5.18 UMECLIDINIUM (as BROMIDE), 62.5 microgram/actuation, inhalation: powder for, 30 actuations, Incruse® Ellipta®, GlaxoSmithKline Australia Pty Ltd

1 Purpose of Application

1.1 The submission proposed the inclusion of umeclidinium on the Pharmaceutical Benefits Scheme (PBS) as a Restricted Benefit listing for treatment of chronic obstructive pulmonary disease (COPD).

2 Requested listing

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
UMECLIDINIUM BROMIDE Inhalation: powder for, 62.5 microgram/actuation, 30 actuations	1	5	Incruse® Ellipta®	GlaxoSmithKline

Restricted benefit:
Chronic obstructive pulmonary disease

2.2 Listing was requested on a cost-minimisation basis with tiotropium.

2.3 The PBAC noted that the proposed restriction is consistent with that of tiotropium (the nominated comparator), glycopyrronium (recommended in November 2013) and aclidinium (recommended in March 2014).

2.4 The PBAC noted that the listing as requested would allow use of umeclidinium for treatment of COPD as monotherapy, in combination with a long acting beta agonist (LABA) and in combination with a LABA and an inhaled corticosteroid (ICS).

3 Background

3.1 The submission was made under TGA/PBAC Parallel Process. At the time of PBAC consideration, the Clinical Evaluation Report, TGA Delegate's Overview and ACPM resolution were available.

3.2 At its June 2014 meeting, the ACPM considered umeclidinium bromide to have an overall positive benefit-risk profile for the following indication:

Umeclidinium bromide is indicated as a long-term, once daily, maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).

3.3 Umeclidinium as monotherapy has not been previously considered by PBAC, however umeclidinium 62.5 micrograms with vilanterol 25 micrograms was rejected by the PBAC at the March 2014 meeting.

4 Clinical place for the proposed therapy

4.1 The submission proposed that umeclidinium 62.5 micrograms as monotherapy will provide an alternative long acting muscarinic antagonist (LAMA) for the symptomatic relief of COPD.

4.2 The submission proposes listing umeclidinium monotherapy as first line treatment for patients with COPD. If symptoms persist in the absence of exacerbations, treatment involves a step-wise approach whereby umeclidinium will be used in combination with a LABA. If a patient then starts to experience exacerbations, treatment may be escalated to a fixed-dose ICS/LABA plus LAMA combination.

5 Comparator

5.1 The submission nominated tiotropium as the comparator.

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 was based on indirect comparisons of two umeclidinium trials and 16 tiotropium trials with placebo as a common comparator. Umeclidinium trials: AC4115408 and DB2113373; Tiotropium trials: SHINE, Brusasco 2003, Casaburi 2000, Casaburi 2002, Chan 2007, Covelli 2005, Donohue 2002, Donohue 2010, Garcia 2007, GLOW2, Moita 2008, Niewoehner 2005, UPLIFT, TIPHON, Verkindre 2006, Vogelmeier 2008

6.4 Details of the trials presented in the submission are provided in the table below.

Trial	Protocol title/ Publication title	Publication citation
Common reference: Placebo		
Umeclidinium		
AC4115408	A 12-week, randomised, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of GSK573719 delivered once-daily via a novel dry powder inhaler in subjects with chronic obstructive pulmonary disease Report number 2011N130819_00.	July 2012
DB2113373	A 24-week, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of GSK573719/GW642444 inhalation powder and the individual components delivered once-daily via a novel dry powder inhaler in subjects with chronic obstructive pulmonary disease.	11 September 2012

