism. 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

Fluxoetine Accord hard capsules are formulated using excipients described in the current Ph Eur, except for the colorants which are controlled according to acceptable in house specifications. All the ingredients of black ink are in compliance with Directive 95/45/EC and are safe for human consumption. All raw materials used in the product are of vegetable origin/ or have 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

One open label, randomised, two-sequence, two-treatment, two-period, single dose bioequivalence study was submitted, in which the test product was compared with Prozac hard capsules with the aim to demonstrate bioequivalence for the parent drug fluoxetine. The choice of a single dose study with demonstration of bioequivalence for the parent drug fluoxetine was considered acceptable. The design of the study was adequate. Fluoxetine was analysed in plasma by a validated LC-MS/MS method. Bioequivalence between the test and the reference product was concluded for fluoxetine since the 90 % confidence intervals were within the stipulated acceptance range of 80-125% for the log-transformed pharmacokinetic parameters C_{max}, AUC_{0-t} and AUC_{0-inf}. Bioequivalence was also demonstrated for the metabolite nor-fluoxetine.

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

Bioequivalence between the test product and the reference product Prozac was demonstrated for fluoxetine as well as for the metabolite nor-fluoxetine in a single dose bioequivalence study.

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 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.

The risk/benefit ratio is considered positive and Fluoxetine Accord, 20 mg, hard capsules is recommended for approval.

VI. APPROVAL

The decentralised procedure for Fluoxetine Accord, 20 mg, hard capsules was successfully finalised on 2010-03-22.

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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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