COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Venlafaxine Aurobindo 37.5 mg, 75 mg and 150 mg, prolonged-release capsules, hard (venlafaxine hydrochloride)

NL/H/6434/001-003/DC

Date: 23 July 2025

This module reflects the scientific discussion for the approval of Venlafaxine Aurobindo 37.5 mg, 75 mg and 150 mg, prolonged-release capsules, hard. The procedure was finalised at 18 December 2014 in Portugal (PT/H/0703/01-03/DC). After a transfer on 26 May 2025, the current RMS is the Netherlands. For information on changes after the finalisation date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed in granting a marketing authorisation for Venlafaxine Aurobindo 37.5 mg, 75 mg and 150 mg, prolonged-release capsules, hard, from Aurobindo Pharma B.V.

The product is indicated for the treatment of major depressive episodes, for prevention of recurrence of major depressive episodes, treatment of generalised anxiety disorder, treatment of social anxiety disorder and treatment of panic disorder, with or without agoraphobia.

A comprehensive description of the indications and posology is given in the current SmPC.

The originator product is Efexor (37.5 mg, 75 mg and 150 mg, prolonged release capsule) by Wyeth Pharmaceuticals.

The marketing authorisation has been granted pursuant to Article 10.1 of Directive 2001/83/EC on 11-02-2015.

This type of application refers to information that is contained in the pharmacological-toxicological and clinical part of the dossier of the authorisation of the reference product. A reference product is a medicinal product authorised and marketed on the basis of a full dossier, i.e. including chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. This information is not fully available in the public domain. Authorisations for generic products are therefore only allowed once the data protection time of the dossier of the reference product has expired. For this kind of application, it has to be demonstrated that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product. This generic product can be used instead of its reference product.

II. QUALITY ASPECTS

II.1 Introduction

Venlafaxine Aurobindo 37.5 mg, prolonged-release capsules, hard
White to off-white spherical to oval pellets filled in Empty hard gelatin capsule shell (size '3') of Opaque Grey color cap and Opaque Peach color body imprinted with "E" on cap and "73" on the body with edible black ink.

Venlafaxine Aurobindo 75 mg, prolonged-release capsules, hard
White to off-white spherical to oval pellets filled in Empty hard gelatin capsule shell (size '1') of Opaque Peach color cap and Opaque Peach color body imprinted with "E" on cap and "74" on the body with edible black ink.

Venlafaxine Aurobindo 150 mg, prolonged-release capsules, hard
White to off-white spherical to oval pellets filled in Empty hard gelatin capsule shell (size '0') of Opaque Dark orange color cap and Opaque Dark orange color body imprinted with "E" on cap and "89" on the body with edible black ink.

Venlafaxine capsules are available in:
Clear PVC/PE/PVDC-Aluminium foil:
Venlafaxine Aurobindo 37.5 mg/75 mg/150 mg: 7, 10, 14, 20, 28, 30, 50, 56, 60, 90, 98 and 100 capsules

HDPE Bottle with polypropylene closure:
Venlafaxine Aurobindo 37.5 mg/75 mg/150 mg: 30, 100 and 500 capsules

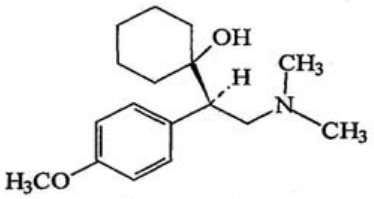
The excipients are:
Sugar spheres (containing sucrose), hypromellose, talc, ethyl cellulose

Shell contents
Cap
Gelatin, Iron oxide red (E172) (for 75 mg and 150 mg only), Iron oxide Black (E172) (for 37.5mg only), Titanium dioxide (E171), Sodium lauryl sulfate

Body
Gelatin, Iron oxide red (E172), Titanium dioxide (E171), Sodium lauryl sulfate

Printing ink:
Shellac, Propylene glycol, Potassium hydroxide, Black iron oxide (E172)

II.2 Drug Substance



and enantiomer . HCl

Venlafaxine hydrochloride

A white or almost white crystalline powder, freely soluble in water and in methanol, soluble in anhydrous ethanol and slightly soluble or practically insoluble in acetone.

The chemical-pharmaceutical documentation and Expert Report in relation to venlafaxine hydrochloride are of sufficient quality in view of the present European regulatory requirements.

II.3 Medicinal Product

Pharmaceutical development
The documentation provided complies with relevant EU guidelines and directives. Manufacture is performed in accordance with cGMP and consistency in quality and homogeneity is demonstrated.
The finished product specification is based on relevant development and stability studies. The development of the product has been described, the choice of excipients is justified and their functions explained.

Quality control of drug product
Appropriate validation data have been provided for the analytical methods. Batch analyses data support the proposed finished product specification.

Stability of drug product
The conditions used in the stability studies are according to the ICH stability guideline. The control tests and specifications for drug product are adequately drawn up. The proposed shelf-life of 3 years for the drug product with no special storage requirements is considered acceptable.

III. NON-CLINICAL ASPECTS

The pharmacodynamic, pharmacokinetic and toxicological properties of venlafaxine hydrochloride are well known. As venlafaxine hydrochloride is a widely used, well-known

active substance, the applicant has not provided additional studies and further studies are not required. An overview based on literature review is, thus, appropriate.

