

5.16 FLUTICASONE FUROATE

Powder for oral inhalation in a breath activated device, 50 mcg, Arnuity® Ellipta®, GlaxoSmithKline Australia Pty Ltd.

1 Purpose of Application

- 1.1 The minor submission requested the listing of fluticasone furoate (FF) 50 mcg (Arnuity® Ellipta®), in addition to the recommended FF 100 mcg and 200 mcg presentations, on the General Schedule as an unrestricted benefit for the treatment of asthma.
- 1.2 The minor submission stated that the FF 100 mcg and 200 mcg presentations are for patients ≥ 12 years of age. The minor submission requested the listing of the FF 50 mcg presentation for patients aged 5 to 11 years of age.

2 Requested listing

- 2.1 The submission requested the same listing as the recommended listing for the FF 100 mcg and 200 mcg presentations.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
FLUTICASONE FUROATE fluticasone furoate 50 microgram/actuation powder for inhalation, 30 actuations	1	5	██████████	Arnuity® Ellipta® GSK

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
Restriction Level / Method:	Unrestricted

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

3 Background

- 3.1 FF 100 mcg and 200 mcg presentations were TGA registered on 11 September 2015 for the maintenance treatment of asthma for patients aged 12 years and over.
- 3.2 FF 50 mcg was approved by the TGA on 14 March 2019 with the approved indication stated as 'for the maintenance treatment of asthma in patients aged 5 years and over'.

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- 3.3 FF (100 mcg and 200 mcg presentations only) was previously considered for the maintenance treatment of asthma for patients aged 12 years and over by the PBAC at its November 2015 and March 2017 meetings.
- 3.4 In November 2015, the PBAC recommended the listing of fluticasone, in the form FF, as an unrestricted benefit. The PBAC recommended listing on a cost-minimisation basis to existing ICS monotherapy fluticasone, in the form of fluticasone propionate (FP). The equi-effective doses were considered to be FF 100 microgram once daily and FP 250 microgram twice daily, and FF 200 microgram once daily and FP 500 microgram twice daily (paragraph 7.1, FF Public Summary Document (PSD), November 2015). The PBAC considered the claim of non-inferior comparative effectiveness and safety compared with FP was reasonable (paragraph 7.3, FF PSD, November 2015). The TGA indication, clinical evidence and financial estimates for the November 2015 submission related to use of FF in patients aged 12 years of age or older.
- 3.5 The November 2015 submission also requested that the PBS legislative instrument (PB71 of 2012) be amended for all FP and FF containing products to reflect the active molecule (i.e. differentiate between FP and FF) instead of the listed drug being fluticasone only, as the two are structurally distinct drugs with different pharmacological and physicochemical properties (paragraph 6.27, FF PSD, November 2015). The PBAC noted the different pharmacology and physicochemical properties of FP and FF and that these resulted in FP and FF having different doses and dosing regimens in clinical practice. However, the PBAC also noted that the outcomes of treatment with FP and FF are not different and on this basis considered it appropriate for FP and FF to continue to be determined as forms of the drug fluticasone for the purposes of the Act (paragraph 7.4, FF PSD, November 2015).
- 3.6 The March 2017 resubmission requested that:
- FF be declared a 'drug' for the purpose of section 85(2) of the *National Health Act 1953* ('the Act'); and
 - The listing instruments for each of Breo[®] Ellipta[®], Seretide[®] and Flixotide[®] be amended to reflect the name of the active moiety of the respective ICS component of each product, being FF in the case of Breo[®] Ellipta[®] and FP in the case of both Seretide[®] and Flixotide[®] (paragraph 1.1, FF PSD, March 2017).
- 3.7 Studies cited in the resubmission addressed physicochemical characteristics, pharmacodynamic properties and pharmacokinetic properties of FF and FP only (paragraph 6.3, FF PSD, March 2017). At the March 2017 meeting the PBAC recommended that FF and FP should be declared as different drugs for the purposes of section 85(2) of the *National Health Act 1953* (the Act). The PBAC therefore recommended the listing of FF, 100 mcg and 200 mcg powder for inhalation, as an unrestricted benefit for the treatment of asthma on a cost-minimisation basis to FP (paragraph 7.1, FF PSD, March 2017). The TGA indication for FF at the March 2017 meeting remained restricted to patients aged 12 years and over (paragraph 4.3, FF PSD, March 2017).

