

5.29 BUDESONIDE, Suppository 4 mg, Budenofalk®, DR FALK PHARMA AUSTRALIA PTY LTD

1 Purpose of Submission

- 1.1 The Category 4 submission requested a General Schedule unrestricted benefit listing of a new form of budesonide (budesonide 4 mg suppository; hereafter referred to as BUS).
- 1.2 The listing was requested on the basis of a cost-minimisation approach versus budesonide foam (rectal foam 2 mg per application, 14 applications, aerosol 16.8 g, 2; hereafter referred to as BUF).

2 Background

Registration status

- 2.1 BUS was TGA registered on 9 July 2024 for short-term treatment of mild to moderate ulcerative colitis, limited to the rectum (ulcerative proctitis), in adult patients.

Previous PBAC consideration

- 2.2 BUS has not been previously considered by the PBAC.

3 Requested listing

- 3.1 The submission requested the listing of BUS under the same conditions as the existing listing for BUF. Suggested additions are in italics:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
BUDESONIDE					
budesonide 2 mg/application foam, 2 x 14 applications	10034D	1	1	3	Budenofalk
<i>budesonide 4 mg suppository, 30</i>	<i>NEW</i>	<i>1</i>	<i>30</i>	<i>3</i>	
Benefit Type: Unrestricted					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners				
	Restriction Type: Unrestricted				
	Administrative Advice: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				

- 3.2 The submission requested listing with a maximum quantity pack of 1, and maximum quantity units of 30.
- 3.3 The submission requested listing with a maximum number of 3 repeats, consistent with the listing of BUF and allowing up to 4 months (16 weeks) of treatment with one script. The TGA Product Information (PI) for BUS states that treatment duration is determined by the physician, however an acute episode generally subsides after 6 to 8 weeks and the duration of treatment period in the clinical studies for the BUS was 8 weeks. The TGA PI for BUF states that treatment should not continue beyond 8 weeks, but this restriction is not present in the PI for BUS. The evaluation noted that the submission estimated the equi-effective doses of BUF and BUS based on the 8-week treatment duration (see 'Economic Analysis' under Section 5 Consideration of the Evidence).
- 3.4 The submission requested an unrestricted benefit listing, consistent with the listing of BUF, though there are other alternative therapies listed as restricted benefits for the treatment of proctitis and ulcerative colitis. The pre-PBAC response stated that these alternative therapies (prednisolone suppositories and hydrocortisone enema) have broader approved TGA indications, which may potentially warrant this level of PBS restriction. The pre-PBAC response also stated that, consistent with BUF, prednisolone enemas have an unrestricted benefit listing.
- 3.5 At its November 2024 meeting, the PBAC reviewed all PBS listings carrying the administrative note pertaining to nurse practitioners prescribing for continuing therapy only. This included BUF (Refer to item 9.01, November 2024 PBAC meeting).

