

**7.10 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 resubmission requested the listing of a new product containing budesonide with eformoterol with a different delivery device to the currently listed Symbicort[®] Turbuhaler[®]. The first submission was considered in July 2017.

2 Requested listing

- 2.1 The resubmission 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. This is unchanged from the July 2017 submission.
- 2.2 The resubmission requests that the PBAC review the proposed indications for asthma and chronic obstructive pulmonary disorder (COPD) individually. The resubmission does not propose to list an alternative brand to the Symbicort[®] 100/6 Turbuhaler[®].
- 2.3 In the pre-PBAC response (p1) the sponsor acknowledged that the restriction had been updated to reflect the PBAC recommendations from the August 2017 Special Meeting to increase the PBS restriction level to Authority Required (STREAMLINED) for ICS/LABA inhalers that have dual listings on the PBS for the treatment of asthma and COPD.

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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 + 1 eformoterol fumarate dihydrate 6 microgram/actuation powder for inhalation, 120 actuations		5	\$ [REDACTED]*	DuoResp Spiromax	Teva Pharma Australia

* The DPMQ price was calculated using the provided AEMP of the submission with appropriate mark-ups added. It has not been adjusted for the revised pricing proposal.

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 type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required <input checked="" 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.

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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 + 1 eformoterol fumarate dihydrate 12 microgram/actuation powder for inhalation, 120 actuations		5	\$ [REDACTED]*	DuoResp Spiromax	Teva Pharma Australia

* The DPMQ price was calculated using the provided AEMP of the submission with appropriate mark-ups added. It has not been adjusted for the revised pricing proposal.

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 type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required <input checked="" 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.
Administrative Advice:	DuoResp Spiromax 400/12 is not recommended nor PBS-subsidised for use as 'maintenance and reliever' therapy.

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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 + 1 eformoterol fumarate dihydrate 6 microgram/actuation powder for inhalation, 120 actuations		5	\$ [REDACTED]*	DuoResp Spiromax	Teva Pharma Australia

* The DPMQ price was calculated using the provided AEMP of the submission with appropriate mark-ups added. It has not been adjusted for the revised pricing proposal.

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 type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required <input checked="" 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.
Population criteria:	Patient must be aged 18 years or over.
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.

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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

* The DPMQ price was calculated using the provided AEMP of the submission with appropriate mark-ups added. It has not been adjusted for the revised pricing proposal.

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 type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required <input checked="" 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.
Population criteria:	Patient must be aged 18 years or over.
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.

3 Background

- 3.1 DuoResp® Spiromax® containing budesonide with eformoterol fumarate dihydrate was TGA registered for asthma and COPD on the ARTG on 19 December 2016. The 400/12 and 200/6 microgram budesonide/eformoterol fumarate dihydrate (DuoResp® Spiromax®) and the 400/12 and 200/6 microgram budesonide/eformoterol fumarate dihydrate (Symbicort® Turbuhaler®) were considered to be bioequivalent by the TGA (DuoResp® Spiromax® TGA approved PI).
- 3.2 DuoResp® Spiromax® was considered by the PBAC at the July 2017 meeting.

4 Comparator

- 4.1 The previous minor submission considered by the PBAC in the July 2017 meeting nominated Symbicort® Turbuhaler® as the comparator. This was unchanged.
- 4.2 The PBAC previously noted 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. In response, the resubmission has again claimed that DuoResp® Spiromax® is easier to use and its delivery of medication does not rely on acquiring a particular technique, and has been proven to improve adherence/compliance. In the pre-PBAC response (p2) the sponsor confirmed that training materials (including placebos) are available to allow education of health care professionals and relevant peak bodies.

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 that no consumer comments were received for this resubmission.

Clinical trials

- 5.3 As a minor resubmission, 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.
- 5.4 The resubmission requests that the PBAC reconsider the listing as the sponsor considers the available strengths of DuoResp® 200/6 and 400/12 Spiromax® meet the criteria for asthma and COPD in adults, the same population as set out in the restriction. The resubmission claims that the two available strengths are sufficient to back titrate with the asthma schedule for adults, and note that international guidelines for back titration set the minimum dosing strength to be 200/6 for adults. The resubmission claims this is in line with the Australian Asthma Handbook. The resubmission also notes that the lowest strength of Symbicort® Turbuhaler® 100/6 accounts for only 3% of overall usage.
- 5.5 The July 2017 submission indicated that the sponsor had a 100/6 formulation under development, which was not TGA registered at the time of the submission. Consequently the sponsor requested the restriction to patients 18 years and over in line with the TGA approval. The PBAC previously considered that this additional restriction would increase the possibility for confusion for prescribers and patients

between the two different delivery devices. In the pre-PBAC response (p2) the sponsor indicated that a DuoResp® 100/6 Spiromax® formulation that meets the necessary criteria to claim bioequivalence for the purposes of a regulatory submission had not yet been developed.

