

Public Assessment Report

Scientific discussion

Fontecare

(fluoxetine, fluoxetine hydrochloride)

5.4.1-2023-29384

This module reflects the scientific discussion for the approval of Fontecare. The procedure was finalised on 2025-03-18. For information on changes after this date please refer to the module ‘Update’.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Fontecare, 4 mg/ml, Oral solution.

The active substance is fluoxetine, fluoxetine hydrochloride. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application for Fontecare, 4 mg/ml, Oral solution, is a generic application submitted according to Article 10(1) of Directive 2001/83/EC. The applicant applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Fontex, 4 mg/ml, oral solution, authorised in SE since 1995, with Eli Lilly Sweden AB as marketing authorisation holder.

Potential similarity with orphan medicinal products

According to the application form and a check of the Community Register of orphan medicinal products

there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacology/Pharmacokinetics/Toxicology

Pharmacodynamic, pharmacokinetic and toxicological properties of fluoxetine are well known. As fluoxetine is a widely used, well-known active substance, no further studies are required and the applicant provides none. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)

Since Fontecare is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Fontecare from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics

The applicant did not submit any studies.

Pharmacokinetic properties of the active substance

Absorption: Fluoxetine is well absorbed from the gastrointestinal tract after oral administration. Maximum plasma concentration is generally achieved 6 to 8 hours after administration.

The bioavailability is not affected by food intake. Therefore, there are no restrictions with respect to food in the SmPC of the originator.

Linearity: Fluoxetine has a non-linear pharmacokinetic profile.

Elimination: The elimination half-life of fluoxetine is 4 to 6 days.

Discussion and overall conclusion

According to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1), bioequivalence studies may be waived if the test product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved oral solution. However, if the excipients may affect gastrointestinal transit, absorption, solubility or stability, a bioequivalence study should be conducted, unless the differences in the amounts of these excipients can be adequately justified by reference to other data. The same requirements for similarity in excipients apply for oral solutions as for BCS-based biowaivers.

According to ICH M9 on biopharmaceutics classification system-based biowaivers (EMA/CHMP/ICH/493213/2018), for BCS Class I drugs, qualitative and quantitative differences in excipients are permitted, except for excipients that may affect absorption, which should be qualitatively the same and quantitatively similar.

The applicant has performed a solubility study, confirming that the highest dose (60 mg) is soluble in 250 ml at three different pHs and in water, i.e. highly soluble. High permeability can also be concluded based on the submitted Caco-2 cell permeability data. Thus, fluoxetine can be classified as a BCS class I substance.

There are quantitative differences in excipients between the test and reference product. However, none of them are classified as excipients that may affect absorption. Thus, absence of bioequivalence study is acceptable.

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Risk Management Plan

The MAH has submitted a risk management plan (version 0.1, DLP 22 Feb 2023, signed 22 Feb 2023), in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Fontecare.

Part II Safety specification

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• None
Missing information	• None

Part III Pharmacovigilance Plan

Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Part V Risk minimisation measures

Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Part VI Summary of the RMP

The Summary of the RMP is endorsed.

Conclusion RMP assessment

The submitted Risk Management Plan, version 0.1, DLP 22 Feb 2023, signed 22 Feb 2023) is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Fluoxetin Sandoz 20 mg dispersible tablet, SE/H/525/001-003, regarding content and Dexamcol 1 mg/ml + 5 mg/ml eye drops, solution, DK/H/3155/001/DC, regarding layout.

The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Fontecare, is found adequate. There are no objections to approval of Fontecare from a non-clinical and clinical point of view. The absence of bioequivalence studies is acceptable. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

Fontecare, 4 mg/ml, Oral solution was approved in the national procedure on 2025-03-18.

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/non approval	Summary/Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)