4 Comparator

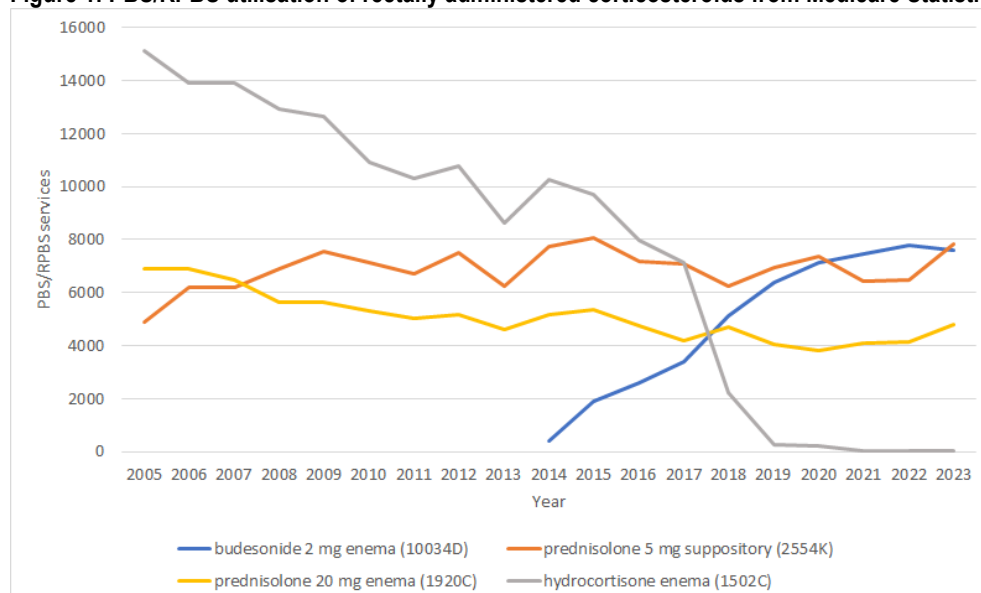
- 4.1 The submission nominated BUF as the main comparator. Other PBS-listed rectal corticosteroids (prednisolone (as sodium phosphate) 20 mg/100 mL enema, 7 x 100 mL, prednisolone (as sodium phosphate) 5 mg suppository, 10, and hydrocortisone acetate 10% enema, 21.1) could be considered appropriate additional comparators.
- 4.2 BUF is registered by the TGA for the treatment of active rectal and rectosigmoid disease in ulcerative colitis. At its July 2013 meeting, the PBAC recommended BUF as an unrestricted benefit on a cost-minimisation basis with prednisolone enema. The accepted equi-effective doses are budesonide 2 mg and prednisolone 20 mg (pg 4, budesonide Public Summary Document (PSD), July 2013 PBAC meeting).
- 4.3 For induction therapy of ulcerative proctitis or distal colitis in adults, the Therapeutic Guidelines states that if the combination of a rectal and an oral 5-aminosalicylate (e.g. mesalazine) is ineffective for induction therapy of ulcerative proctitis or distal

colitis, a rectal corticosteroid therapy should be added¹. The Therapeutic Guidelines states that the following rectal corticosteroids can be added.

- budesonide 2 mg/applicator foam 1 applicator rectally, once daily OR
- hydrocortisone acetate 10% foam 1 applicator rectally, once or twice daily OR
- prednisolone 20 mg/100 mL enema rectally, once or twice daily OR
- prednisolone 5 mg suppository rectally, once or twice daily (for isolated proctitis).

4.4 The pre-PBAC response noted that PBS utilisation data shows a significant decrease in the use of hydrocortisone acetate enemas following the PBS listing of BUF (Figure 1) and claimed that this makes it a less relevant comparator for BUS.

Figure 1: PBS/RPBS utilisation of rectally administered corticosteroids from Medicare Statistics



Source: Figure 1 of the pre-PBAC response.

Note: Each service for the enema preparations is estimated to provide treatment for 28 days (budesonide, prednisolone and hydrocortisone) compared with 15 days for the prednisolone suppositories, based on TGA approved doses (see equi-effective doses in Table 2 below). Budesonide 2 mg enema is the foam formulation.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

5.2 The PBAC noted and welcomed the input from one organisation via the Consumer

¹ Ulcerative colitis in adults [published 2022 August]. In: Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; accessed 5 September 2024. <https://www.tg.org.au>

Comments facility on the PBS website. The comments from Crohn’s and Colitis Australia support the requested listing, emphasising that BUS offers several benefits over BUF for ulcerative colitis patients including ease of self-administration, reduced toxicity compared to prednisolone suppository, and improved delivery to inflamed areas.

Clinical trials

5.3 The submission was based on evidence from a phase 3, randomised, double-blind, double-dummy, active controlled, non-inferiority trial (BUS-4/UCA). Details of the trial are summarised in Table 1 below.

