

**7.14 UMECLIDINIUM+VILANTEROL, umeclidinium (as bromide) 62.5 microgram/actuation + vilanterol (as trifenate) 25 microgram/actuation inhalation: powder for, 30 actuations, Anoro<sup>®</sup> Ellipta<sup>®</sup>, GlaxoSmithKline Australia Pty Ltd**

**1 Purpose of Application**

1.1 To request a Authority Required (Streamlined) listing for the treatment of adult patients with chronic obstructive pulmonary disease (COPD) where symptoms persist despite regular bronchodilator treatment with a long acting muscarinic antagonist (LAMA) and/or long acting beta<sub>2</sub>-agonist (LABA); or for the treatment of adult patients who have been stabilised on a combination of a LAMA and a LABA in separate devices.

**2 Requested listing**

2.1 The submission requested the following restriction:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
UMECLIDINIUM + VILANTEROL Inhalation: powder for, Umeclidinium (as bromide) 62.5 microgram + vilanterol (as trifenate) 25 microgram, 30	1	5	Anoro <sup>®</sup>	GSK

<p><b><u>Authority required (STREAMLINED)</u></b> Chronic obstructive pulmonary disease</p> <p>Patient must have symptoms that persist despite regular bronchodilator treatment with a long acting muscarinic antagonist and/or long acting beta2 agonist; Or Patients must have been stabilised on a combination of long-acting muscarinic antagonist and long acting beta2 agonist.</p>
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2.2 Listing was sought on a cost-minimisation basis with umeclidinium/vilanterol compared to tiotropium with indacaterol.

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

**3 Background**

3.1 Umeclidinium + vilanterol (UMEC/VI) was TGA registered on 4 July 2014 for long-term once daily maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).

3.2 UMEC/VI was considered by the PBAC in March 2014. The PBAC rejected the submission as the FDC was cost-minimised to the sum of the component products and this was not justified by the evidence presented as the price of the FDC would be approximately twice the cost of monotherapy in the absence of evidence to demonstrate an incremental benefit of this magnitude.

- 3.3 As the incremental gain in FEV<sub>1</sub> of the FDC was not able to be translated into more clinically relevant measures of effect (e.g. frequency of exacerbations, hospitalisations), the PBAC considered it was unable to determine and value the incremental benefit associated with use of the FDC compared with use of components given concurrently. Therefore, the committee was unable to determine an appropriate price for the FDC.
- 3.4 The PBAC also noted that the treatment algorithm for COPD is changing given the potential safety risks associated with inhaled corticosteroid (ICS) use, therefore there is potential for greater switching from ICS/LABA than what was considered in the original submission.

#### **4 Clinical place for the proposed therapy**

- 4.1 The listing of UMEC/VI FDC would provide an alternative in one inhaler for a LABA/LAMA combination, rather than LABA + LAMA in two inhaler devices.

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

#### **5 Comparator**

- 5.1 The initial major submission nominated indacaterol with tiotropium as the main comparator and indacaterol/glycopyrronium FDC as a supportive comparator. This was accepted by the PBAC in March 2014.

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

#### **6 Consideration of the evidence**

##### ***Sponsor hearing***

- 6.1 There was no hearing for this item.

##### ***Consumer comments***

- 6.2 The PBAC noted that no consumer comments were received for this item.

##### ***Clinical trials***

- 6.3 The submission has presented a new trial which claims an incremental benefit in FEV<sub>1</sub> of 112mL over tiotropium monotherapy. As this is a minor submission, this trial has not been evaluated.

##### ***Clinical claim***

- 6.4 As in March 2014, the submission claimed the UMEC/VI combination therapy has comparable effectiveness to indacaterol 150 microgram plus tiotropium 18 microgram at 12 weeks. The submission claimed that UMEC/VI combination therapy has a mostly benign and similar safety profile to indacaterol plus tiotropium.

- 6.5 The PBAC considered that the claim of non-inferior comparative effectiveness to indacaterol plus tiotropium was reasonable.
- 6.6 The PBAC considered that the claim of non-inferior comparative safety was reasonable.
- 6.7 The PBAC recalled its primary concern in March 2014 that the incremental benefit of the combination product over monotherapy could not be translated into clinically relevant measures of effect and therefore an appropriate price could not be determined.
- 6.8 The submission attempted to address the PBAC concerns by calculating the incremental benefit of the FDC using a price per mL improvement in FEV<sub>1</sub> over monotherapy and then discounting the resulting price to deal with some of the uncertainty in this approach. It was noted that this approach to calculating cost has not previously been considered or accepted by PBAC. This approach assumes that each additional gain in FEV<sub>1</sub> is clinically relevant to the patient. It also assumes that each additional gain in FEV<sub>1</sub> is equivalent. Although the PBAC considered that these assumptions were not appropriately justified, it accepted that under the proposed approach, the listing of the FDC would be associated with both benefits and cost savings for patients who are already using individual LAMA and LABA in separate devices.
- 6.9 The PBAC further noted that while improvement in FEV<sub>1</sub> has previously been accepted as a surrogate outcome in the treatment of COPD, they were concerned that this may not translate into clinically meaningful benefits to the patient. The PBAC noted that reduction in exacerbations and hospitalisations are outcomes that could potentially be used to measure effectiveness of COPD therapies.
- 6.10 The PBAC recalled that in March 2014, aclidinium (a LAMA), was recommended for listing on the PBS at the lower price requested by the sponsor. The PBAC noted that the Department's advice at the meeting that the Minister (through his Delegate) intends to declare aclidinium as a pharmaceutical benefit under section 85(2) of the *National Health Act 1953* and that the PBS listing will proceed with the lower price. As the main comparators in this submission, indacaterol and tiotropium are cost-minimised to aclidinium (the former via tiotropium), the PBAC considered it is appropriate for the new lower aclidinium price to be used in calculating the price for umeclidinium/vilanterol.

