LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Efexor Depot
(venlafaxine hydrochloride)

SE/H/936/04/DC

This module reflects the scientific discussion for the approval of Efexor Depot. The procedure was finalised at 2014-10-02. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Efexor Depot, prolonged-release capsules, 225 mg, is an extension application made according to Article 8(3) of Directive 2001/83/EC, known active substance. The applicant, Pfizer AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and BE, ES, LU, PT and UK as concerned member states (CMS). The active substance, venlafaxine hydrochloride, is the same as in Efexor Depot, prolonged-release capsules, marketed by Pfizer AB, since 1997.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Efexor Depot is presented in the form of prolonged-release capsules containing 255 mg of venlafaxine hydrochloride, which corresponds to 225 mg of the active entity venlafaxine . The excipients are microcrystalline cellulose, ethyl cellulose, hypromellose, talc, gelatin, black iron oxide, yellow iron oxide, red iron oxide, titanium dioxide, shellac, propylene glycol, sodium hydroxide and povidone. The prolonged-release capsules are packed in blisters.

II.2 Drug Substance

Venlafaxine hydrochloride has a monograph in the Ph. Eur.

Venlafaxine hydrochloride is a white or almost white powder, which is freely soluble in water. The structure of venlafaxine hydrochloride 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, 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

Efexor Depot prolonged-release capsules are formulated using excipients described in the current Ph. Eur., except for the iron oxides which are controlled according to acceptable in-house specifications. All raw materials used in the product 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 product development has taken into consideration the physico-chemical characteristics of the active substance, such as polymorphism.

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.

III. NON-CLINICAL ASPECTS

Efexor Depot prolonged-release capsules contain venlafaxine hydrochloride as the active substance. The pharmacodynamic, pharmacokinetic and toxicological properties of venlafaxine are well-known.

The Efexor Depot prolonged-release capsules 225 mg utilise the same formulation as the lower strength capsules (37.5, 75 and 150 mg) previously approved. The excipients are well-known and there is no cause for toxicological concern.

III.1 Ecotoxicity/environmental risk assessment

The approval of the Efexor Depot prolonged-release capsules 225 mg strength is not expected to result in an increased environmental exposure.

III.2 Discussion on the non-clinical aspects

From a non-clinical perspective, no new information is available that changes the risk/benefit of the product. The product can be recommended for market authorisation.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

The new strength applied for (225 mg) consists of encapsulated coated venlafaxin spheroids that are common to all strengths and the 225 mg dose is already approved for and in clinical use. Given the formulation similarity, no formal comparative pharmacokinetic data between the new strength and the previously approved strengths were requested.

Descriptive pharmacokinetic data of the new strength and the previously approved strengths were included in the application. After administration of venlafaxine ER capsules, venlafaxine and O-desmethylvenlafaxine exposure (Cmax and AUC) increased in a linearly dose-proportional manner over the dose range studied (37.5-225 mg).

IV.2 Discussion on the clinical aspects

From a pharmacokinetic perspective, the new strength has been sufficiently characterised. Further, from a general clinical perspective, no new information is available that changes the risk/benefit of the product. The product can be recommended for market authorisation.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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 Efexor depot 37,5 mg, 75 mg, 150 mg prolonged-release capsuels, hard, SE/H/0936/001-003/R/001. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Efexor Depot, prolonged-release capsules, 225 mg, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Efexor Depot, prolonged-release capsules, 225 mg, was successfully finalised on 2014-10-02.

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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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