

6.14 FLUTICASONE WITH FORMOTEROL

Pressurised inhalation containing fluticasone propionate 250 micrograms with formoterol fumarate dihydrate 10 micrograms per dose, 120 doses;

Pressurised inhalation containing fluticasone propionate 125 micrograms with formoterol fumarate dihydrate 5 micrograms per dose, 120 doses;

Pressurised inhalation containing fluticasone propionate 50 micrograms with formoterol fumarate dihydrate 5 micrograms per dose, 120 doses

Flutiform[®], Mundipharma Pty Limited

Note: The LI and schedule name of eformoterol is currently being updated to formoterol in line with international harmonisation of drug names.

1 Purpose of Application

- 1.1 The minor submission requested the current Authority Required (STREAMLINED) listing of fluticasone propionate with formoterol fumarate dihydrate pressurised inhalation (hereafter referred to as fluticasone/formoterol) be amended to a Restricted Benefit.

2 Requested listing

- 2.1 The minor submission requested a change of restriction level for the existing asthma indication only. No other changes to existing listings were requested.

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Background

- 3.1 Fluticasone/formoterol was TGA registered on 14 June 2013 for the regular maintenance treatment of asthma where the use of a combination product (an inhaled corticosteroid (ICS) and a long-acting β 2-agonist (LABA)) is appropriate. This includes patients not adequately controlled with maintenance ICS and inhaled short-acting β 2-agonist used on an 'as required' basis. Fluticasone/formoterol does not have a TGA approved indication for use in Chronic Obstructive Pulmonary Disease (COPD).
- 3.2 In July 2013, the PBAC recommended the listing of fluticasone/formoterol for maintenance treatment of asthma on a cost-minimisation basis with fluticasone with

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salmeterol pressurised metered dose inhalers (Section 12, fluticasone/formoterol Public Summary document (PSD), July 2013). The PBAC noted that TGA approval for fluticasone/formoterol is restricted to patients aged 12 years and over (Section 7, fluticasone/formoterol PSD, July 2013). Fluticasone/formoterol was listed as a Restricted benefit on the PBS for this indication in December 2013. The population criteria of the PBS restriction states that patients must be aged 12 years or over.

- 3.3 An increase in the restriction level from Restricted Benefit to Authority Required (STREAMLINED) for all ICS/LABA fixed dose combinations (FDC) on the PBS came into effect on 1 August 2018. This change, among others, resulted from two Reviews which were considered by the PBAC:
- *Post-Market Review of PBS Medicines Used to Treat Asthma in Children* (hereafter referred to as the Asthma in Children Review)
 - *Post-Market Review of COPD medicines* (hereafter referred to as the COPD Review).
- 3.4 At its August 2017 meeting, the PBAC noted that the ICS/LABA PBS item codes for COPD have dual indications for asthma. The PBAC also noted that ICS/LABA FDCs were available as Restricted Benefit in COPD despite guideline recommendations that ICS should only be used after LAMA and LABA therapy in COPD and only where there is evidence of repeated exacerbations and where FEV1 is <50% predicted. The PBAC discussed separating the item codes for COPD and asthma and only increasing the restriction level on the COPD item codes. However, the creation of separate PBS listings for COPD with a higher restriction level (STREAMLINED) was considered unlikely to be effective in modifying prescribing habits to use ICS/LABAs to be in line with the guideline recommendations for COPD. The PBAC therefore supported increasing the restriction for high dose ICS/LABA item codes on the PBS that have dual listings for COPD and asthma. The PBAC considered that an Authority Required (STREAMLINED) listing for high dose ICS/LABAs in asthma would not be a burden on prescribers and would act as a reminder that ICS/LABAs should be used second line to other monotherapy preventers in patients initiating asthma treatment. This change was not considered to be a significant burden on prescribers by the Reference Group and the PBAC.
- 3.5 In March 2018, the PBAC came to a similar conclusion regarding the Evaluation Report of the 2014 Asthma in Children Review. The PBAC noted that the percentage of children initiating asthma treatment with an ICS/LABA FDC remained unacceptably high, and that this prescribing and use was not consistent with clinical guidelines. The PBAC recommended the increase in restriction level to Authority Required (STREAMLINED) for all ICS/LABA FDC inhalers to encourage prescribers to consider first line treatment with ICS alone (March 2018 PBAC Outcomes – Other Matters PSD, March 2018).

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

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

Consumer comments

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

Current situation

- 4.3 The minor submission requested that the March 2018 PBAC recommendation to increase the restriction level to Authority Required (STREAMLINED) for all ICS/LABA FDC inhalers be set aside for fluticasone/formoterol and that the Restricted benefit listing be reinstated.
- 4.4 The minor submission stated that ‘the sponsor was not actively involved in the Review process, since fluticasone/formoterol was appropriately excluded from the Terms of Reference’ of the COPD Review and Asthma in Children Review.
- 4.5 The minor submission argued that as fluticasone/formoterol does not have a PBS listing or a TGA indication for use in COPD it could not be included as relevant medicine in the COPD review. The minor submission noted that fluticasone/formoterol was not included in the item codes affected by the PBAC recommendation from the August 2017 meeting to increase the PBS restriction level to Authority Required (STREAMLINED) for ICS/LABAs that have dual listings on the PBS for the treatment of COPD and asthma.
- 4.6 The minor submission argued that fluticasone/formoterol was not included in the Terms of Reference for the Asthma in Children Review, as it is not TGA nor PBS-indicated for use in children below 12 years of age and hence should not be covered by the subsequent DUSC review or PBAC decisions that directly arise from the review.
- 4.7 The minor submission and pre-PBAC response argued the PBS listings should be separated into adult/adolescent (≥ 12 years) and children’s PBS items (4 to 12 years) where necessary and change the restriction level for items that are indicated for use in children only. The PBAC noted that term ‘children’ was used in relation to patients aged 0 to 18 years of age in the Asthma in Children Review.
- 4.8 The minor submission stated that the results of the Evaluation Report of the 2014 Asthma in Children Review indicate fluticasone/formoterol is an infrequently used asthma therapy in children. The minor submission also stated that while the Evaluation Report identified a small amount of prescribing of fluticasone/formoterol in younger children, the bulk of prescribing is appropriate in those 12 years or older, with prescribing of fluticasone/formoterol outside the restriction representing only 2% of all age-inappropriate ICS/LABA prescribing to children. The PBAC noted that in

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2015–2016 1883 children received fluticasone/formoterol and that almost a third (32.9%) of those children were less than 12 years of age (Table 1).