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

4 Population and disease

- 4.1 Asthma is a heterogenous disease, usually characterised by chronic airway inflammation and defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow. These clinical features are seen in school aged children, adolescents and adults.
- 4.2 The goal of asthma management is to achieve and maintain asthma control and reduce the risk of exacerbations. The key asthma guidelines for Australian clinicians are the Australian Asthma Handbook (AAH)¹, updated in March 2019, and the Global Strategy for Asthma management and prevention². Both key asthma guidelines split asthma management and recommendations by age group: adults and adolescents (aged 12 years and over); children aged 6 to 11 years; children 5 years and younger.
- 4.3 The minor submission stated that 'according to the AAH, similar to adults, the clinical management of asthma in children 5 years of age and over involves a stepped approach to adjusting medication'. While the AAH recommends a stepped approach to clinical management for both adults and children aged 6 to 11 years the treatment strategies are different. For adults, the AAH stepped approach to adjusting asthma medication recommends that few patients receive short acting beta2-agonist (SABA) as needed only, with most patients recommended to receive a low-dose regular preventer (ICS) plus an as needed SABA. For children aged 6 to 11 years, the AAH stepped approach to adjusting asthma medication recommends that many children should use as needed SABA only with only some children requiring regular preventer (low-dose ICS or montelukast) plus as needed SABA.

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

5 Comparator

- 5.1 The major submission considered by the PBAC in November 2015 nominated FP as the appropriate comparator. This was accepted by the PBAC (paragraph 7.2, FF PSD, November 2015).
- 5.2 The current minor submission nominated FP 100 mcg administered twice daily as the appropriate comparator. The minor submission stated that it is anticipated that FF 50 mcg once daily would replace FP 100 mcg administered twice daily.

¹ National Asthma Council Australia. *Australian Asthma Handbook*, Version 2.0. National Asthma Council Australia, Melbourne, 2019. Website. Available from: <http://www.asthmahandbook.org.au> (accessed 28 May 2019)

² Global Initiative for Asthma (GINA). *Pocket guide for asthma management and prevention*. Updated 2019. GINA, Fontana, 2019. Website. Available from: <https://ginasthma.org> (accessed 28 May 2019)

- 5.3 The minor submission stated that FP comprised 97% of the market share of all ICS monotherapy scripts dispensed for children with asthma aged 5 to 11, based on a sample of 10% of PBS scripts in 2018.

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 as it was a minor submission.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from organisations (2) via the Consumer Comments facility on the PBS website. The comments described the benefits of treatment with FF 50 mcg including adherence advantages, reduced burden of disease for paediatric patients and fewer occasions of emergency health care utilisation, while also highlighting the importance of provider education to ensure that the product is prescribed, accessed and used appropriately and safely.

Clinical trials

- 6.3 The minor submission was based on one 12-week Phase IIb, randomised, double-blind, placebo- and active-controlled study (HZA106855) conducted in children aged 5-11 years with inadequately controlled asthma, and was the same study provided to the TGA to support the change in PI. The treatment arms were:
- placebo (N=119);
 - FF 25 mcg once daily (N =118);
 - FF 50 mcg once daily (N=120);
 - FF 100 mcg once daily (N = 118);
 - FP (active control) 100 mcg twice daily (N = 118).
- 6.4 Supporting safety information from two additional trials, HZA107112 (leg growth) and HZ107118 (HPA Axis), was included in an appendix to the submission.
- 6.5 Details of the trials presented in the submission are provided in Table 1.

Table 1: Trials and associated reports presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Direct randomised trial(s)		
Primary study HZA106855	Oliver, A. J., et al. Randomized Trial of Once-Daily Fluticasone Furoate in Children with Inadequately Controlled Asthma. HZA106855 CSR Randomized Trial of Once-Daily Fluticasone Furoate in Children with Inadequately Controlled Asthma. GSK Clinical Study Report	Journal of Pediatrics 2016; 178: 246-253
Supplementary randomised trial(s)		
Safety study (leg growth) HZA107112	Wolthers, O.D., et al. Knemometry assessment of short-term growth in children with asthma receiving fluticasone furoate for 2 weeks: a randomized, placebo-controlled, crossover trial.	Clinical Therapeutics 2017; 39(6): 1191-1199
Safety study (HPA axis) HAZ107118	A randomised, double blind, placebo-controlled, parallel group study of once daily inhaled Fluticasone Furoate Powder on the Hypothalamic-pituitary-adrenocortical Axis of Children Aged 5-11 Years With Asthma. GSK Clinical Study Report, 2017	

Source: Table 14, p27 of minor submission

6.6 The primary outcome of study HZA106855 was the mean change from baseline in daily pre-dose morning peak expiratory flow (PEF) averaged over weeks 1 to 12. As HZA106855 was not a non-inferiority trial, the minor submission nominated a non-inferiority acceptance limit of -12mL/min for the primary outcome from the literature (von Berg 2007 and Pederson 2006). Hence, the minor submission stated that non-inferiority would be determined if the lower limit of the 95% confidence interval (CI) for differences between treatment groups was greater than -12mL/min.