Table 1: Trial presented in the submission

Study ID	Publication title	Publication citation
BUS-4/UCA	Randomised, double-blind, double-dummy, multicentre study to compare the efficacy and safety of once daily novel 4 mg budesonide suppository versus once daily 2 mg budesonide foam in patients with acute ulcerative proctitis. Dr. Falk Pharma.	NIHR - Innovation Observatory 2021
	Novel Budesonide Suppository and Standard Budesonide Rectal Foam Induce High Rates of Clinical Remission and Mucosal Healing in Active Ulcerative Proctitis: a Randomised, Controlled, Non-inferiority Trial. Kruis et al., 2022	Journal of Crohn's and Colitis. 2022a;16(11):1714-24.
	Novel Budesonide Suppository and Budesonide Rectal Foam Induce Mucosal Healing in Acute Ulcerative Proctitis. Kruis et al., 2021	Gastroenterology. 2021;160(6):S-92.
	Rectal budesonide formulations are well accepted by patients with ulcerative proctitis and improve work productivity and quality of life. Kruis et al., 2022	Gastroenterology. 2022b;162(7):S-976-S-7.
	Euctr HU. Novel budesonide suppository vs. budesonide foam in acute ulcerative proctitis.	2017 https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-001921-15/HU
	Novel budesonide suppository vs. budesonide foam in acute ulcerative proctitis	2016 EUCTR2016-001921-15-DE.

Source: Adapted from Table 8 of the submission main body.

5.4 The submission presented results from the analysis of two primary endpoints: 1) rates of clinical remission and 2) mucosal healing. The submission stated that the findings from these analyses (full analysis set (FAS) and per protocol set (PPS)) were statistically consistent, indicating that BUS is non-inferior to BUF in terms of effectiveness (Table 2).

Table 2: Co-primary endpoints: Rates for clinical remission and mucosal healing by the end of treatment or discontinuation (PPS and FAS)

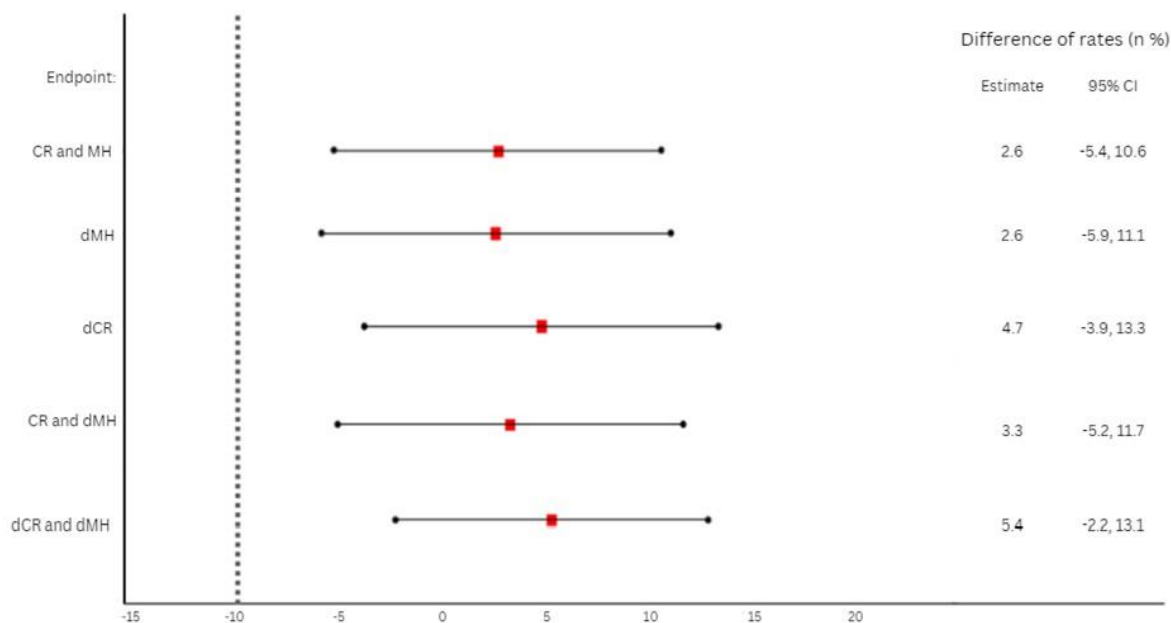
	BUS n/N (%)	BUF n/N (%)	Difference BUS – BUF Estimate (95% CI)	P-value
PPS				
Clinical remission				
Yes	197/250 (78.8%)	194/261 (74.3%)	4.5% (-3.0%, 11.9%)	0.00007
No	53/250 (21.2%)	67/261 (25.7%)		
Mucosal healing				
Yes	203/250 (81.2%)	212/261 (81.2%)	0.0% (-6.9%, 6.9%)	0.00224
No	47/250 (18.8%)	49/261 (18.8%)		
FAS				
Clinical remission				
Yes	211/281 (75.1%)	204/290 (70.3%)	4.7% (-2.6%, 12.1%)	0.00004
No	70/281 (24.9%)	86/290 (29.7%)		
Mucosal healing				
Yes	214/281 (76.2%)	220/290 (75.9%)	0.3% (-6.7%, 7.3%)	0.00209
No	67/281 (23.8%)	70/290 (24.1%)		