Trial	Protocol title/ Publication title	Publication citation
Tiotropium		
SHINE	Dual bronchodilation with QVA149 versus bronchodilator therapy: the SHINE study,	Bateman ED, Ferguson GT, Barnes N, et al., 2013. 'ERJ Express, 42(6):1484-1494
Brusasco, 2003	Health outcomes following treatment for six months with once daily tiotropium compared with twice daily salmeterol in patients with COPD	Brusasco V, Hodder R, Miravitlles M. 2003. Thorax, 58:399-404
Casaburi, 2000	The spirometric efficacy of once-daily dosing with tiotropium in stable COPD: A 13-week multicentre trial	Casaburi R, Briggs DD, Donohue JF et al., 2000., Chest, 118:1294-1302
Casaburi, 2002	A long-term evaluation of once-daily inhaled tiotropium in chronic obstructive pulmonary disease	Casaburi R, Mahler DA, Jones PW et al., 2001. , European Respiratory Journal, 19:217-224
Chan, 2007	A randomized controlled trial to assess the efficacy of tiotropium in Canadian patients with chronic obstructive pulmonary disease	Chan CKN, Maltais F, Sigouin C, et al., 2007., Canadian Respiratory Journal, 14(8):465-472
Covelli, 2005	Absence of electrocardiographic findings and improved function with once-daily tiotropium in patients with chronic obstructive pulmonary disease	Covelli H, Bhattacharya S, Cassino C, et al., 2005, Pharmacotherapy, 25(12):1708-1718
Donohue, 2002	A 6-month, placebo-controlled study comparing lung function and health status changes in COPD patients treated with tiotropium or salmeterol	Donohue JF, Bateman ED, Langley S, et al., 2002. Chest, 122:47-55
Donohue, 2010	Once-daily bronchodilators for chronic obstructive pulmonary disease: indacaterol versus tiotropium.	Donohue JF, Fogarty C, Lotvall J et al., 2010. , American Journal of Respiratory and Critical Care Medicine, 182(2):155-162
Garcia, 2007	A randomised, double-blind, placebo-controlled, 12 week trial to evaluate the effect of tiotropium inhalation capsules on the magnitude of exercise, measured using accelerometer, in patients with chronic obstructive pulmonary disease (COPD).	Garcia RF. 2007. Boehringer Ingelheim Clinical Trial Register.
GLOW 2	Efficacy and safety of NVA237 versus placebo and tiotropium in patients with COPD: the GLOW2 study.	Kerwin E, Hebert J, Gallagher N, et al., 2012. European Respiratory Journal, 40:1106-1114
Moita, 2008	Tiotropium improves FEV_1 in patients with COPD irrespective of smoking status.	Moita J, Barbara C, Cardoso J, et al., 2008. , Pulmonary Pharmacology & Therapeutics, 21(1)
Niewoehner, 2005	Prevention of exacerbations of chronic obstructive pulmonary disease with tiotropium, a once-daily inhaled anticholinergic bronchodilator.	Niewoehner DE, Rice K, Cote C et al., 2005. , Annals of Internal Medicine, 143(5):317-327
UPLIFT	A 4-year trial of tiotropium in chronic obstructive pulmonary disease. Mortality in the 4-year trial of tiotropium (UPLIFT) in patients with chronic obstructive pulmonary disease'	Tashkin DP, Celli B, Senn S et al., 2008. The New England Journal of Medicine, 359(15):1543-1554 Celli B, DeCramer M, Kesten S et al., 2009. American Journal of Respiratory Critical Care Medicine, 180:948-955
TIPHON	Effect of tiotropium on health-related quality of life as a primary efficacy endpoint of COPD.	Tonnel AB, Perez T, Grosbois JM et al., 2008. International Journal of COPD, 3(2):301-310
Verkindre , 2006	The effect of tiotropium on hyperinflation and exercise capacity in chronic obstructive pulmonary disease.	Verkindre C, Bart F, Aguilaniu B et al., 2006. , Respiration, 73:420-427

Trial	Protocol title/ Publication title	Publication citation
Vogelmeier , 2008	Formoterol mono- and combination therapy with tiotropium in patients with COPD: A 6-month study.	Vogelmeier C, Kardos P, Harari S et al., 2008. Respiratory Medicine, 102:1511-1520
Common reference: Umeclidinium 125 mcg; Umeclidinium 62.5 mcg + Vilanterol 25 mcg		
DB2113374	A multicentre trial comparing the efficacy and safety of GSK573719/GW642444 with GSK573719 and with Tiotropium over 24 weeks in subjects with COPD	17 September 2012
Common reference: Vilanterol 25 mcg		
DB2113360	A multicentre trial comparing the efficacy and safety of GSK573719/GW642444 with GW642444 and with Tiotropium over 24 weeks in subjects with COPD	14 September 2012

Source: Table 6, pp31-33; of the submission
COPD: chronic obstructive pulmonary disease; n/a: not available;

6.5 The key features of the randomised trials included in the indirect comparison, using placebo as common reference are summarised in the table below.