Comparative effectiveness

6.7 The Intent-To-Treat (ITT) population was the primary population for all analyses of efficacy measures, comprising of all subjects randomised to treatment and who received at least one dose of trial medication.

6.8 The results for the primary outcome and secondary efficacy endpoints presented in the minor submission³ are presented in Table 2.

³ Additional secondary outcomes of study HZA106855 included change from baseline in: daily pre-dose evening PEF averaged during the treatment, morning and evening PEF over the last 7 days of the treatment period and the number of withdrawals due to lack of efficacy during the treatment period.

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Table 2: Results for the primary and selected secondary outcomes of study HZA106855 (ITT population)^a

	Placebo	FF 25 OD	FF 50 OD	FF 100 OD	FP 100 BD
Primary outcome: Mean change from baseline in AM PEF (L/min) averaged over weeks 1 to 12					
n/N (%)	119/119 (100%)	117/118 (99%)	118/120 (98%)	118/118 (100%)	117/118 (100%)
LS mean	198.9	217.5	218.4	211.3	212.9
LS mean change (SE)	3.3 (2.63)	21.9 (2.66)	22.8 (2.65)	15.8 (2.64)	17.3 (2.64)
Mean difference vs. placebo (95% CI), p-value		18.6 (11.3, 26.0) p<0.001	19.5 (12.1, 26.9) p<0.001	12.5 (5.1, 19.8) p<0.001	14.0 (6.7, 21.4) p<0.001
Secondary outcome: Mean change from baseline in PM Trough FEV1 (L) at Week 12					
n/N (%)	102/119 (86%)	96/118 (81%)	112/120 (93%)	96/118 (81%)	102/118 (86%)
LS mean	1.524	1.650	1.545	1.557	1.587
LS mean change (SE)	0.128 (0.0264)	0.254 (0.0272)	0.150 (0.0252)	0.162 (0.0272)	0.192 (0.0262)
Mean difference vs. placebo (95% CI), p-value		0.126 (0.051, 0.201) p<0.001	0.022 (-0.050, 0.094) p=0.551	0.033 (-0.041, 0.108) p=0.379	0.064 (-0.010, 0.137) p=0.089
Secondary outcome: change from baseline in percentage of rescue-free 24 hour periods					
n/N (%)	119/119 (100%)	117/118 (99%)	118/120 (98%)	118/118 (100%)	117/117 (100%)
LS mean change (SE)	16.5 (3.01)	24.9 (3.03)	26.3 (3.03)	28.7 (3.02)	22.7 (3.01)
Mean difference vs. placebo (95% CI), p-value		8.4 (0.0, 16.9) P=0.050	9.8 (1.3, 18.2) p=0.023	12.2 (3.8, 20.5) p=0.004	6.2 (-2.1, 14.6) p=0.143
Secondary outcome: Change from baseline in percentage of symptom-free 24-hour periods					
n/N (%)	119/119 (100%)	117/118 (99%)	119/120 (98%)	118/118 (100%)	117/118 (100%)
LS mean change (SE)	19.0 (2.90)	21.0 (2.92)	24.7(2.90)	22.9 (2.91)	22.0 (2.91)
Mean difference vs. placebo (95% CI), p-value		2.1 (-6.1, 10.2) P=0.619	5.8 (-2.3, 13.9) p=0.161	3.9 (-4.1, 12.0) p=0.340	3.0 (-5.0, 11.1) p=0.459

^a Analysis performed using ANCOVA with covariates of baseline, actual pre-screening ICS use, region, sex, age and treatment
Source: Tables 27-30 pp 43-46 of minor submission. BD = twice daily, OD = once daily

6.9 The minor submission stated that a statistically significant difference from placebo was observed for the primary outcome (mean change in AM PEF averaged over 12 weeks) for all FF treatment groups and for the active control group (FP 100 mcg twice daily). In contrast, a statistically significant adjusted treatment difference in the change from baseline in PM trough FEV1 at week 12 was only observed for the FF 25 mcg once daily group compared with placebo but not for the other treatment comparisons. The minor submission stated the reason for the lack of difference with trough FEV1 is unclear but may be partly due to the difficulties in achieving quality spirometry readings in young children. Mean change in baseline trough (evening) FEV1 at 24 weeks was the primary outcome used in the November 2015 PBAC consideration of the FF 100 mcg and 200 mcg presentations. Change from baseline in trough (evening) FEV1 at the end of the 12 week treatment period was a key outcome used in the November 2018 PBAC consideration of tiotropium for the treatment of severe

asthma in children and adolescents aged 6–17 years (paragraph 6.11, tiotropium PSD, November 2018).