III.1 Environmental risk assessment (ERA)

An Environmental Risk Assessment has not been performed as the product is intended for generic substitution. A disposal advice has been added to the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

To support the application, the applicant has submitted 3 bioequivalence studies. According to the guideline, CPMP/EWP/280/96 three studies under fasting, fed and multiple dose (MD) conditions are required at the highest strength (in casu 150 mg). A biowaiver is adequately addressed and justified. Therefore, waiving bioequivalence studies for the 37.5 mg and 75 mg strengths is acceptable.

IV.2 Pharmacovigilance system

A Summary of the Pharmacovigilance System (version not specified dated 29-04-2014) was submitted.
A declaration signed by the representative of the applicant and the qualified person responsible for pharmacovigilance (QPPV) was submitted, stating that the applicant has at its disposal a QPPV, who resides and carries out duties in Spain and that it has the necessary means to fulfil the tasks and responsibilities listed in Title IX of Directive 2001/83/EC, further described in the applicants pharmacovigilance system master file.

IV.3 Risk Management Plan

Routine pharmacovigilance activities are considered sufficient for the product.

V. USER CONSULTATION

The package leaflet has been evaluated 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. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the RMS considered that the application for Venlafaxine Aurobindo 37.5 mg , 75 mg and 150 mg, prolonged-release capsules, hard, is approvable.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
PT/H/0703/1-3/001/G	Change in the name and/or address of a manufacturer/importer of the finished product (including batch release or quality control testing sites) -The activities for which the manufacturer/importer is responsible do not include batch release + Deletion of manufacturing sites (including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier)).	No Yes	12 February 2016	Approved	N.A.
PT/H/0703/1-3/IB/002	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	6 June 2016	Approved	N.A.
PT/H/0703/1-3/IB/003	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of a generic/hybrid/biosimilar medicinal products following assessment of the same change for the reference product Implementation of change(s) for which no new additional data are submitted by the MAH	Yes	21 August 2017	Approved	N.A.

PT/H/0703/1-3/IB/004	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	6 April 2018	Approved	N.A.
PT/H/0703/1-3/IB/005	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of human medicinal products intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority under Articles 45 or 46 of Regulation 1901/2006SmPCSmPC -update Summary of Product Characteristics	Yes	12 April 2018	Approved	N.A.
PT/H/0703/1-3/IA/006	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - New certificate from a new manufacturer (replacement or addition)	No	3 January 2019	Approved	N.A.
PT/H/0703/1-3/IA/007/G	Change in the name and/or address of a manufacturer/importer of the finished product (including batch release or quality control testing sites) -The activities for which the manufacturer/importer is responsible do not	No	2 May 2019	Approved	N.A.

	include batch release + Deletion of manufacturing sites (including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier)). + Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product Secondary packaging site	Yes No			
PT/H/0703/1-3/R/001	Renewal	No	29 July 2019	Approved	N.A.
PT/H/0703/1-3/IA/008	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products update Summary of Product Characteristics and Patient leaflet	Yes	31 August 2019	Approved	N.A.
PT/H/0703/1-3/IB/009	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of a generic/hybrid/biosimilar medicinal products following assessment of the same change for the reference product Implementation of change(s) for which no new additional data are submitted by the MAH	Yes	19 July 2021	Approved	N.A.
PT/H/0703/1-3/IA/010	Change to importer, batch release arrangements and quality control testing of the finished product	No	4 February 2020	Approved	N.A.

	Replacement or addition of a site where batch control/testing takes place				
PT/H/0703/1-3/IA/011	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. -Updated certificate from an already approved manufacturer	No	14 May 2020	Approved	N.A.
PT/H/0703/1-3/IB/012	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	26 October 2020	Approved	N.A.
PT/H/0703/1-3/IB/013	Other variation: Update of the Summary of Product Characteristics and Package leaflet to be in line with PRAC recommendations (EMA/PRAC/257435/2020)	Yes	19 July 2021	Approved	N.A.
PT/H/0703/1-3/IA/014	Other variation: to update product information with reference to the recommendations by PRAC wordings (EMA/PRAC/513083/2020)	Yes	4 February 2021	Approved	N.A.
PT/H/0703/1-3/IB/015	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan	No	10 September 2021	Approved	N.A.

PT/H/0703/1-3/IA/016/G	Change in the name and/or address of a manufacturer/importer of the finished product (including batch release or quality control testing sites) + Deletion of manufacturing sites (including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier)). + Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product Secondary packaging site	No Yes No	27 March 2023	Approved	N.A.
PT/H/0703/1-3/IA/017	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of human medicinal products intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority under Articles 45 or 46 of Regulation 1901/2006SmPCSmPC Implementation of wording agreed by the competent authority	Yes	13 September 2023	Approved	N.A.
PT/H/0703/1-3/IA/018	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of human medicinal products intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority under Articles 45	Yes	2 May 2024	Approved	N.A.

	or 46 of Regulation 1901/2006SmPCSmPC Implementation of wording agreed by the competent authority				
PT/H/0703/1-3/IA/019	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - Updated certificate from an already approved manufacturer	No	3 August 2024	Approved	N.A.