Source: Table ES.3 of submission executive summary.

Abbreviations: BUF budesonide foam; BUS budesonide suppositories; CI confidence interval; FAS full analysis set; PPS per protocol set.

5.5 The submission further stated that the outcomes of the secondary endpoints supported non-inferiority of BUS compared to BUF in terms of effectiveness (Figure 2) and reported that there was overall acceptance of BUS compared to BUF.

Figure 2: Key secondary endpoints: Remission rates by the end of treatment or discontinuation (PPS)



Source: Figure ES.2 of submission executive summary.

Abbreviations: CI, confidence interval; CR, clinical remission; dCR, deepened clinical remission; dMH, deepened mucosal healing; MH, mucosal healing; PPS, per protocol set.

Dotted line indicates non-inferiority margin of -10%.

- 5.6 The submission stated the BUS-4/UCA trial demonstrated that BUS is non-inferior to BUF in terms of safety as it was well tolerated and its safety outcomes were consistent with the established safety profile of BUF.
- 5.7 The submission highlighted that BUS was associated with a higher incidence of treatment-emergent adverse events (TEAEs; Table 3), particularly the incidence of serum-cortisol decrease, compared to BUF (BUS - 22.4%; BUF - 11.7%). However, as there were no symptoms suggestive of adrenal insufficiency in majority of the patients, BUS was considered safe for this patient group and that overall, the adverse effects were manageable.

Table 3: Summary of adverse events (SFS)

	BUS (N = 286)	BUF (N = 291)	Odds Ratio [95% CI]	Risk Ratio [95% CI]	Risk Difference [95% CI]
	n (%)	n (%)			
AEs	160 (55.9%)	143 (49.1%)	1.31 [0.95, 1.82]	1.14 [0.97, 1.33]	0.07 [-0.01, 0.15]
Mild	126 (44.1%)	114 (39.2%)	1.22 [0.88, 1.70]	1.12 [0.93, 1.37]	0.05 [-0.03, 0.13]
Moderate	21 (7.3%)	17 (5.8%)	1.28 [0.66, 2.47]	1.26 [0.68, 2.33]	0.02 [-0.03, 0.06]
Severe	1 (0.3%)	2 (0.7%)	0.51 [0.05, 5.62]	0.51 [0.05, 5.58]	0.00 [-0.02, 0.01]
Pre-TAEs	16 (5.6%)	10 (3.4%)	1.67 [0.74, 3.73]	1.63 [0.75, 3.53]	0.02 [-0.01, 0.06]
TEAEs	141 (49.3%)	119 (40.9%)	1.41 [1.01, 1.95]	1.21 [1.01, 1.45]	0.08 [0.00, 0.17]
PTAEs	45 (15.7%)	46 (15.8%)	0.99 [0.64, 1.56]	1.00 [0.68, 1.45]	0.00 [-0.06, 0.06]
ADRs	89 (31.1%)	64 (22.0%)	1.60 [1.10, 2.33]	1.41 [1.07, 1.87]	0.09 [0.02, 0.16]
TEAEs	79 (27.6%)	52 (17.9%)	1.75 [1.18, 2.61]	1.55 [1.13, 2.11]	0.10 [0.03, 0.17]
PTAEs	11 (3.8%)	13 (4.5%)	0.86 [0.38, 1.94]	0.86 [0.39, 1.89]	-0.01 [-0.04, 0.03]
SAEs	2 (0.7%)	5 (1.7%)	0.40 [0.08, 2.09]	0.41 [0.08, 2.08]	-0.01 [-0.03, 0.01]
TEAEs	2 (0.7%)	3 (1.0%)	0.68 [0.11, 4.08]	0.68 [0.11, 4.03]	0.00 [-0.02, 0.01]
PTAEs	0 (0.0%)	2 (0.7%)	0.20 [0.01, 4.23]	0.20 [0.01, 4.22]	-0.01 [-0.02, 0.00]
SADR	0 (0.0%)	0 (0.0%)	NE	NE	0.00 [0.00, 0.00]
AEs leading to tx discontinuation	9 (3.1%)	7 (2.4%)	1.32 [0.48, 3.59]	1.31 [0.49, 3.47]	0.01 [-0.02, 0.03]
TEAEs	10 (3.5%)	7 (2.4%)	1.47 [0.55, 3.92]	1.45 [0.56, 3.77]	0.01 [-0.02, 0.04]
AEs leading to death	0 (0.0%)	0 (0.0%)	NE	NE	0.00 [0.00, 0.00]