- 6.10 The pre-PBAC response argued that PEF was employed as the primary outcome in Study HZA106855 as this is an accepted measure of lung function in asthma trials and offers practical advantages in the paediatric population where spirometry can prove to be challenging⁴. The pre-PBAC response noted that in their second-round clinical evaluation the TGA had considered that the sponsor had adequately substantiated the choice of PEF as the primary endpoint on the basis of feasibility of lung function measures in this age group (CPMP/EWP/4151/00 Rev. 1).
- 6.11 The minor submission stated that a greater change in the percentage of rescue-free 24 hour periods was observed in all treatment groups, however, the difference compared to placebo was only significant in the FF 50 mcg once daily and FF 100 mcg once daily groups (Table 2). No significant differences from baseline in the percentage of symptom-free 24 hour periods were observed for any of the treatment groups.
- 6.12 The minor submission also included results from other endpoints in study HZA106855 including the change from baseline in the childhood Asthma Control Test (cACT) score at week 12 and the change from baseline in the Standardised Paediatric Asthma Quality of Life Questionnaire, or PAQLQ(S), score at week 12. The results from these endpoints are presented in Table 3.

⁴ Loeb J, et al. Acceptability and repeatability of spirometry in children using updated ATS/ERS criteria. *Pediatric Pulmonology* 2008;43:1020-1024.

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Table 3: Results for the change from baseline in cACT and PAQLQ(s) scores of study HZA106855

	Placebo	FF 25 OD	FF 50 OD	FF 100 OD	FP 100 BD
Change from Baseline in cACT score at Week 12^a					
n/N (%)	70/119 (59%)	97/118 (82%)	89/120 (74%)	84/118 (71%)	89/118 (75%)
LS mean change (SE)	3.7 (0.39)	4.0 (0.33)	4.4 (0.35)	3.5 (0.36)	4.1 (0.34)
Mean difference vs. placebo (95% CI), p-value		0.2 (-0.8, 1.3) P=0.637	0.7 (-0.4, 1.7) p=0.198	-0.2 (-1.3, 0.8) p=0.696	0.3 (-0.7, 1.4) p=0.518
Percentage of Subjects Controlled at Week 12^b					
n/N (%)	70/119 (59%)	97/118 (82%)	89/120 (74%)	84/118 (71%)	89/118 (75%)
cACT score <20	16 (23)	24 (25)	16 (18)	17 (20)	18 (20)
cACT score ≥20	54 (77)	73 (75)	73 (82)	67 (80)	71 (80)
Odds Ratio (95% CI), p-value		0.99 (0.45, 2.15) p=0.979	1.63 (0.71, 3.72) p=0.249	1.40 (0.61, 3.22) p=0.432	1.35 (0.60, 3.03) p=0.465
Change from Baseline in Total PAQLQ(S) total score at Week 12					
n/N (%)	52/119 (44%)	61/118 (52%)	71/120 (59%)	57/118 (48%)	64/118 (54%)
LS mean change (SE)	0.8 (0.11)	0.9 (0.10)	0.9 (0.09)	1.0 (0.10)	1.1 (0.10)
Mean difference vs. placebo (95% CI), p-value		0.1 (-0.2, 0.4) p=0.423	0.2 (-0.1, 0.4) p=0.349	0.2 (-0.1, 0.5) p=0.112	0.3 (0.0, 0.6) p=0.036

^a Analysis performed using ANCOVA with covariates of baseline, actual pre-screening ICS use, region, sex, age and treatment.

^b Logistic regression adjusted for baseline, actual pre-screening ICS use, region, sex, age and treatment.

Source: Tables 31-33 pp 46 to 47 of minor submission

6.13 The minor submission stated that no significant changes from baseline in cACT score or PAQLQ(S) scores were reported at week 12 (Table 3).

