6.15 TIOTROPIUM BROMIDE WITH OLODATEROL HYDROCHLORIDE
solution for oral inhalation containing tiotropium 2.5 micrograms (as bromide monohydrate) with olodaterol 2.5 micrograms (as hydrochloride) per dose, 60 doses
Spiolto® Respimat®, Boehringer Ingelheim Pty Ltd.

1 Purpose of Application

1.1 The minor submission requested a change to the current Authority Required (STREAMLINED) listing for tiotropium with olodaterol fixed dose combination (FDC) to allow patients who have symptoms that persist despite regular bronchodilator treatment with either a long acting muscarinic antagonist (LAMA) or long acting beta-2 agonist (LABA) to move straight to the FDC, in addition to those stabilised on a combination of a LAMA and LABA treatment.

2 Requested listing

2.1 The submission requested the following wordings in place of the current listing:

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
TIOTROPIUM WITH OLODATEROL solution for oral inhalation containing tiotropium 2.5 µg (as bromide monohydrate) with olodaterol 2.5 µg (as hydrochloride) per dose, 60	1	5	$89.48	Spiolto® Respimat®	Boehringer Ingelheim Pty Limited

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☒ Nurse practitioners ☐ Optometrists ☐ Midwives
Restriction Level / Method:	☒ Streamlined
Clinical criteria:	Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting muscarinic antagonist (LAMA) OR Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting beta 2 agonist (LABA) OR Patient must have been stabilised on a combination of a LAMA and a LABA.
Administrative Advice	This product is not PBS-subsidised for the treatment of asthma. This product is not indicated for the initiation of bronchodilator therapy in COPD. The treatment must not be used in combination with an ICS/LABA, or LAMA or LABA monotherapy. A LAMA includes tiotropium, glycopyrronium, aclidinium or umeclidinium. A LABA includes indacaterol, salmeterol or eformoterol.

2.2 The submission requested amendments to the restriction to include patients who have persistent chronic obstructive pulmonary disease (COPD) symptoms despite regular monotherapy with a LAMA or LABA.

For more detail on PBAC's view, see section 7 "PBAC outcome"

3 Background

3.1 At the July 2015 meeting, the PBAC recommended the listing of tiotropium with olodaterol FDC on a cost-minimisation basis to the existing LAMA/LABA FDCs as a once-daily maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD already stabilised on concomitant LAMA and LABA therapy. All LAMA/LABA FDCs were listed with the current restriction, which requires patients to be stabilised on separate LABA and LAMA inhalers before moving to an FDC.

3.2 Tiotropium monotherapy is PBS listed for patients with COPD. Olodaterol monotherapy is not available on the PBS.

3.3 There are three other LAMA/LABA FDCs that are currently listed on the PBS: umeclidinium with vilanterol, aclidinium with eformoterol, and indacaterol with glycopyrronium. The restrictions for these LAMA/LABA FDCs are the same as the current restriction for tiotropium with olodaterol.

3.4 Umeclidinium with vilanterol and indacaterol with glycopyrronium were recommended by the PBAC at the July 2014 PBAC meeting as Authority required (STREAMLINED) benefits for the treatment of COPD for patients already stabilised on concomitant LAMA and LABA therapy. The PBAC accepted that the LAMA/LABA FDCs have a place in therapy for patients already stabilised on individual LAMA and LABA in separate devices. However, the PBAC also noted the DUSC's concern that patients could be initiated on the combination earlier than clinically appropriate without the adequate titration of individual components (July 2014 PBAC Public Summary Document). Aclidinium with eformoterol was recommended at the July 2015 PBAC meeting as an Authority required (STREAMLINED) benefit for the treatment of COPD for patients already stabilised on concomitant LAMA and LABA therapy.

