

An addendum to this public summary document has been included at the end of the document

**6.12 BUDESONIDE with GLYCOPYRRONIUM and
FORMOTEROL,
Pressurised inhalation containing budesonide
160 micrograms with glycopyrronium 7.2 micrograms
and formoterol fumarate dihydrate 5 micrograms per
dose, 120 doses
Breztri Aerosphere® DFP-EvoCap,
AstraZeneca Pty Ltd**

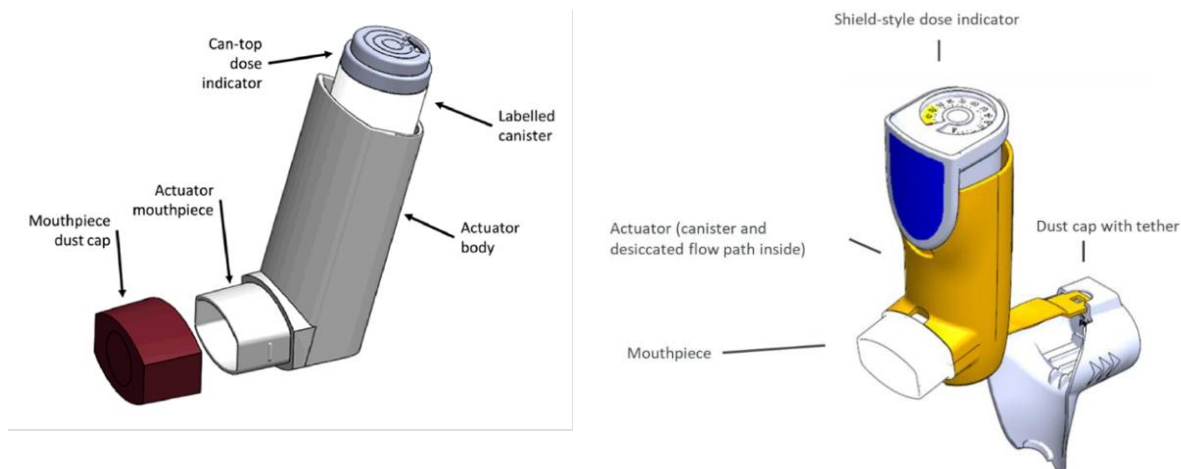
1 Purpose of Submission

- 1.1 The Category 4 submission provided notification that the existing budesonide with glycopyrronium and formoterol pressurised metered dose inhaler (pMDI) (Breztri Aerosphere®) is to be phased out and replaced with a pMDI with a desiccated flow path (Breztri Aerosphere® DFP-EvoCap, herein referred to as DFP-EvoCap).

2 Background

- 2.1 Budesonide with glycopyrronium and formoterol is currently listed on the PBS as an Authority Required (STREAMLINED) benefit for the long-term maintenance treatment of chronic obstructive pulmonary disease (COPD) (PBS item code 12672Y). Breztri Aerosphere is the only listed brand of this medicine.
- 2.2 The existing Breztri Aerosphere inhaler is a pMDI delivering budesonide 160 micrograms, glycopyrronium 7.2 micrograms and formoterol (eformoterol) fumarate dihydrate 5 micrograms per actuation. The submission stated that the DFP-EvoCap (see Figure 1) delivers an equivalent amount of active ingredients while reducing the risk of drug deposition and improving on the function of the dose indicator. The device components changed include the:
- desiccated flow path (DFP) – reduces moisture in the internal drug flow path by desiccating through a hole in the valve stem, reducing the risk of clogging.
 - ‘shield-style’ dose indicator – provides a reading of the remaining doses and reduces unintentional firing of the MDI and inadvertent increases in dose count.
 - tethered dust cap – closes the mouthpiece when not in use.

Figure 1: Appearance of the existing Breztri Aerosphere inhaler (left) and the DFP-EvoCap inhaler (right)



Source: Figure 1, p3 of the submission.

