IPAR

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Salbutamol CFC-Free Inhaler 100 micrograms per metered dose, pressurised inhalation, suspension

SALBUTAMOL

PA1987/001/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Salbutamol CFC-Free Inhaler 100 micrograms per metered dose, pressurised inhalation, suspension, from Cetus Pharma CV on 27th May 2011 for the relief and prevention of bronchial asthma and conditions associated with reversible airways obstruction.

This application for a marketing authorisation was submitted in accordance with Article 10(1) of Directive 2001/83/EC and is referred to as a 'generic' application. Salbutamol CFC-Free Inhaler 100 micrograms per metered dose has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Ventolin Inhaler 100 micrograms Pressurised Metered-dose Inhaler.

The Summary of Product Characteristics for (SPC) for this medicinal product is available on the HPRA's website at www.HPRA.ie

Name of the product	Salbutamol CFC-Free Inhaler
Name(s) of the active substance(s) (INN)	Salbutamol
Pharmacotherapeutic classification (ATC code)	R03 AC02
Pharmaceutical form and strength(s)	100 micrograms
Marketing Authorisation Number(s) in Ireland (PA)	PA1987/001/001
Marketing Authorisation Holder	VALEAS SPA

II QUALITY ASPECTS

II.1. Introduction

This application is for Salbutamol CFC-Free Inhaler 100 micrograms per metered dose, pressurised inhalation, suspension.

II.2 Drug substance

The active substance is Salbutamol Sulphate Ph. Eur., an established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The product is a pressurised inhalation suspension supplied in an aluminium canister fitted with a metering valve. There is a plastic actuator and dust cap.

Each metered dose contains salbutamol 100 µg, as Salbutamol Sulphate Ph. Eur. The pressurised inhalation also contains oleic acid, anhydrous ethanol, and norflurane.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites. The manufacturing process has been validated according to relevant ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances)*

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the monograph for Salbutamol Pressurised Inhalation B.P. and the general Ph. Eur. monograph for pressurised metered-dose preparations for inhalation. The tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The product is presented as a pressurised inhalation suspension supplied in an aluminium canister fitted with a metering valve.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines demonstrating the stability of the product for 3 years when stored at or below 30 °C.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Salbutamol CFC-Free Inhaler 100 micrograms per metered dose, pressurised inhalation, suspension.

III NON-CLINICAL ASPECTS

III.1 Introduction

This active substance has been available on the European/Irish market for more than ten years. Preclinical data have been superseded by clinical experience and therefore no preclinical assessment report is available.

IV CLINICAL ASPECTS

IV.1 Introduction

Salbutamol sulphate is a well known active substance with established efficacy and tolerability.

The content of the SPC approved during the national procedure is in accordance with that accepted for the reference product Ventolin marketed by Glaxo Smith Kline.

For this generic application, the applicant has submitted a therapeutic equivalence in which the pharmacodynamic profile of the test product Salbutamol CFC-Free inhaler is compared with the pharmacodynamic profile of the reference product Ventolin pressurised metered dose inhaler.

The HPRA has been assured that GCP standards were followed in an appropriate manner in the studies conducted.

The Marketing Authorisation Holder submitted a set of documents describing the Pharmacovigilance System, including information on the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

IV.6 Discussion on the clinical aspects

A rising dose, single blind, crossover therapeutic equivalence study was carried out in 29 asthmatic subjects at a single investigative centre in the Netherlands. Valeas HFA 100 µg ex-actuator (test product) was compared to the reference product Ventolin pMDI 100 µg ex-actuator in asthmatic subjects, using cumulative doses up to a maximum of 800 µg Improvement in lung function (FEV1) was the principal assessment criterion. Based on the pharmacodynamic effects on the subjects' lung function the relative potency of the test and reference of active substances was calculated to be 0.97 (90% Confidence Interval (0.086 to 0.99). The difference was not considered to be clinically meaningful.

V OVERALL CONCLUSIONS

Salbutamol CFC-Free inhaler, a pressurised metered dose inhaler is a generic form of Ventolin pMDI, a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the CHMP guidance documents. The SPC is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted considered that Salbutamol CFC-free inhaler demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI REVISION DATE

27th May 2011