3.5 In August 2015, the PBAC recommended a Post-market Review of COPD Medicines to review the utilisation, safety, efficacy and cost-effectiveness of the PBS listed COPD medicines, and to address quality use of medicines concerns associated with the apparent use of multiple products. The Review was approved by the Minister for Health on 28 September 2015 and is currently underway. One of the aims of this review is to compare the PBS restrictions to current clinical guidelines. Another aim is to conduction an evaluation of whether the current utilisation of multiple therapies and the latest evidence relating to safety and efficacy justifies a review of cost-effectiveness for some or all medicines indicated for COPD. Whilst tiotropium with olodaterol was listed after the Post-market Review was announced, the outcomes will be relevant to this medicine, as well as the other LAMA/LABA FDCs.

For more detail on PBAC's view, see section 7 "PBAC outcome"

4 Clinical place for the proposed therapy

4.1 The submission argued that the current PBS criteria are likely to delay access for patients who are uncontrolled on a single long acting bronchodilator and would benefit from a LAMA/LABA FDC.

4.2 The Sponsor claimed that proposed change to the prescribing restriction is to make this consistent with the treatment algorithm in the COPD-X Plan, which is jointly developed and updated by the Thoracic Society of Australia and New Zealand (TSANZ) and Lung Foundation Australia (LFA). The guidelines (GOLD COPD-X 2016) state that for patients with COPD:

1. The first step is treatment with a short acting bronchodilator [short acting muscarinic antagonist (SAMA) or short acting β2 agonist (SABA)].
2. For patients receiving short-acting bronchodilators who have persistent troublesome dyspnoea, a long acting bronchodilator [a LAMA or a LABA] should be initiated.
3. LAMA/LABA FDCs in a single inhaler are available for patients who remain symptomatic despite monotherapy with either alone.
4. For patients with forced expiratory volume in 1 second (FEV1) <50% predicted and ⩾2 exacerbations in 12 months, the COPD-X Plan recommends initiation of an inhaled corticosteroid (ICS)/LABA FDC and discontinue LABA monotherapy.

4.3 The PBAC noted that the clinical treatment guidelines do not require patients to be stabilised on separate inhalers prior to commencing treatment with a LAMA/LABA FDC, whilst the current PBS restriction does. However, the PBAC also noted that this potential issue had already been recognised and as a result the concordance of PBS restrictions with clinical guidelines was one of the focus areas of the Post-market Review of COPD medicines currently underway.

4.4 The PBAC also noted that PBS restrictions do not always align with clinical treatment guidelines, primarily because the latter do not explicitly consider cost-effectiveness.

For more detail on PBAC's view, see section 7 "PBAC outcome"

5 Consideration of 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 health care professionals (3) and organisations (2) via the Consumer Comments facility on the PBS website. The comments described the potential benefits from a convenience and quality use of medicines perspective of allowing treatment with tiotropium with olodaterol FDC if stabilisation is not achieved with LAMA or LABA monotherapy.

5.3 The PBAC noted the advice received from the Lung Foundation Australia and the Royal Australian College of General Practitioners (RACGP). Both organisations were of the view that it is clinically appropriate to allow patients who have symptoms that persist despite regular bronchodilator treatment with either a LAMA or LABA to move straight to a LAMA/LABA FDC. The PBAC also noted the advice that the current

process of trialling patients on two separate devices was cumbersome and, as monotherapy for olodaterol is not available on the PBS, patients need to be trialled on another LABA before being switched to combination therapy or trialled on tiotropium plus an ICS/LABA combination which also poses potential quality use of medicines issues.

Estimated PBS usage & financial implications

5.4 The minor submission updated the estimates provided with their July 2015 major submission to account for the higher uptake of the FDC without prior use of each individual LABA and LAMA. This change resulted in a net save of less than $10 million per year in year 5 of listing, with a total net save of less than $10 million to the PBS over the first 5 years of listing. This is summarised in the table below:

Table 1: Estimated financial implications

Description	Year 1	Year 2	Year 3	Year 4	Year 5
Total cost to (R)PBS current PBS listing	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Total cost to (R)PBS proposed PBS listing	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to PBS/RPBS	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]

Source: Page ix of the minor submission

For more detail on PBAC's view, see section 7 "PBAC outcome"

6 PBAC Outcome

6.1 The PBAC decided to defer the requested change to the Authority Required (STREAMLINED) listing for tiotropium with olodaterol FDC to allow patients taking either a LAMA or LABA to move straight to the FDC until after the PBAC has considered the Post-market Review of COPD Medicines.