Trial	N[a]	Design/ duration	Risk of bias	COPD Patient population [c]	Outcomes
Umeclidinium vs. Placebo					
12 weeks					
AC4115408	137	R, DB, 12 wks	Low	Mild – Severe $FEV_1 \leq 70\%$	FEV_1 @ 12 weeks; TDI focal score; rescue medication; SGRQ
24 weeks					
DB2113373	698	R, DB, 24 wks	Low	Mild – Severe $FEV_1 \leq 70\%$	FEV_1 @ 12 weeks; FEV_1 @ 24 weeks; TDI focal score; rescue medication; SGRQ
Tiotropium vs. Placebo					
10-14 weeks					
Casaburi, 2000	470	R, DB, 13 wks	Low	Moderate – Severe $FEV_1 \leq 65\%$	FEV_1 @ 12 weeks;
Covelli, 2005	196	R, DB[b], 12 wks	Low	Moderate – Severe $FEV_1 \leq 60\%$	FEV_1 @ 12 weeks
Garcia, 2007	250	R, DB, 12 wks	Low	Moderate – Severe $FEV_1 \leq 60\%$	Only safety results presented in submission
Moita, 2008	304	R, DB[b], 12 wks	Low	Moderate – Severe $FEV_1 \leq 70\%$	FEV_1 @ 12 weeks;
Verkindre, 2006	100	R, DB, 12 wks	Low	Moderate – Severe $FEV_1 \leq 50\%$	FEV_1 @ 12 weeks; TDI focal score; rescue medication; SGRQ
22-26 weeks					
SHINE	712	R, OL, 26 wks	Low	Mild –Severe COPD $FEV_1 \geq 30\%$ and $\leq 80\%$	FEV_1 @ 12 weeks; FEV_1 @ 24 weeks; TDI focal score;
Brusasco, 2003	802	R, DB[b], 24 wks	Low	Mild – Severe $FEV_1 \leq 65\%$	FEV_1 @ 24 weeks
Donohue, 2002	410	R, DB, 24 wks	Low	Moderate - Severe $FEV_1 \leq 60\%$	FEV_1 @ 24 weeks
Donohue, 2010	833	R, OL, 26 wks	Low	Mild – Severe $FEV_1 \geq 30\%$ and $\leq 80\%$	FEV_1 @ 12 weeks; FEV_1 @ 24 weeks; TDI focal score; SGRQ
Niewoehner, 2005	1,829	R, DB, 6 mths	Low	Moderate - Severe $FEV_1 \leq 60\%$	FEV_1 @ 12 weeks; FEV_1 @ 24 weeks;
Vogelmeier, 2008	430	R, OL, 24 wks	Low	Mild - Severe $FEV_1 \leq 70\%$	Only safety results presented in submission
36 weeks					

Trial	N[a]	Design/ duration	Risk of bias	COPD Patient population [c]	Outcomes
TIPHON	554	R, DB, 36 wks	Low	Mild - Severe FEV_1 ≥20% and ≤70%	SGRQ
48 - 56 weeks					
Casaburi, 2002	921	R, DB, 56 wks	Low	Mild - Severe FEV_1 ≤ 65%	TDI focal score
Chan, 2007	913	R, DB, 48 wks	Low	Mild - Severe FEV_1 ≤ 65%	FEV_1 @ 12 weeks;
GLOW 2	535	R, OL, 52 wks	Low	Mild - Severe FEV_1≥ 30% and ≤80%	FEV_1 @ 12 weeks; FEV_1 @ 24 weeks; TDI focal score; SGRQ
4 years					
UPLIFT	5,992	R, DB, 4 yrs	Low	Mild - Severe FEV_1 ≤ 70%	FEV_1 @ 24 weeks;

DB=double blind; FEV_1: forced expiratory volume in 1 second; OL=open label; R=randomised; SGRQ: St George Respiratory Questionnaire (Disease-specific instrument designed to measure impact on overall health, daily life, and perceived well-being in patients with obstructive airways disease).; TDI = transition dyspnoea index; Source: Table 2, p5 of the commentary.