Economic analysis

- 5.6 The resubmission requested a cost minimisation to the currently listed Symbicort® Turbuhaler® formulations. The Secretariat notes that, while not a matter for the PBAC, a recommendation to list DuoResp® Spiromax® would result in a 16% statutory price reduction under section 99ACC of the *National Health Act 1953*.
- 5.7 Following the pre-PBAC response, the sponsor submitted a revised pricing proposal to deliver a ■■■% reduction on the current ex-manufacturer price for DuoResp® Spiromax®.
- 5.8 The minor resubmission estimated there to be no financial implications to the PBS beyond those resulting from the above noted statutory price reduction. The PBAC noted that the revised price offer would result in a saving over and above that normally achieved on the listing of the first generic brand of a medicine.

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of a new brand of budesonide with eformoterol fumarate dehydrate, DuoResp® 200/6 and 400/12 Spiromax® as an alternative brand to the currently listed Symbicort brand.
- 6.2 The PBAC noted that the DuoResp® Spiromax® is available in two strengths (200/6 and 400/12), whereas Symbicort® Turbuhaler® is available and PBS listed in 100/6, 200/6 and 400/12 strengths. The PBAC noted that a DuoResp® 100/6 Spiromax® formulation meeting bioequivalence criteria for the purposes of a regulatory submission had not yet been developed.
- 6.3 The PBAC recalled previous concerns that for patients with asthma the DuoResp® Spiromax® does not cover all dose levels of the comparator for maintenance therapy due to the non-availability of the 100/6 strength. The PBAC noted that the restriction was limited to patients aged 18 years and over. The PBAC recalled that at its November 2016 meeting it had not recommended the listing of 500/50 microgram fluticasone/salmeterol (AirFluSal® Forspiro®) due to the inability to back titrate the dose with a similar device.
- 6.4 The PBAC noted the data provided in the resubmission indicating that Symbicort® 100/6 Turbuhaler® accounts for only 3% of use. In addition, the PBAC noted the evidence provided in the resubmission regarding the ease of use of the Spiromax® device and the potential for improved adherence. The PBAC considered that, as only a very small proportion of the market would potentially be affected by the omission of the DuoResp® 100/6 Spiromax® strength, the claimed ease of use and potential

for improved adherence most likely outweighed previous concerns.

- 6.5 The PBAC noted that Symbicort® 200/6 Turbuhaler® is not listed for COPD. The PBAC considered that the listing of DuoResp® Spiromax® for COPD should be consistent and recommended the listing of the DuoResp® 400/12 Spiromax® only for this condition.
- 6.6 The PBAC noted that listing would be associated with net overall savings to the PBS/RPBS based on the impact of the offered price reduction.
- 6.7 The PBAC noted that the delivery device for DuoResp® Spiromax® was different to the delivery device for Symbicort® Turbuhaler® and would require training for the patient in its use.
- 6.8 The PBAC noted that in the pre-PBAC response (p2) the sponsor indicated it would provide training for pharmacists (in addition to prescribers and practice nurses) if the Committee considered an 'a' flag was appropriate.
- 6.9 The PBAC considered that any differences in the devices could be managed in the course of the regular patient education and counselling on the use of the devices that is provided to patients by prescribers and pharmacists, and that these differences were not sufficient to preclude marking the two brands as equivalent.
- 6.10 The PBAC recommended that the DuoResp® 200/6 and 400/12 Spiromax® and the Symbicort® 200/6 and 400/12 Turbuhaler® could be marked as equivalent in the Schedule of Pharmaceutical Benefits for the purposes of substitution by the pharmacist at the point of dispensing.
- 6.11 The PBAC advised that budesonide with eformoterol fumarate dehydrate is suitable for prescribing by nurse practitioners, as is the case for currently listed products.
- 6.12 The PBAC recommended that the Safety Net 20 Day Rule should not apply, as is the case for currently listed products.

Outcome:

Recommended

7 Recommended listing

- 7.1 Add new item:

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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 type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required <input checked="" 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.

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Administrative Advice:	DuoResp Spiromax 400/12 is not recommended nor PBS-subsidised for use as 'maintenance and reliever' therapy.

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BUDESONIDE+ EFOMOTEROL budesonide 400 microgram/actuation + 1 efomoterol fumarate dihydrate 12 microgram/actuation powder for inhalation, 120 actuations	1	5	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 type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required <input checked="" 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.
Population criteria:	Patient must be aged 18 years or over.
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.

8 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.

9 Sponsor's Comment

The sponsor had no comment.