

5.21 BUDESONIDE WITH EFORMOTEROL,

Powder for oral inhalation in breath actuated device containing budesonide 200 micrograms with eformoterol fumarate dihydrate 6 micrograms per dose, 120 doses;

Powder for oral inhalation in breath actuated device containing budesonide 400 micrograms with eformoterol fumarate dihydrate 12 micrograms per dose, 120 doses

DuoResp® Spiromax®, Teva Pharma Australia Pty Limited

1 Purpose of Application

- 1.1 The minor submission requested the listing of a new product containing budesonide with eformoterol with a different delivery device to the currently listed Symbicort® Turbuhaler®.

2 Requested listing

- 2.1 The submission requested the following listings based on the listing for alternative brands of the Symbicort® 200/6 and 400/12 Turbuhaler® with the only change requested in the population criteria for the treatment of asthma, being restricted to patients 18 years and over. The submission did not propose to list an alternative brand to the Symbicort 100/6 Turbuhaler. The Secretariat did not propose any changes to the requested listing.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
BUDESONIDE+ EFORMOTEROL budesonide 200 microgram/actuation + eformoterol fumarate dihydrate 6 microgram/actuation powder for inhalation, 120 actuations	1	5	\$ [REDACTED]*	DuoResp Spiromax	Teva Pharma Australia

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Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Asthma
PBS Indication:	Asthma
Treatment phase:	Initial/Continuing
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	Patient must have previously had frequent episodes of asthma while receiving treatment with oral corticosteroids or optimal doses of inhaled corticosteroids; OR Patient must have experienced frequent asthma symptoms while receiving treatment with oral or inhaled corticosteroids and require single maintenance and reliever therapy; OR Patient must have experienced frequent asthma symptoms while receiving treatment with a combination of an inhaled corticosteroid and long acting beta-2 agonist and require single maintenance and reliever therapy.
Population criteria:	Patient must be aged 18 years or over.

* The DPMQ price was calculated using the provided AEMP with appropriate mark-ups added.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
BUDESONIDE+ EFORMOTEROL budesonide 400 microgram/actuation + eformoterol fumarate dihydrate 12 microgram/actuation powder for inhalation, 120 actuations	1	5	\$ [REDACTED]*	DuoResp Spiromax	Teva Pharma Australia

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Asthma
PBS Indication:	Asthma
Treatment phase:	Initial/Continuing

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Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	Patient must have previously had frequent episodes of asthma while receiving treatment with oral corticosteroids or optimal doses of inhaled corticosteroids.
Population criteria:	Patient must be aged 18 years or over.
Administrative Advice:	DuoResp Spiromax 400/12 is not recommended nor PBS-subsidised for use as 'maintenance and reliever' therapy.

* The DPMQ price was calculated using the provided AEMP with appropriate mark-ups added.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
BUDESONIDE+ EFORMOTEROL budesonide 400 microgram/actuation + eformoterol fumarate dihydrate 12 microgram/actuation powder for inhalation, 120 actuations	1	5	\$ [REDACTED]*	DuoResp Spiromax	Teva Pharma Australia

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Chronic obstructive pulmonary disease (COPD)
PBS Indication:	Chronic obstructive pulmonary disease (COPD)
Treatment phase:	Initial/Continuing
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	Patient must have a forced expiratory volume in 1 second (FEV1) less than 50% of predicted normal prior to therapy, AND Patient must have a history of repeated exacerbations with significant symptoms despite regular beta-2 agonist bronchodilator therapy, AND The treatment must be for symptomatic treatment.
Administrative Advice:	Patient must not be on a concomitant single agent long-acting beta-2 agonist. This product is not indicated for the initiation of bronchodilator therapy in COPD.

* The DPMQ price was calculated using the provided AEMP with appropriate mark-ups added.