[a] for treatment arms included in analysis

[b] Alternative inhalers were reported (or not reported) for alternative treatment arms

[c] Source: Australian/NZ COPDX based on predicted FEV_1: Mild = 60-80%; Moderate = ≥ 40% and ≤60%; Severe = <40%;

6.6 The PBAC agreed with the ESC who considered the age, gender and severity of patients in the included trials to be appropriate to the PBS population and that the evaluation of trials including the concomitant use of ICS/LABA would have been informative.

Comparative effectiveness

6.7 Umeclidinium results in statistically significant and clinically relevant difference of 136 mL (95% CI 110 mL to 170 mL) in trough FEV_1 at 12 weeks compared to placebo treatment. Tiotropium results in a similar clinically relevant improvement compared to placebo treatment. There is statistical heterogeneity in trough FEV_1 across the tiotropium trial (p-value: 0.023). A summary of the efficacy outcomes is presented in the table below.

Outcome	Umeclidinium trials		Tiotropium trials		Indirect estimate of effect MD (95% CI)
	N trials (n)	LS MD UMEC vs. PBO (95% CI)	N trials (n)	LS MD TIO vs PBO (95% CI)	
Week 12					
Change in trough FEV_1 (L); MD	[redacted]	[redacted]	9[b] (10,756)	**0.118 (0.10, 0.14)** I^2 = 54.9%	[redacted]
TDI focal score, MD	[redacted]	[redacted]	5[c] (2,657)	**0.73 (0.48, 0.97)** I^2 = 11.7%	[redacted]
Change in rescue medication, MD[h]	[redacted]	[redacted]	1[d] (100)	-0.13 (-0.62, 0.36)	[redacted]
Change in SGRQ; MD	[redacted]	[redacted]	4[e] (2,024)	**-2.67 (-4.3, -1.1)** I^2 = 44.5%	[redacted]
Week 24					
Change in trough FEV_1 (L); MD	1[f] (698)	**0.115 (0.08, 0.16)**	7[g] (10,756)	**0.111 (0.10, 0.13)** I^2 = 33.2%	0.004 (-0.04, 0.05)

Source: Table 46, p109, Tables 50-51, pp111-112, Table 53, p114, Table 56 -58, pp115-117, Tables 61-62, pp118-119, Table 64, p121 of the submission; Table 17, p37 Attachment 3 of the submission;

CI = confidence interval; FEV_1 = forced expiratory volume in one second; LS MD = least square mean difference; N = number of trials; n= number in meta-analysis; TDI = transitional dyspnoea index; SGRQ = St George's respiratory questionnaire; UMEC = umeclidinium; TIO = tiotropium; PBO = placebo; **Bold** = statistically significant outcome

[a] AC4115408, DB2113373

[b] SHINE, Casaburi 2000, Chan, Covelli, Donohue 2010, GLOW 2, Moita, Niewoehner, Verkindre

[c] SHINE, Casaburi 2000, Donohue 2010, GLOW 2, Verkindre

[d] Verkindre

[a] Donohue 2010, GLOW 2, TIPHON ,Verkindre
[f] DB2113373
[g] SHINE, Brusasco, Donohue 2002, Donohue 2010, GLOW 2, Niewoehner, UPLIFT
[h] measured in puffs per day of salbutamol

Comparative harms

6.8 Indirect comparisons of umeclidinium and tiotropium using placebo as a common comparator based on trials reporting safety at similar time points were conducted during the evaluation. Meta-analyses were performed for the tiotropium trials reporting safety at similar end points using a random effects model. Indirect comparisons were performed using the Bucher method. Umeclidinium was not associated with a greater risk of adverse events when compared to tiotropium at both 12 and 24 weeks.

Benefits/harms

6.9 A summary of the comparative benefits and harms for umeclidinium and tiotropium compared to placebo is presented in the table below.