- 2.3 While the delivered dose of active ingredients in the DFP-EvoCap is the same as the existing Breztri Aerosphere inhaler, due to a decreased formulation overage, the amount of the two excipients (calcium chloride dihydrate and distearoylphosphatidylcholine) per actuation is increased.
- 2.3 The DFP-EvoCap was approved by the TGA with AUST R number 386646 on 5 August 2022 and registered on the ARTG on 11 August 2022 for the same indications as the existing Breztri Aerosphere inhaler. The TGA approval letter states: “BREZTRI AEROSPHERE (AUST R 386646) was previously supplied as BREZTRI AEROSPHERE (AUST R 339070). The two products are the same, apart from their formulations and other pharmaceutical chemistry variations that will not affect rate and extent of absorption. On this basis, they are bioequivalent.”
- 2.4 While not a matter for the PBAC, the sponsor has made a separate submission to the Department requesting for the DFP-EvoCap to be recognised as a new presentation.

Previous PBAC consideration

- 2.5 Budesonide with glycopyrronium and formoterol was recommended for this indication by the PBAC at its July 2021 meeting for patients not adequately treated by a combination of an inhaled corticosteroid (ICS) with a long-acting beta2-agonist (LABA), or LABA with a long-acting muscarinic antagonist (LAMA).
- 2.6 There have been no further submissions to the PBAC for budesonide with glycopyrronium and formoterol.

For more detail on PBAC’s view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 The submission requested that the existing PBS item code and authority code be retained for the listing of the DFP-EvoCap.
- 3.2 The Australian Digital Health Agency has advised that the Australian Medicines Terminology (AMT) for the DFP-EvoCap’s listing description (medicinal product pack) is unchanged from the existing Breztri Aerosphere, but the Trade Product Pack (TPP) for the DFP-EvoCap is BREZTRI AEROSPHERE 160/7.2/5 (DFP-EvoCap), which differs from the TPP for Breztri Aerosphere.
- 3.3 If recommended, the DFP-EvoCap will be assigned a new TPP and listed as a new brand under the same PBS item code as the existing Breztri Aerosphere.
- 3.4 The sponsor requested an Administrative Note to be added to the PBS listing to explain that the inhaler has changed, but the sponsor did not provide any suggested wording. Apart from the addition of the Administrative Note, there were no further changes requested to the current restrictions for Breztri Aerosphere. The Secretariat provided suggested wording for the Administrative Note (see Section 3.5).
- 3.5 Suggested additions are in italics. An abridged version is presented.

Amend existing listing as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
budesonide + glycopyrronium + formoterol (eformoterol)					Breztri Aerosphere®
budesonide 160 microgram/actuation + glycopyrronium 7.2 microgram/actuation + formoterol (eformoterol) fumarate dihydrate 5 microgram/actuation inhalation, 120 actuations	12672Y	1	1	5	Breztri Aerosphere® DFP-EvoCap

<i>Administrative Advice: Breztri Aerosphere® DFP-EvoCap includes a desiccated flow path, whereas Breztri Aerosphere® does not. Ensure the patient is provided instruction on optimal inhaler technique for both inhalers.</i>
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For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The submission proposed a new inhaler for budesonide with glycopyrronium and formoterol and nominated the currently listed inhaler of the same drug as the comparator. The submission nominated the comparator on the basis that the new inhaler is expected to replace the existing inhaler.
- 4.2 The PBAC considered cost-minimisation to the lowest cost alternative agent would be appropriate. Alternative comparators include any combinations of LAMA, LABA and

corticosteroid used together for the treatment of COPD, whether in fixed dose combinations or open combination (i.e. individual products).

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from individuals (1), and organisations (1) via the Consumer Comments facility on the PBS website. The patient comment described a willingness to access budesonide with glycopyrronium and formoterol to treat their condition, via the listing of a new inhaler device on the PBS.
- 5.3 The PBAC welcomed the input from the Lung Foundation Australia, which reported the results of a targeted survey of 200 patients experiencing mild to moderate and severe COPD and their families. The survey responses showed strong support for the listing. Respondents considered it would offer an additional treatment choice for clinicians to match to patient characteristics and disease stage, and that the new device potentially offered more effective treatment with fewer exacerbations, higher adherence and a reduced the burden of taking multiple medications. In addition to positive impacts on wellbeing and quality of life for those affected, the survey respondents also considered that there could be wider benefits to having all three medicines in one device for environmental sustainability and cost-effectiveness.