6.2 The PBAC acknowledged the consumer comments received from health care professionals and organisations that indicated support for the proposed change to the restriction. The PBAC noted that the proposed changes would align the restrictions with the treatment algorithm in the COPD-X Plan.

6.3 The PBAC noted that, if recommended, either the listing for tiotropium with olodaterol would be inconsistent with the other LAMA/LABA FDCs or there would need to be flow-on restriction changes for the three other LAMA and LABA FDCs listed on the PBS (umeclidinium with vilanterol, aclidinium with eformoterol, and indacaterol with glycopyrronium). The PBAC also noted that the consistency of PBS restrictions with recommended clinical guidelines; and an evaluation of whether the current utilisation of multiple therapies and the latest evidence relating to safety and efficacy justifies a review of cost-effectiveness for some or all medicines indicated for COPD, are key components of the Post-market Review of COPD medicines, the outcome of which will be relevant to such a decision. Therefore, the PBAC considered that it would be more appropriate to wait for the outcome of the Review before recommending any changes to the listings.

Outcome:
Deferred

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 had no comment.

November 2017 addendum to the November 2016 PBAC Minutes:

4.05 TIOTROPIUM BROMIDE WITH OLODATEROL HYDROCHLORIDE
solution for oral inhalation containing tiotropium 2.5 micrograms (as bromide monohydrate) with olodaterol 2.5 micrograms (as hydrochloride) per dose, 60 doses
Spiolto® Respimat®,
Boehringer Ingelheim Pty Ltd

9 Background

At the November 2016, the PBAC deferred the requested change to the Authority Required (STREAMLINED) listing for tiotropium bromide with olodaterol FDC to allow patients taking either a LAMA or LABA to move straight to the FDC until after PBAC has considered the Post-market Review (PMR) of Chronic Obstructive Pulmonary Disease (COPD) Medicines.

The PBAC noted that the consistency of PBS restrictions with recommended clinical guidelines. Further the PBAC noted an evaluation of whether the current utilisation of multiple therapies and the latest evidence relating to safety and efficacy justifies a review of cost-effectiveness for some or all medicines indicated for COPD, are key components of the PMR of COPD medicines, the outcome of which will be relevant to such a decision. Therefore, the PBAC considered that it would be more appropriate to wait for the outcome of the Review before recommending any changes to the listings.

With the outcome of the PMR of COPD medicines now finalised, the sponsor requests that

the PBAC reconsider the submission to change the Authority Required (STREAMLINED) listing for tiotropium bromide with olodaterol FDC.

10 PBAC Outcome

The PBAC recommended the requested change to the Authority Required (STREAMLINED) listing for tiotropium bromide with olodaterol FDC to allow patients who have persistent COPD symptoms despite regular monotherapy with a LAMA or LABA to be eligible for PBS subsidised FDC.

The PBAC noted that the outcome of the PMR of COPD medicines supported the removal of 'the requirement to stabilise patients on a LAMA and LABA separately, prior to initiation of a LAMA/LABA FDC'. The PBAC therefore considered it would be appropriate to recommend the requested change to the PBS listing consistent with the outcome of PMR.

The PBAC also noted that there are three other LAMA/LABA FDC currently listed on the PBS (aclidinium with eformoterol, indacaterol with glycopyrronium and umeclidinium with vilanterol), where the individual components are not available separately on the PBS. The PBAC considered that the change of existing listing of tiotropium with olodaterol should also apply to these LAMA/LABA FDCs.