Benefits								
Change in trough FEV_1 (L); MD at 12 weeks [indirect comparison]								
	Umeclidinium trials		**Tiotropium trials**				**Indirect estimate of effect MD (95% CI)**	
Trial ID	**N trials (n)**	**LS MD UMEC vs. PBO (95% CI)**	**N trials (n)**	**LS MD UMEC vs. PBO (95% CI)**				
Umeclidinium	[redacted]	[redacted]						
Tiotropium			[redacted]	[redacted]				
Indirect comparison: Umeclidinium vs. Tiotropium							[redacted]	
Harms at 24 weeks								
	UMEC	**PBO**	**TIO**	**RR (95% CI)**	**Event rate/100 patients/24 weeks**			**RD (95% CI)**
					UMEC	**PBO**	**TIO**	
Any Adverse Event								
DB2113373	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]		[redacted]
Tiotropium (2 trials)[b]		216/441	354/701	0.97 (0.86, 1.05)		49	50	-0.02 (-0.08, 0.04)
Indirect comparison: UMEC vs. TIO				[redacted]				[redacted]
COPD exacerbations								
[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]		[redacted]
Tiotropium (3 trials)[c]		417/1356	416/1,615	**0.82 (0.73, 0.92)**		31	26	**-0.06 (-0.09, -0.02)**
Indirect comparison: UMEC vs. TIO				[redacted]				[redacted]
Any Serious Adverse Event								
[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]		[redacted]
Tiotropium (2 trials)[d]		169/1,147	181/1,394	0.99 (0.77, 1.27)		8	8	-0.01 (-0.03, 0.02)
Indirect comparison: UMEC vs. TIO				[redacted]				[redacted]

RD = risk difference; RR = relative risk; UMEC = umeclidinium; PBO = placebo; TIO = tiotropium; LS MD = least square mean difference; CI = confidence interval

Source: Table 4, p7 of the commentary
[a] AC4115408, DB2113373
[b] SHINE, Vogelmeier
[c] SHINE, Niewoehner, Vogelmeier
[d] SHINE, Niewoehner

6.10 Based on an indirect comparison using placebo as the common comparator, umeclidinium appears to be no worse than tiotropium in the treatment of COPD. The outcomes assessed were airway function, breathlessness, and use of additional rescue medication.

6.11 On the basis of the indirect comparison presented, the frequency of adverse effects appears to be the same between umeclidinium and tiotropium.

Clinical claim

6.12 The submission described umeclidinium 62.5 mcg is non-inferior in terms of effectiveness and non-inferior in terms of safety when compared to tiotropium 18 mcg.

6.13 The following concerns were raised by the ESC:
- The submission provides only evidence for the use of umeclidinium as monotherapy; and
- There is heterogeneity within the trials included in the meta-analysis for the main comparator, tiotropium, which is likely to be related to differences in patient characteristics among the trials.

6.14 The ESC advised that on the basis of the indirect comparison, there was no significant difference between umeclidinium and tiotropium with respect to airway function, exacerbations and adverse effects, and that the claim of non-inferiority was adequately supported by the clinical evidence.

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

Economic analysis

6.15 The submission presents a cost-minimisation analysis using a comparison of drug costs only.

6.16 Umeclidinium 62.5 mcg once daily and tiotropium 18 mcg once daily are claimed to be equi-effective. The claim is based on an indirect comparison of data from 18 key randomised trials, two for umeclidinium and 16 for tiotropium.

6.17 The PBAC noted the concerns raised by ESC around the potential for patients to inappropriately use greater than one daily dose of umeclidinium due to the ease of use of the inhaler device, when compared to other devices currently listed on the PBS, which require the patient to place a capsule inside the inhaler device for each dose. This would potentially lead to increased and unquantifiable costs.

6.18 The proposed cost-minimisation of umeclidinium to tiotropium is shown in the table below.

Product	Strength (mcg)	Max Qty	Pack size	DPMQ
Tiotropium	18	30	1	$73.65
Umeclidinium	62.5	30	1	$73.65

Source: Table 99 p.169 of the submission.

6.19 The expected cost per patient of umeclidinium per year is $897, assuming 12.16 scripts per year, similar to the cost of tiotropium.

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

Estimated PBS usage & financial implications

6.20 This submission was not considered by DUSC. The submission uses a market share approach to estimate utilisation and financial implications of umeclidinium over a five-year time horizon. Market share data are taken from the Medicare Australia website and include all PBS/RPBS services for LAMAs. The submission's estimates are presented in the table below.