Source: Table ES.4 of submission executive summary.

Abbreviations: ADR adverse drug reaction; AE adverse event; BUF budesonide foam; BUS budesonide suppositories; IMP investigational medicinal product; pre-TAE pre-treatment adverse event; PTAE post-treatment adverse event; SADR serious adverse drug reaction; SAE serious adverse event; SFS safety set; TEAE treatment-emergent adverse event; tx treatment

Note: Treatment differences calculated post-hoc for the purposes of the submission

- 5.8 The TGA Clinical Evaluation Report (CER) stated that the results from study BUS-4/UCA overall demonstrate non-inferiority of the 4 mg budesonide suppository to the 2 mg foam enema and secondary endpoints were supportive of this result (p55, Budenofalk 4 mg suppositories, Round 2 CER).
- 5.9 The TGA CER also stated that the sponsor had emphasised the reduced systemic effects of budesonide in comparison to other corticosteroids but had not actually presented evidence of this. The sponsor advised it did not have access to pharmacodynamic data specifically related to prednisolone suppositories, though stated that budesonide is known to have significantly lower systemic bioavailability

compared to systemically active corticosteroids which is associated with a reduction in systemic exposure, potentially resulting in fewer systemic adverse events. The TGA accepted the sponsor’s response although it stated that without a direct comparison to prednisolone, direct comments on the difference in systemic effects are not able to be verified (p102, Budenofalk 4 mg suppositories, Round 2 CER).

5.10 As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

5.11 The submission claimed non-inferior comparative effectiveness and comparative safety of BUS compared with BUF.

Economic analysis

5.12 The submission presented a cost-minimisation approach of BUS compared with BUF.

5.13 The equi-effective doses were estimated as BUS 4 mg daily over 8 weeks and BUF 2 mg daily over 8 weeks.

5.14 The submission indicated that the equi-effective doses were made based on evidence from the BUS-4/UCA clinical trial regarding the duration of acute treatment.

5.15 The submission had requested the same approved ex-manufacturer price (AEMP) for BUS as the existing listing of BUF (Table 4).

Table 4: Cost minimisation approach

Row	Parameter	Input	Source / calculation
BUF (PBS 10034D)			
A	Price (AEMP) per pack	\$127.07	https://www.pbs.gov.au/info/industry/pricing/ex-manufacturer-price (April 2024)
B	Units per pack	28	https://www.pbs.gov.au/medicine/item/10034D
C	Units per course	56	Equi-effective dose: 2 mg daily for 8 weeks
D	Packs per patient	2.00	C/B
E	Cost per unit	\$4.54	A/B
F	Cost per course (AEMP)	\$254.14	C*E
BUS			
G	Units per pack	30	Proposed pack size
H	Units per course	56	Equi-effective dose: 4 mg daily for 8 weeks
I	Packs per patient	1.87	H/G
J	Cost per unit	\$4.54	F/H
K	Cost per course	\$254.14	H*J
L	Cost (AEMP) per pack	\$127.07	K/I (Rounding up no. of packs to account for wastage)

Source: Table 28 of the submission main body.