Outcome:
Recommended

11 Recommended listing

Amend existing listing as follows (changes to the existing listing are shown in italics and strikethrough):

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
TIOTROPIUM WITH OLODATEROL solution for oral inhalation containing tiotropium 2.5 µg (as bromide monohydrate) with olodaterol 2.5 µg (as hydrochloride) per dose, 60	1	5	Spiolto® Respimat® Boehringer Ingelheim Pty Limited

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☒ Nurse practitioners ☐ Optometrists ☐ Midwives
Restriction Level / Method:	☒ Streamlined
PBS indication	Chronic obstructive pulmonary disease (COPD)
Clinical criteria:	*Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting muscarinic antagonist (LAMA)* *OR* *Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting beta 2 agonist (LABA)* *OR* Patient must have been stabilised on a combination of a LAMA and a LABA.
Administrative Advice	This product is not PBS-subsidised for the treatment of asthma. This product is not indicated for the initiation of bronchodilator therapy in COPD. The treatment must not be used in combination with an ICS/LABA, or LAMA or LABA monotherapy. A LAMA includes tiotropium, glycopyrronium, aclidinium or umeclidinium. A LABA includes indacaterol, salmeterol or eformoterol.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
ACLIDINIUM WITH EFORMOTEROL powder for oral inhalation in breath actuated device containing aclidinium 340 micrograms (as bromide) with eformoterol fumarate dehydrate 12 micrograms per dose, 60	1	5	Brimica Genuair A. Menarini Australia Pty Limited

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☒ Nurse practitioners ☐ Optometrists ☐ Midwives
Restriction Level / Method:	☒ Streamlined
PBS indication	Chronic obstructive pulmonary disease (COPD)
Clinical criteria:	*Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting muscarinic antagonist (LAMA)* *OR* *Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting beta 2 agonist (LABA)* *OR* Patient must have been stabilised on a combination of a LAMA and a LABA.
Administrative Advice	This product is not PBS-subsidised for the treatment of asthma. This product is not indicated for the initiation of bronchodilator therapy in COPD. The treatment must not be used in combination with an ICS/LABA, or LAMA or LABA monotherapy. A LAMA includes tiotropium, glycopyrronium, aclidinium or umeclidinium. A LABA includes indacaterol, salmeterol or eformoterol.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
INDACATEROL WITH GLYCOPYRRONIUM				
Capsule containing powder for oral inhalation indacaterol 110 micrograms (as maleate) with glycopyrronium 50 micrograms (as bromide) (for use in Breezhaler)	30	5	Ultibro breezhaler 110/50	Novartis Pharmaceuticals Australia Pty Limited

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☒ Nurse practitioners ☐ Optometrists ☐ Midwives
Restriction Level / Method:	☒ Streamlined
PBS indication	Chronic obstructive pulmonary disease (COPD)
Clinical criteria:	*Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting muscarinic antagonist (LAMA)* *OR* *Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting beta 2 agonist (LABA)* *OR* Patient must have been stabilised on a combination of a LAMA and a LABA.
Administrative Advice	This product is not PBS-subsidised for the treatment of asthma. This product is not indicated for the initiation of bronchodilator therapy in COPD. The treatment must not be used in combination with an ICS/LABA, or LAMA or LABA monotherapy. A LAMA includes tiotropium, glycopyrronium, aclidinium or umeclidinium. A LABA includes indacaterol, salmeterol or eformoterol.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
UMECLIDINIUM WITH VILANTEROL				
powder for oral inhalation in breath actuated device containing umeclidinium 62.5 micrograms (as bromide) with vilanterol 25 micrograms (as trifenatate) per dose, 30	1	5	Anoro Ellipta 62.5/25	GlaxoSmithKline Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☒Nurse practitioners ☐Optometrists ☐Midwives
Restriction Level / Method:	☒Streamlined
PBS indication	Chronic obstructive pulmonary disease (COPD)
Clinical criteria:	*Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting muscarinic antagonist (LAMA)* *OR* *Patient must have COPD symptoms that persist despite regular bronchodilator treatment with a long acting beta 2 agonist (LABA)* *OR* Patient must have been stabilised on a combination of a LAMA and a LABA.
Administrative Advice	This product is not PBS-subsidised for the treatment of asthma. This product is not indicated for the initiation of bronchodilator therapy in COPD. The treatment must not be used in combination with an ICS/LABA, or LAMA or LABA monotherapy. A LAMA includes tiotropium, glycopyrronium, aclidinium or umeclidinium. A LABA includes indacaterol, salmeterol or eformoterol.

12 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.

13 Sponsor's Comment

The sponsor had no comment.