LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Salbutamol Neutec
(salbutamol sulfate)

SE/H/2104/01/DC

This module reflects the scientific discussion for the approval of Salbutamol Neutec. The procedure was finalised on 2023-04-19. 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 Salbutamol Neutec, 2,5 mg, Nebuliser solution.

The active substance is salbutamol sulfate. 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 Salbutamol Neutec, 2,5 mg, nebulisation solution, is submitted according to Article 10(3) of Directive 2001/83/EC. The applicant, Neutec lnhaler lreland Limited applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and BE, DE, DK, ES, FI, FR, IE, IS, NL, NO and UK(NI) as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Ventoline 1 mg/ml lösning för nebulisator authorised in SE since 1982, with GlaxoSmithKline AB as marketing authorisation holder.

European Reference Product (ERP)
A European Reference Product is used in CMS BE, DE and ES: Ventoline 1 mg/ml lösning för nebulisator authorised in SE since 1982, with GlaxoSmithKline AB as marketing authorisation holder. The justification to use this product is based on RMS's own files. The ERP information was circulated during validation period.

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 salbutamol sulphate are well known. As salbutamol 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 Salbutamol Neutec is intended for substitution with marketed products containing the same active substance, 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 product name from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
According to the Guideline for Orally Inhaled Products (OIP) (CPMP/EWP/4151/00 Rev.1, 2009), a step-wise approach should be considered when demonstrating therapeutic equivalence for an orally inhaled product. The first step consists of pharmaceutical data, the second step of pharmacokinetic data and the third step is represented by pharmacodynamic/clinical efficacy and safety data. Therapeutic equivalence of the developed medicinal product with the reference medicinal product is based on the comparative evaluation of *in vitro* data alone; i.e. in accordance with Step 1 in the OIP guideline (CPMP/EWP/4151/00 Rev. 1).

No pharmacokinetic studies have been conducted with Salbutamol Neutec. As the *in vitro* data comply with all criteria required in the OIP-guideline, the lack of comparative pharmacokinetic data is acceptable.

Pharmacodynamics/Clinical efficacy/Clinical safety
Salbutamol is a selective β2-agonist providing short-acting (4-6 hours) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction. The use of short acting β2-agonists (SABA) for the treatment of bronchospasm is a standard therapy in asthma for the treatment of breakthrough symptoms, prevention of exercise induced symptoms and for additional bronchodilation in acute severe asthma and is recommended as the initial bronchodilator of choice in the treatment of COPD patients including during exacerbations

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. As therapeutic equivalence with the originator product has been demonstrated through provision of satisfactory *in vitro* data, additional data is not necessary.

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 Salbutamol Neutec.

Safety specification

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 submitted Risk Management Plan, version 0.3 signed 17/04/2023 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 Ventoline 1 mg/ml lösning för nebulisator. 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, Salbutamol Neutec, is found adequate. There are no objections to approval of Salbutamol Neutec, from a non-clinical and clinical point of view. The absence of pharmacokinetic 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

The decentralised procedure for Salbutamol Neutec, 2,5 mg, Nebuliser solution was positively finalised on 2023-04-19.

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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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