LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Azelastine /Fluticasone Substipharm
(fluticasone propionate, azelastine hydrochloride)

SE/H/2293/01/DC

This module reflects the scientific discussion for the approval of Azelastine /Fluticasone Substipharm. The procedure was finalised on 2024-04-24. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Azelastine /Fluticasone Substipharm, 125 mikrogram + 50 mikrogram per actuation, Nasal spray, suspension.

The active substance is fluticasone propionate and azelastine 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 Azelastine /Fluticasone Substipharm, 125 mikrogram + 50 mikrogram per actuation, nasal spray, suspension, is a hybrid application submitted according to Article 10(3) of Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and the following concerned member states (CMS): FR, IT, DK, NO.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Dymista, 125 mikrogram + 50 mikrogram per actuation, nasal spray, suspension authorised in Sweden since 2013, with Meda 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 active substance are well known. As active substance 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)
An environmental risk assessment has been provided. The ERA contains a justification that approval of Azelastine/Fluticasone Substipharm 125 mikrogram + 50 mikrogram per actuation, nasal spray, suspension will not lead to an increased exposure to the environment, and that ERA studies are therefore not needed. Based on sales data, it is agreed that approval of Azelastine/Fluticasone Substipharm 125 mikrogram + 50 mikrogram per actuation, nasal spray, suspension, it not expected to result in a significant increase in environmental exposure to fluticasone propionate.

IV. CLINICAL ASPECTS

Pharmacokinetics/Pharmacodynamics/Clinical efficacy/Clinical safety
No clinical pharmacokinetic studies or additional clinical studies to demonstrate efficacy and safety have been conducted, as the applicant claims therapeutic equivalence based on *in vitro* equivalence data. The principle of showing qualitative *in vitro* equivalence as a surrogate for clinical study/ies is considered acceptable.

It can be concluded that equivalence between the test and the reference product has been shown *in vitro*. See assessment in the Quality assessment report. The absence of clinical data is considered acceptable.

Risk Management Plan
The MAH has submitted a risk management plan, 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 Azelastine /Fluticasone Substipharm.

Safety specification

Table SVIII.1: Summary of safety concerns

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

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

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

Summary of the RMP
The MAH has satisfactorily responded to the questions raised and updated the RMP accordingly. Issue is resolved. The submitted Risk Management Plan, version 0.2 signed 13 February 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

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 language used for the purpose of user testing the PL 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

The quality of the product, Azelastine /Fluticasone Substipharm, is found adequate. There are no objections to approval of Azelastine /Fluticasone Substipharm from a non-clinical and clinical point of view. The absence of bioequivalence studies is acceptable. It can be concluded that equivalence between the test and the reference product has been shown *in vitro*. The product information is acceptable. The benefit/risk is considered positive, and the applications are 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

The decentralised procedure for Azelastine /Fluticasone Substipharm, 125 mikrogram + 50 mikrogram per actuation, nasal spray, suspension was positively finalised on 2024-04-24.

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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)

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