Clinical trials

- 5.4 The submission presented a comparability report comparing the DFP-EvoCap with the existing Breztri Aerosphere inhaler, which found that they were equivalent both for delivered dose and aerodynamic particle size (see Table 1).
- 5.5 The submission also provided a justification document providing further context for the DFP-EvoCap (see Table 1).
- 5.6 The submission stated that, as in-vitro equivalence has been demonstrated, no formal bioequivalence assessments were required for TGA approval. The TGA registered the DFP-EvoCap on 11 August 2022 and determined it to be bioequivalent to the existing Breztri Aerosphere inhaler (see paragraph 2.3).
- 5.7 As a Category 4 submission, the clinical evidence has not been independently evaluated.

*Public Summary Document – November 2022 PBAC Meeting with June 2023 OOS
Addendum*

Table 1: Comparability studies provided with the submission

Document name	Publication Title
Justification Document	Justification Document. Device transition to Desiccated Flow Path and EvocapXS, budesonide, glycopyrronium bromide and formoterol fumarate dihydrate, pressurised inhalation suspension, respiratory use, 160+7.2+4.8 µg, 120 and 28 inhalations
Comparability Document	Comparability Report for the Proposed Change to a Desiccated Flow Path and EvocapXS Actuator for Budesonide, Glycopyrronium Bromide and Formoterol Fumarate Dihydrate, Pressurised Inhalation Suspension, Respiratory Use, 160/7.2/4.8 µg 120 and 56 Inhalation Products, 21 September 2021

Source: Table 4, p6 of the submission

Clinical claim

- 5.8 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of the DFP-EvoCap compared with the existing Breztri Aerosphere inhaler, based on the in-vitro assessment of equivalence.

Economic analysis

- 5.9 The submission provided a cost-minimisation approach comparing the DFP-EvoCap with the existing Breztri Aerosphere inhaler. The equi-effective doses were estimated as one DFP-EvoCap actuation to one existing Breztri Aerosphere actuation.
- 5.10 As a Category 4 submission, the economic analysis has not been independently evaluated.

Estimated PBS utilisation and financial implications

- 5.11 The submission requested the same AEMP per pack of the DFP-EvoCap as the current AEMP per pack for Breztri Aerosphere.
- 5.12 The submission used a market share approach to generate utilisation and financial estimates for listing of the DFP-EvoCap. The submission stated that listing the DFP-EvoCap is not expected to increase the overall size of the market for triple-therapy combination treatments for COPD, but rather the DFP-EvoCap is expected to replace the existing Breztri Aerosphere inhaler by year 2 of listing. Therefore, the submission claimed that this listing is expected to have nil financial impact on the PBS.
- 5.13 Breztri Aerosphere is subject to a Deed of Agreement with expenditure caps. The sponsor has acknowledged that the DFP-EvoCap would be subject to the same arrangements.
- 5.14 As a Category 4 submission, the financial estimates have not been independently evaluated.

For more detail on PBAC’s view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC held no objections to the planned replacement of the existing pMDI containing budesonide, glycopyrronium and formoterol (Breztri Aerosphere) with a pMDI with a desiccated flow path (Breztri Aerosphere® DFP-EvoCap).
- 6.2 The PBAC noted that the submission requested the same AEMP per pack of the DFP-EvoCap as the current AEMP per pack for Breztri Aerosphere.
- 6.3 The PBAC considered that the DFP-EvoCap should be cost-minimised to the lowest cost alternative agent, including any combination of LAMA, LABA and corticosteroid used for the treatment of COPD, whether in fixed dose combinations or open combination (i.e. individual products).
- 6.4 The PBAC noted that the TGA had determined that Breztri Aerosphere and DFP-EvoCap were bioequivalent.
- 6.5 The PBAC noted that the new DFP-EvoCap would retain the same listing description as Breztri Aerosphere and would therefore be listed under the same PBS item code as an additional brand.
- 6.6 The PBAC recommended the addition of an Administrative Note to the listing to advise prescribers of the differences between the two brands and to encourage them to instruct patients on optimal inhaler technique.
- 6.7 The PBAC advised, under Section 101 (4AACD) of the *National Health Act*, that DFP-EvoCap and Breztri Aerosphere should be considered equivalent for the purposes of substitution (i.e. a-flagged in the Schedule).
- 6.8 The PBAC noted the intention of the sponsor to replace the existing Breztri Aerosphere inhaler with the DFP-EvoCap and considered that a formal request to delist the existing Breztri Aerosphere inhaler would be required.
- 6.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Amend existing/recommended listing as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
budesonide + glycopyrronium + formoterol (formoterol)					Breztri Aerosphere®
budesonide 160 microgram/actuation + glycopyrronium 7.2 microgram/actuation + formoterol (eformoterol) fumarate dihydrate 5 microgram/actuation inhalation, 120 actuations	12672Y	1	1	5	Breztri Aerosphere® DFP-EvoCap