6.14 As noted in paragraph 6.7 study HZA106855 was not designed as a non-inferiority trial. The minor submission presented a *post hoc* analysis of the mean change from baseline in AM PEF averaged over the 12 week treatment period for FF versus FP. The results of this analysis are presented in Table 4.

Table 4: Post hoc statistical analysis of change from baseline in AM PEF FF 50 mcg daily vs FP 100 mcg twice daily

Treatment group	Mean change from baseline AM PEF L/min (SE)	Mean difference, 95% CI
FF 50 mcg once daily (N = 118)	22.8 (2.7)	5.5 (-1.9, 12.8)
FP 100 mcg twice daily (N = 117)	17.3 (2.6)	

Source: Table 34 p 48 of minor submission

6.15 The minor submission stated that the *post hoc* analysis identified a mean treatment difference between FF 50 mcg once daily and FP 100 mcg twice daily of 5.5L/min (95% CI: -1.9, 12.8), which met the non-inferiority acceptance limit of -12mL/min, where the lower limit of the 95% confidence interval for treatment differences is greater than -12mL/min.

Comparative harms

6.16 The minor submission stated that safety findings from the HZA106855 trial were consistent with those reported in adult and adolescent subjects. On-treatment

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adverse reactions occurring in $\geq 3\%$ of subjects treated with FF 50 mcg and greater than placebo were bronchitis, pharyngitis, and viral infection. The proportion of subjects experiencing on-treatment adverse events was comparable between the FF 50 mcg once daily and FP 100 mcg twice daily groups (32% and 31%) and slightly higher than the placebo group (29%). It was also stated that two on-treatment non-fatal serious adverse events were reported, but neither were related to the study treatment. An overview of adverse events is presented in Table 5.

Table 5: Overview of adverse events in study HZA106855 (ITT population)

Type of Adverse Event	Number (%) subjects				
	Placebo N=119	FF 25 OD N=118	FF 50 OD N=120	FF 100 OD N=118	FP 100 BD N=118
All AEs					
On-treatment	35 (29)	43 (36)	38 (32)	39 (33)	36 (31)
On-treatment drug-related	2(2)	1(<1)	0	1(<1)	0
On-treatment leading to withdrawal	2(2)	0	1(<1)	3(3)	1(<1)
Post-treatment	2(2)	1(<1)	1(<1)	0	0
SAEs					
On-treatment	0	0	1(<1)	1(<1)	0
On-treatment drug-related	0	0	0	0	0
On-treatment fatal	0	0	0	0	0
Post-treatment	0	0	0	0	0

Source: Table 35 p 49 of minor submission

Clinical claim

- 6.17 The submission claimed that FF 50 mcg once daily is non-inferior, in terms of both efficacy and safety, to FP 100 mcg administered twice daily in patients aged 5 to 11 years with asthma.
- 6.18 The PBAC had previously considered that the claim of non-inferior comparative effectiveness and safety compared to FP was reasonable for FF 100 mcg and 200 mcg presentations (paragraph 7.3, FF PSD, November 2015).
- 6.19 The PBAC considered that the claims of non-inferior comparative effectiveness and non-inferior comparative safety compared to FP 100 mcg was reasonable for FF 50 mcg.

Economic analysis

- 6.20 Based on the claim of non-inferior efficacy and safety of FF compared to FP, the equi-effective doses were stated to be FF 50 mcg once daily and FP 100 mcg twice daily.
- 6.21 The minor submission stated the calculation of equi-effective doses was based on a direct randomised trial where doses of all treatments were fixed and consistent with

existing (FP) and proposed (FF) use in clinical practice as per the TGA approved PI for these products.

- 6.22 The minor submission stated that there are no differences between FF and FP in paediatric patients aged 5 to 11 years with asthma with respect to administration, monitoring or safety. Given this, the difference between FF and FP was based on a comparison of drug costs alone based on equi-effective doses. Using the PBS-listed price of FP, a cost-comparison analysis of FF 50 mcg once daily versus FP 100 mcg twice daily was presented in the submission (see Table 6 below). The requested price for FF 50 mcg was derived from the current approved price to pharmacist for FP 100 mcg.