Abbreviations: AEMP, ex-manufacturer price; BUS, budesonide suppository; BUF, budesonide foam; CMA, cost-minimisation analysis

5.16 In the context of the cost-minimisation approach taken by the submission, a further consideration for the PBAC is that, under Section 101(3B) of the *National Health Act 1953*, the PBAC could only recommend listing BUS at a higher price than the alternative therapy or therapies if it is satisfied that it provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies. The pre-PBAC response presented a revised pricing scenario for BUS, incorporating all of the alternative PBS-listed rectally administered

corticosteroids, with the relative weightings determined using PBS/RPBS utilisation data for the 2023/2024 financial year (Table 5). The weighted cost-minimisation price (AEMP) equated to \$118.77. The pre-PBAC response cited the PBAC’s consideration of oral budesonide (Entocort®) in July 2018 as a precedent for a weighted comparator approach, however the pre-PBAC response did not provide a clinical justification for using the approach (Entocort®; July 2018 PSD).

Table 5: Comparison of PBS-listed rectally administered intestinal anti-inflammatory corticosteroids

Medicine (form)	Item code	Max Qty (packs)	Max Qty (units)	Equi-effective daily doses ^c	Dose/day	Treatment days / pack	AEMP (\$)	DPMQ (\$)	AEMP/day (\$)	Weighting ^d
budesonide 4 mg suppository, 30 ^a	NEW	1	1	-	QD 4 mg	30	118.77	151.92	3.96	N/A
budesonide 2 mg/application foam, 2 x 14 applications ^a	10034D	1	1	2 mg QD	QD 2 mg	28	127.07	151.92	4.54	47.9%
prednisolone (as sodium phosphate) 20 mg/100 mL enema, 7 x 100 mL ^a	1920C	4	28	20 mg QD	QD 20 mg	7	38.54	182.51	5.51	23.8%
					BID 40 mg	3.5			11.01	
prednisolone (as sodium phosphate) 5 mg suppository, 10 ^b	2554K	3	3	5 mg BID	QD 5 mg	10	8.46	40.77	0.85	28.2%
					BID 10 mg	5			1.69	
hydrocortisone acetate 10% enema, 21.1 g ^b	1502C	2	2	1 app QD	1 app QD 1.5 g	14	13.76	43.05	0.98	0.2%
					1 app BID 3 g	7			1.97	

Source: PBS website, September 2024 Ex-manufacturer spreadsheet. Compiled during the evaluation and Table 2 of pre-PBAC response
Abbreviations: AEMP = approved ex-manufacturer price, DPMQ = dispensed price for maximum quantity, QD = once daily, BID = twice daily

^a unrestricted benefit

^b restricted benefit for the treatment of proctitis and ulcerative colitis

^c Equi-effective doses are as per Table 5 of the Submission Overview.

^d Weighting is determined using the relative days of treatment utilisation

5.17 As a Category 4 submission, the economic analysis has not been independently evaluated.

Estimated PBS usage and financial implications

5.18 Table 6 presents the estimated extent of use, cost of BUS to the PBS/RPBS and the net financial implications to the PBS/RPBS and. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

5.19 The submission adopted a market share approach to estimate the utilisation and financial impact of listing BUS. The submission determined the utilisation of BUS by using the PBS utilisation data for BUF (PBS item: 10034D), which includes data from patients with distal ulcerative colitis and not only ulcerative proctitis due to the unrestricted Benefit PBS listing of BUF.