	Administrative Advice: Breztri Aerosphere® DFP-EvoCap includes a desiccated flow path, whereas Breztri Aerosphere® does not. Ensure the patient is provided instruction on optimal inhaler technique for both inhalers.
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8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.

Addendum to the November 2022 PBAC Public Summary Document

10 Purpose

- 10.1 The Category 4 submission requested that PBAC reconsider its November 2022 recommendation regarding the pricing basis of Breztri Aerosphere® DFP-EvoCap.

11 Background

- 11.1 At its November 2022 meeting, the PBAC considered a Category 4 submission to list budesonide with glycopyrronium and formoterol pressurised metered dose inhaler (Breztri Aerosphere® DFP-EvoCap) which was intended to replace the existing listing (Breztri Aerosphere®).
- 11.2 The PBAC recommended the listing of DFP-EvoCap and advised that DFP-EvoCap should be cost-minimised to the lowest cost alternative agent, including any combination of LAMA, LABA and corticosteroid used for the treatment of COPD, whether in fixed dose combinations or open combination (i.e. individual products).
- 11.3 At its November 2022 meeting, the PBAC also noted that the new DFP-EvoCap was proposed to be listed as an additional brand under the same PBS item code as Breztri Aerosphere.
- 11.4 The sponsor, AstraZeneca, made a subsequent Category 4 submission to the PBAC which contested the November 2022 recommendation with regards to pricing comparator.
- 11.5 The resubmission noted that supply of Breztri Aerosphere would be exhausted soon and requested listing of Breztri with the DFP-EvoCap inhaler device by 1 August 2023 to ensure continued supply to Australian patients.
- 11.6 The resubmission reiterated its November 2022 submission request that DFP-EvoCap be listed at the same AEMP as the current listing for budesonide with glycopyrronium and formoterol. Additionally, the resubmission proposed that DFP-EvoCap could be supplied under the existing Breztri Aerosphere brand name.

12 PBAC Outcome

- 12.1 The PBAC recalled its November 2022 recommendation that DFP-EvoCap should be cost-minimised to the lowest cost alternative agent, including any combination of LAMA, LABA and corticosteroid used for the treatment of COPD, whether in fixed dose combinations or open combination (i.e. individual products).
- 12.2 The PBAC recalled that, at its November 2022 meeting, it had noted that Breztri Aerosphere DFP-EvoCap would be listed as a new brand under the same PBS item code as Breztri Aerosphere.

- 12.3 The PBAC noted the proposal in the resubmission that the new inhaler could be supplied under the existing listing for Breztri Aerosphere. The PBAC considered that only certain components of the inhaler device were being changed, and that Breztri Aerosphere DFP-EvoCap and Breztri Aerosphere were not sufficiently different as to require them to have separate listing descriptions on the PBS.
- 12.4 Therefore, the PBAC held no objections to the replacement of Breztri Aerosphere with an updated inhaler device, noting that the Department would take into consideration Australian Medicines Terminology, pharmaceutical item descriptions appearing in the legislative instruments and software vendor requirements before finalising the details of any new listings on the PBS.
- 12.5 The PBAC noted that should Breztri Aerosphere with the DFP-EvoCap inhaler device be supplied under the currently listed brand and pharmaceutical item, it was appropriate for the price to remain unchanged, consistent with previous PBAC consideration of items where a change to an existing delivery device does not require amendments to the legal instruments enacting the current PBS listing.

Outcome:

Advice Provided

13 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

14 Sponsor's Comment

The sponsor had no comment.