Table 6: Prices of FF and FP based on cost-comparison analysis

Drug	Form	Max Qty	Pack size	AEMP	DPMQ
FP	Powder for oral inhalation in breath actuated device containing FP 100 micrograms per dose, 60 doses	1	1	■	■
FF	Powder for oral inhalation in breath actuated device containing FF 50 micrograms per dose, 30 doses	1	1	■	■

Source: Table 43 p 58 of minor submission

Estimated PBS usage & financial implications

- 6.23 The minor submission stated that currently there are four ICS monotherapy agents available on the PBS in this therapeutic area, however, FP 100 mcg is used predominantly (96.5%) in paediatric patients. The minor submission noted that the DPMQ for both FP 100 mcg (Flixotide Junior MDI) and FP 50 mcg (Flixotide Junior Accuhaler) is \$18.74, with the DPMQ for the remaining three ICS monotherapy agents used in children 5 to 11 years of age ranging from \$20.43 to \$28.74.
- 6.24 The minor submission estimated there to be no financial implications to the PBS or changes in PBS usage as the submission expects FF 50 mcg to only substitute for FP 100 mcg and both drugs have the same price.

Table 7: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	■	■	■	■	■	■
Estimated financial implications of FF						
Cost to PBS/RPBS	■	■	■	■	■	■
Co-payments	■	■	■	■	■	■
Cost to PBS/RPBS less co-payments	■	■	■	■	■	■
Estimated financial implications for FP						
Cost to PBS/RPBS	■	■	■	■	■	■
Co-payments	■	■	■	■	■	■
Cost to PBS/RPBS less co-payments	■	■	■	■	■	■
Net financial implications						
Net cost to PBS/RPBS	■	■	■	■	■	■

Source: Table 48-50, pp63-65 of minor submission.

The redacted table shows that the estimated number of scripts dispensed over 6 years is less than 10,000 and the net cost to the PBS is less than \$10 million.

- 6.25 The PBAC previously accepted that the listings of FF 100mcg and 200mcg would be cost neutral as substitution would likely only occur from within the existing ICS market.

For more detail on PBAC’s view, see section 7 PBAC outcome.

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of fluticasone furoate (FF) 50 mcg on the General Schedule as an unrestricted benefit. The PBAC recommended that the listing be on a cost-minimisation basis to fluticasone propionate (FP) 100 mcg at equi-effective doses of FF 50 mcg once daily and FP 100 mcg twice daily.
- 7.2 The PBAC reiterated its previous advice that FP was the appropriate comparator.
- 7.3 The PBAC noted the key clinical trial evidence supporting the FF 50 mcg listing and considered the primary outcome of mean change in AM PEF over 12 weeks versus placebo to be reasonable in the trial population. The PBAC acknowledged the difficulty in the measurement of lung function in the paediatric population and considered that PEF appeared to be more reproducible than FEV1 in this population, at least up to 8 years of age.
- 7.4 The PBAC noted that study HZA106855 was not designed as a non-inferiority trial. However, with respect to the *post hoc* statistical analysis of change from baseline in AM PEF for FF 50 mcg once daily versus FP 100 mcg twice daily, the PBAC noted the mean difference of 5.5L/min (95% CI: -1.9, 12.8) and considered that the literature based non-inferiority margin specified in the submission (-12 mL/min for the lower limit of the CI) had been met. The PBAC therefore considered that the claim of non-inferior comparative effectiveness was reasonable.

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- 7.5 The PBAC noted that the proportion of patients experiencing adverse events was comparable between the FF 50 mcg once daily and FP 100 mcg twice daily groups (32% and 31%) and slightly higher than the placebo group (29%). The PBAC considered that there were no statistical differences between the groups nor adverse event signals, and therefore considered that the claim of non-inferior comparative safety of FF 50 mcg and FP 100 mcg was reasonable.
- 7.6 The PBAC considered that, assuming no growth in the market and based on the equi-effective doses of FF and FP outlined in paragraph 7.1 (and at the PBS-listed price of FP 100 mcg) there would be no financial impact associated with the new listing.
- 7.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because FF is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over FP, or not expected to address a high and urgent unmet clinical need over FP, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 7.8 The PBAC reiterated its previous advice that FF is suitable for prescribing by nurse practitioners.
- 7.9 The PBAC reiterated its previous advice that the Early Supply Rule should apply to FF.
- 7.10 The PBAC reiterated its previous advice that FF should be treated as interchangeable on an individual patient basis with FP and ciclesonide.
- 7.11 The submission is not eligible for an Independent Review, because the PBAC made a positive recommendation.

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	
FLUTICASONE FUROATE fluticasone furoate 50 microgram/actuation powder for inhalation, 30 actuations	1	5	Arnuity® Ellipta®	GSK

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
Restriction Level / Method:	Unrestricted

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

The sponsor had no comment.