Table 1. Dispensing of FDCs by age and population inconsistent with age recommendations

Medicine	Strength, Number of children in 2015-2016 (N), Number of dispensings in 2015-2016 (D)	Product Information age recommendation
Fluticasone with Salmeterol	50/25mcg; 100/50mcg; N=38309 children; D=66996 dispensings;	Recommended age >=4 years, Outside recommendation: N=2561 (6.7%) D=4122 (6.2%)
Fluticasone with Salmeterol	125/25mcg; 250/50mcg N=44861 children; D=79171 dispensings;	Recommended age >=12 years, Outside recommendation: N=18968 (42.3%) D=33419 (42.2%)
Fluticasone with Salmeterol	250/25mcg; 500/50mcg; N=19289 children; D=33410 dispensings;	Recommended age >=12 years, Outside recommendation: N=2618 (13.6%) D=4556 (13.6%)
Fluticasone with Salmeterol	Distinct children: 79476; Total dispensings: 179577	Outside recommendation: Distinct children: 19967 (25.1%); Total dispensings: 42097 (23.4%)
Budesonide with Formoterol	50/3mcg; 100/3mcg; 100/6mcg; 200/6mcg; N=29707 children; D=44816 dispensings;	Recommended age >=12 years, Outside recommendation: N=6384 (21.5%) D=9209 (20.5%)
Budesonide with Formoterol	400/12mcg N=1674 children; D=2916 dispensings;	Recommended age >=18 years, Outside recommendation: N=1244 (74.3%) D=2150 (73.7%)
Budesonide with Formoterol	Distinct children: 26672; Total dispensings: 47732;	Outside recommendation: Distinct children: 6621 (24.8%); Total dispensings: 11359 (23.8%)
Fluticasone with Formoterol	50/5mcg; 125/5mcg; 250/10mcg; N=2227 children; D=3637 dispensings; Distinct children: 1883;	Recommended age >=12 years Outside recommendation: N=715 (32.1%) D=1157 (31.8%) Distinct children: 620 (32.9%);
Fluticasone with Vilanterol	100/25mcg; 200/25mcg N=2443 children; D=4802 dispensings; Distinct children: 1994;	Recommended age >=12 years, Outside recommendation: N=261 (10.7%); D=456 (9.5%); Distinct children: 232 (11.6%);
ALL FDC products	Distinct children: 107882; Total dispensings: 235748	Outside recommendations: Distinct children: 27123 (25.1%); Total dispensings: 55069 (23.4%)

Source: Table 2, p26-27 Evaluation Report of the 2014 Asthma in Children Review

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC did not recommend amending the current Authority Required (STREAMLINED) listing of fluticasone/formoterol to a Restricted Benefit listing. The PBAC reaffirmed its March 2018 recommendation to increase the restriction level to Authority Required (STREAMLINED) for all ICS/LABA FDC inhalers to encourage prescribers to consider first line treatment with ICS alone in asthma management.
- 5.2 The PBAC recalled that the March 2018 recommendation was made following its consideration of the findings of the Evaluation Report of the 2014 Asthma in Children Review. The PBAC did not accept the minor submissions claim that fluticasone/formoterol should not be covered by PBAC decisions from the Asthma in Children Review as it is not TGA or PBS-indicated for use in children below 12 years of age. The PBAC advised that in both the 2014 Asthma in Children Review report and the subsequent Evaluation Report of the review, the term children was used in relation to patients aged 0 to 18 years of age. The PBAC also noted that the change to an Authority Required (STREAMLINED) listing had been applied to other ICS/LABA FDC products whose use is restricted to those aged 12 years and over.
- 5.3 The PBAC noted that fluticasone/formoterol was included in the Evaluation Report of the 2014 Asthma in Children Review, and that all sponsors, including the sponsor of fluticasone/formoterol, had been informed of and provided an opportunity to respond to the Evaluation Report of the 2014 Asthma in Children Review prior to the implementation of the change to restriction level.
- 5.4 The PBAC considered that concerns regarding high levels of initiation of asthma treatment with an ICS/LABA FDC rather than an ICS alone were relevant to both children and adults with the condition. As such the PBAC reiterated that its recommendation to increase the restriction level to Authority Required (STREAMLINED) remained appropriate for all ICS/LABA FDC inhalers, including fluticasone/formoterol.
- 5.5 The PBAC considered that the increase in restriction level of all ICS/LABA formulations does not limit or delay the appropriate use of ICS/LABA FDCs in the populations which were prescribed these medicines under the previous Restricted Benefit listing. The PBAC noted that the clinical criteria which determines patients' eligibility for PBS subsidy of ICS/LABAs was not changed, despite the restriction level being increased to Authority Required (STREAMLINED).
- 5.6 The PBAC noted that this submission is not eligible for an Independent Review as an Independent Review is not available in response to a request to modify an existing restriction.

Outcome:
Rejected

6 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.

7 Sponsor's Comment

The sponsor had no comment.