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated extent of use					
Total number of LAMA scripts [a]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Market share of UMEC	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
UMEC scripts	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimated net cost to PBS/RPBS					
Cost of UMEC to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost offsets PBS/RPBS, TIO	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Cost to MBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Estimated total net cost					
Net cost to PBS/RPBS	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**

Source: Tables 100-104 pp.172-175 of the submission

[a] The number of LAMA scripts were incorrectly presented in the submission, however the calculations presented in the submission for the number of umeclidinium scripts are correct.

UMEC = umeclidinium; LAMA = long acting muscarinic antagonist; TIO = tiotropium

6.21 The listing of umeclidinium is estimated by the submission to result in nil total cost to the PBS/RPBS over the first five years as the DPMQ for umeclidinium is the same as for other LAMAs, and it is likely that direct substitution from within the existing LAMA market will occur. The PBAC noted that, at the lower price recommended for aclidinium, the listing of umeclidinium will be cost saving to the PBS and the RPBS over the first five years compared to estimates in the submission.

6.22 The number of scripts and PBS/RPBS cost may be higher or lower due to:

- The assumption that umeclidinium will only replace LAMAs (underestimate);
- There will not be an increase in the LAMA market, due to listing of umeclidinium (underestimate);
- Uptake rate of umeclidinium, which is based on internal sales forecast (over- or under-estimate).

6.23 The submission claims no financial implications for Medicare. This seems reasonable.

6.24 The extent of use of umeclidinium is uncertain, and may be higher or lower than estimated in the submission due to the recent PBS listing of glycopyrronium and recommendation for listing aclidinium for the same indication.

7 PBAC Outcome

7.1 The PBAC recommended listing of umeclidinium as a restricted benefit for the treatment of chronic obstructive pulmonary disease with a maximum quantity of one pack with five repeats on the basis of non-inferiority to tiotropium. The PBAC considered that the cost-effectiveness of umeclidinium would be acceptable if it were cost-minimised against aclidinium, which was recommended for listing by PBAC in March 2014 for the same indication, also on the basis of non-inferiority to tiotropium but at the lower price requested by the sponsor of aclidinium. 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.

7.2 The PBAC accepted that tiotropium is the appropriate comparator but also considered that glycopyrronium bromide (recommended at the November 2013 PBAC meeting) and aclidinium (recommended at the March 2014 PBAC meeting) may also be relevant comparators.

7.3 The equi-effective doses are umeclidinium 62.5 microgram once daily and tiotropium 18 microgram once daily.

7.4 The PBAC considered that the data provided adequately supported the submission's claim that umeclidinium is non-inferior in terms of comparative effectiveness and comparative safety to tiotropium. The PBAC noted the ESC concerns that data presented in the submission was only for umeclidinium as monotherapy, and that there was heterogeneity in the trials included in the meta-analysis, but on balance, the PBAC considered that the data presented supported the submission's claim of non-inferior comparative efficacy and comparative safety of umeclidinium over tiotropium.

7.5 The PBAC considered that a cost-minimisation analysis was the correct approach based on the evidence presented.

7.6 The PBAC noted that unlike tiotropium, the price for umeclidinium incorporates the cost of the included inhaler device, whereas patients prescribed tiotropium are required to purchase an inhaler device separately.

7.7 The PBAC recommended that the Safety Net 20 Day Rule should apply.

7.8 The PBAC advised that umeclidinium is suitable for inclusion in the PBS medicines for prescribing by nurse practitioners within collaborative arrangements.

7.9 Advice to the Minister under Section 101 3BA of the *National Health Act*
The PBAC advised the Minister that under Section 101 3BA of the *National Health Act 1953,* umeclidinium should be treated as interchangeable on an individual patient basis with tiotropium, glycopyrronium and aclidinium.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
UMECLIDINIUM (as BROMIDE) Inhalation: powder for, 62.5 microgram/actuation, 30 actuations	1	5	Incruse® Ellipta®	GSK

Condition:	Chronic obstructive pulmonary disease
Restriction:	Restricted Benefit

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 Incruse for the treatment of COPD on the PBS.