3 Background

- 3.1 DuoResp® Spiromax® containing budesonide with eformoterol fumarate dihydrate was TGA registered for asthma and chronic obstructive pulmonary disease (COPD) on the ARTG on 19 December 2016. In pharmacokinetic studies with and without a charcoal blockage, DuoResp Spiromax was evaluated by comparing it against the innovator fixed-dose combination inhalation product containing the same active substances. Budesonide and eformoterol have been shown to be equivalent in both pulmonary and systemic deposition of the 200/6 and 400/12 doses. (TGA approved PI).
- 3.2 DuoResp® Spiromax® has not been considered by the PBAC previously.
- 3.3 The PBAC has recently considered a submission at the November 2016 meeting where a sponsor sought a listing of a new brand of an existing combination product with a single high strength inhaler for the treatment of asthma and COPD (fluticasone with salmeterol). The comparator/original product was available in multiple lower dose strengths allowing for back titration of patients with a similar delivery device. The PBAC did not recommend the listing of the new brand based on the inability to easily back titrate the dose using a similar device which limited the ability of prescribers to avoid possible adverse events, and may mean that some patients would remain on a clinically inappropriate high dose (fluticasone with salmeterol PSD, November 2016).

4 Comparator

- 4.1 The minor submission nominated Symbicort® Turbuhaler® as the comparator.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from organisations (2) via the Consumer Comments facility on the PBS website. The comments described a range of issues in regards to the treatment of asthma and COPD with budesonide with eformoterol including the ability to back titrate dosages and the need to correctly educate

patients on the correct use of new inhaler devices, with particular emphasis on the need to restrict pharmacy level substitution (“a” flagging) for new delivery devices of existing medications.

Clinical trials

- 5.3 As a minor submission, no clinical trials were presented in the submission. The clinical trials used to support TGA registration were summarised in the TGA approved Product Information which were the same clinical trials as in the Symbicort® Turbuhaler® TGA Product Information.

Economic analysis

- 5.4 The submission requested a cost minimisation to the currently listed Symbicort® Turbuhaler® formulations. The PBAC noted that while not a matter for PBAC consideration, the listing of DuoResp® Spiromax® would result in a 16% statutory price reduction under section 99ACD of the *National Health Act 1953* (the Act), as this product would be considered bioequivalent to the equivalent strength presentations of Symbicort Turbuhaler for the purposes of the Act.
- 5.5 The minor submission estimated there to be no financial implications to the PBS beyond those resulting from the above noted statutory price reduction.

6 PBAC Outcome

- 6.1 The PBAC decided not to recommend a Restricted Benefit listing of a new brand of budesonide with eformoterol, DuoResp Spiromax®, for the treatment of asthma and COPD due to the inability to back titrate the dose with a similar device.
- 6.2 The PBAC considered that the inability to easily back titrate the dose using a similar device limited the ability of prescribers to avoid possible adverse events, and may mean that some patients would remain on a clinically inappropriate high dose of budesonide with eformoterol.
- 6.3 The PBAC considered that Symbicort® Turbuhaler® was the appropriate comparator for DuoResp Spiromax®.
- 6.4 The PBAC also noted that the delivery device for DuoResp Spiromax® was different to the delivery device for Symbicort® Turbuhaler® which would require additional patient training in its use which may be confusing to the consumer and may result in lack of compliance.

- 6.5 The PBAC noted from the pre-PBAC response that the sponsor has a 100/6 microgram budesonide with eformoterol fumarate dehydrate formulation under development, but that it was not TGA registered at the time of the submission. Consequently the sponsor requested the restriction to patients 18 years and over. The PBAC considered that this additional restriction would increase the possibility for confusion for prescribers and patients between the two different delivery devices.
- 6.6 The PBAC concluded that there was no clinical need for listing this new brand of an existing drug, especially as not all dose combinations were available in the DuoResp Spiromax® format in comparison to the comparator brand.
- 6.7 The PBAC noted that this submission was not eligible for an Independent Review as it was for a new brand of existing drugs.

Outcome:

Rejected

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

The sponsor will work with the department to address the identified concerns.