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

### **Economic analysis**

- 6.11 The submission did not present a new economic model.

### **Estimated PBS usage & financial implications**

- 6.12 The PBAC noted the DUSC's concern over the likelihood that the introduction of a fixed dose combination (FDC) could grow the overall market and that patients could be initiated on the combination earlier than clinically appropriate without the adequate titration of individual components. DUSC has noted emerging trends with some FDC products, such as a higher proportion of patients commencing de novo and FDCs increasing the market rather than substituting within current markets (DUSC Outcome Statement February 2013).

- 6.13 In March 2014, the PBAC considered that a risk sharing arrangement would be required to manage the risk associated with higher than estimated usage and cost however no details have been proposed by the sponsor.

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

## **7 PBAC Outcome**

- 7.1 The PBAC recommended the listing of UMEC/VI as an Authority required (STREAMLINED) benefit for the treatment of chronic obstructive pulmonary disease for patients already stabilised on concomitant LAMA and LABA therapy.
- 7.2 The PBAC considered, amongst other matters, that the cost-effectiveness of UMEC/VI would be acceptable if it were priced using the methodology proposed by the submission (see Section 6) but with the calculation based on the new lower acclidinium price in place of the current tiotropium price as proposed.
- 7.3 While other treatments for COPD are currently listed as Restricted Benefits, the PBAC considered it would be appropriate for UMEC/VI to be listed as Streamlined Authority as proposed by the sponsor in an attempt to address inappropriate prescribing of the product, particularly in the first-line setting. The PBAC noted that the sponsor had sought the advice of the Thoracic Society of Australia and New Zealand, which confirmed that initial treatment will be as monotherapy and patients are likely to be transitioned to FDC treatment only when clinically necessary.
- 7.4 The PBAC noted that the primary concerns raised in the March 2014 submission were not adequately addressed in the resubmission as the incremental benefit of the combination product could not be translated into clinically relevant measures of effect. However, the Committee accepted that there are both benefits and cost savings for patients who are already using individual LAMA and LABA in separate devices.
- 7.5 The clinically equi-effective doses are umeclidinium/vilanterol 62.5/25 to tiotropium 18 microgram with indacaterol 150 microgram.
- 7.6 The PBAC noted that there is significant confusion among prescribers regarding medicines used in COPD and as such, names of individual LAMAs and LABAs should be noted in the restriction.
- 7.7 The PBAC accepted that umeclidinium/vilanterol has a place in therapy for patients already stabilised on individual LAMA and LABA in separate devices.
- 7.8 Advice to the Minister under Subsection 101 3BA of the *National Health Act*  
In accordance with subsection 101(3BA) of the *National Health Act* 1953, the PBAC advised that it is of the opinion that umeclidinium/vilanterol should be treated as interchangeable on an individual patient basis with indacaterol/glycopyrronium.
- 7.9 The PBAC advised that umeclidinium/vilanterol is suitable for prescribing by nurse practitioners.
- 7.10 The PBAC recommended that the Safety Net 20 Day Rule should apply.

### **Outcome:**

Recommended

**8 Recommended listing**

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
UMECLIDINIUM + VILANTEROL Inhalation: powder for, Umeclidinium (as bromide) 62.5 microgram + vilanterol (as trifenate) 25 microgram	1	5	Anoro <sup>®</sup> GSK

Condition:	Chronic Obstructive Pulmonary Disease
Restriction:	Authority required (STREAMLINED)
Clinical criteria:	Patient must have been stabilised on a combination of a long acting muscarinic antagonist and long acting beta-2 agonist.
Administrative Advice	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. This product is not PBS-subsidised for the treatment of asthma. This product is not indicated for the initiation of bronchodilator therapy in COPD.

**9 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.

**10 Sponsor's Comment**

GlaxoSmithKline welcomes the PBAC's recommendation to list Anoro for the treatment of COPD on the PBS.