الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Breztri®

Type of Application: New drug application.

Type of Product: New chemical entity.

Active Pharmaceutical Ingredient(s): Formoterol Fumarate, Glycopyrronium Bromide, Budesonide.

ATC code: R03AL.

Dosage Form: Pressurized inhalation, suspension.

Dosage Strength: 5 - 7.2 – 160 µg.

Pack Size: 1.

Shelf life: 30 months.

Storage Conditions: Store below 30°C.

Reference Product in SA (if applicable): NA.

Marketing Authorization Holder: AstraZeneca.

Manufacturer: AstraZeneca Dunkerque Production (AZDP).

Registration No.: 1705222041.

Date of Decision: Approved on 25/04/2022.

Proposed Indications:

Breztri Aerosphere is indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist or combination of a long-acting beta2-agonist and a long-acting muscarinic antagonist.

Product Background

This product is considered as a new chemical entity, for Saudi regulatory purposes. Furthermore, this product is qualified to follow the SFDA's regulatory pathway abridged approval.

The SFDA approval for Breztri Aerosphere® (Formoterol fumarate dehydrate 5 micrograms, Glycopyrronium bromide 7.2 micrograms and Budesonide 160 micrograms) is based on a review of the quality, safety and efficacy as summarised hereinafter:

Quality Aspects

Drug Substance

- Budesonide is a white or almost white powder. Budesonide is practically insoluble in water, freely soluble in methylene chloride and sparingly soluble in ethanol. Budesonide does not have chirality.

- Polymorphism has not been observed. Formoterol fumarate dihydrate is a white to almost white or slightly yellow powder. Formoterol fumarate dihydrate is slightly soluble in water, soluble in methanol, slightly soluble in 2-propanol, practically insoluble in acetonitrile. Formoterol fumarate dihydrate does not have chirality. Polymorphism has not been observed.

- Glycopyrronium Bromide is a white or almost white crystalline powder. Glycopyrronium Bromide is soluble in water and in alcohol, and practically insoluble in chloroform and ether. Glycopyrronium Bomide does not have chirality. Polymorphism has not been observed.

- The drug substance (DS) is manufactured by a multiple-step chemical synthesis. The structure of budesonide, formoterol fumarate dihydrate and Glycopyrronium Bromide has been fully elucidated using several spectroscopic techniques.

- The drug substance specification includes relevant tests for proper quality control. The control methods are validated according to international guidelines.

- Appropriate stability data have been presented and justify the established re-test period.

Drug Product

- The finished product is available as pressurized inhalation, white suspension. Each actuation contains 160 µg of Budesonide, 7.2 µg of Budesonide and 5 µg of formoterol fumarate dihydrate.

- the composition of the drug product (DP) is adequately described, qualitatively and quantitatively. Suitable pharmaceutical development data have been provided for the finished product composition and manufacturing process.

- The manufacturing process is described narratively and in sufficient detail, taking into account pharmaceutical development data. Batch manufacturing formulas and in-process controls are included. Satisfactory validation data pertaining to the commercial manufacturing process are provided.
- The drug product specification covers appropriate parameters for this dosage form which allow for proper control of the finished drug product. The control methods are validated according to international guidelines.
- Batch data show a consistent quality of the drug product.
- The drug product is packaged in coated aluminium can fitted with a metering valve, a white plastic actuator, a grey plastic dust cap, and a can-top dose indicator.
- Appropriate stability data have been generated in the packaging material intended for commercial use and following relevant international guidelines. The data show a good stability of the finished product and support the proposed shelf life 24 months.

Clinical Aspects

Efficacy and Safety

The clinical development program for Breztri Aerosphere consisted of two pivotal clinical studies (PT010006 and PT010005) to prove the efficacy and safety of the product for the proposed indication.

Summary of the clinical studies presented hereafter:

- PT010006 Study: A phase III randomized, double blind, parallel group, multi-center, chronic-dosing study. The primary objective was to assess the effects of Budesonide, Glycopyrronium, and formoterol fumarate - Metered dose inhaler (BGF MDI), Glycopyrronium and formoterol fumarate - Metered dose inhaler (GFF MDI), Budesonide and formoterol fumarate - Metered dose inhaler (BFF MDI), and Symbicort® Turbuhaler (TBH). The trial interventions were tested for lung function for a duration of 24 weeks in 1902 participants with moderate to very severe chronic obstructive pulmonary disease (COPD) who were symptomatic despite receiving two or more inhaled COPD maintenance treatments.
- PT010005 Study: A phase III, randomized, double-blinded multicenter parallel group trial. The primary objective was to assess the effect of BGF MDI relative to GFF MDI and BFF MDI on the rate of moderate or severe COPD exacerbations in 8588 participants with moderate to very severe COPD who had a history of moderate or severe COPD exacerbations and remained symptomatic (CAT 10) having received two to three inhaled maintenance therapies.

The clinical pharmacology, efficacy and safety results from the aforementioned studies were assessed by the SFDA efficacy and safety department. Based on the review of the submitted

evidence, the benefit/risk balance of Breztri Aerosphere is considered positive. Therefore, we recommend the approval of the marketing authorization of Breztri Aerosphere.

Product Information

The approved Summary of Product Characteristics (SPC) with the submission can be found in Saudi Drug Information System (SDI) at: https://sdi.sfda.gov.sa/

The date of revision of this text corresponds to that of the Saudi PAR. New information concerning the authorized medicinal product in question will not be incorporated into the Saudi PAR. New findings that could impair the medicinal product's quality, efficacy, or safety are recorded and published at (SDI or Summary Saudi-PAR report).

For inquiry and feedback regarding Saudi PAR, please contact us at Saudi.PAR@sdfa.gov.sa