- 5.20 The submission estimated approximately 30% of BUF usage is in patients with ulcerative proctitis (UP) based on previous studies.^{2 3}
- 5.21 The submission estimated the proportion of BUS prescriptions in the overall rectal budesonide market for UP (BUS vs BUF) would increase to approximately 60% by year 3 and subsequently stabilise (Table 6).
- 5.22 The submission estimated 5,000 to < 10,000 BUS scripts would be supplied over the first six years of listing (500 to < 5,000 in Year 1 and 500 to < 5,000 in Year 6).
- 5.23 The submission used ABS data for the population growth rate for adults to estimate the annual rate of growth. As BUF has been PBS-listed since 2014, historic PBS-data should be used to calculate the forward estimates for annual growth.
- 5.24 The submission claimed the cost to PBS/RPBS for listing BUS would be offset by the cost savings resulting from its substitution with BUF and would result in nil net financial impact to the PBS/RPBS.

Table 6: BUS utilisation and net financial impact to the PBS/RPBS

Parameter	2025	2026	2027	2028	2029	2030
Impact on utilisation						
Estimated BUF script volume	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Proportion attributed to UP	30%	30%	30%	30%	30%	30%
Proportion replaced by BUS	40%	50%	60%	60%	60%	60%
BUS scripts proposed	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
BUF scripts substituted	-█ ²	-█ ²	-█ ²	-█ ²	-█ ²	-█ ²
Financial impact of BUS						
BUS total costs	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³
Less co-payments	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴
Net cost to PBS/RPBS	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³
Replaced BUF costs	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴
Less co-payments	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³
Net cost to PBS/RPBS	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴	-█ ⁴
Overall net cost to PBS/RPBS	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³

Source: Table 29 of submission main body

Abbreviations: BUF, budesonide foam; BUS, budesonide suppository; PBS, Pharmaceutical Benefits Scheme; RPBS, Repatriation Pharmaceutical Benefits Scheme; UP, ulcerative proctitis

The redacted values correspond to the following ranges:

¹ 5,000 to < 10,000

² 500 to < 5,000

³ \$0 to < \$10 million

⁴ net cost saving

- 5.25 The pre-PBAC response presented revised utilisation and financial estimates using historic PBS data for BUF to linearly extrapolate and calculate the annual growth forward estimates. This resulted in a slight increase in script volume of BUS over the

² Fumery et al., 2018. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. Clin Gastroenterol Hepatol. 2018 Mar;16(3):343-356.e3. doi: 10.1016/j.cgh.2017.06.016. Epub 2017 Jun 16. PMID: 28625817; PMCID: PMC6658168.

³ Ng et al., 2013. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. Gastroenterology. 2013 Jul;145(1):158-165.e2. doi: 10.1053/j.gastro.2013.04.007. Epub 2013 Apr 9. PMID: 23583432.

first six years of listing (500 to < 5,000 vs 500 to < 5,000 in Year 1 and 500 to < 5,000 vs 500 to < 5,000 in Year 6; Table 7).

Table 7: Revised BUS utilisation and net financial impact to the PBS/RPBS

Parameter	2025	2026	2027	2028	2029	2030
Impact on utilisation						
Estimated BUF script volume	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Proportion attributed to UP	30%	30%	30%	30%	30%	30%
Proportion replaced by BUS	40%	50%	60%	60%	60%	60%
BUS scripts proposed	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
BUF scripts substituted	-█ ²	-█ ²	-█ ²	-█ ²	-█ ²	-█ ²

Source: Table 3 of pre-PBAC response

Abbreviations: BUF, budesonide foam; BUS, budesonide suppository; UP, ulcerative proctitis

The redacted values correspond to the following ranges:

¹ 5,000 to < 10,000

² 500 to < 5,000

- 5.26 The submission assumed that BUS is expected to only substitute for BUF, and did not consider any substitution from other PBS-listed rectal corticosteroids. However, in its pre-PBAC response, the sponsor provided the net financial implication of BUS listing if each of the three main comparators were 100% substituted (Table 8).
- 5.27 The revised cost model estimated the proposed listing would result in a cost of \$0 to < \$10 million to the PBS/RPBS over six years (\$0 to < \$10 million in Year 1 to \$0 to < \$10 million in Year 6).

Table 8: Net financial implications of BUS listing depending on which comparator is substituted (at the revised price)

Parameter	2025	2026	2027	2028	2029	2030
BUS utilisation						
BUS scripts proposed	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
Net cost to PBS/RPBS (at revised DPMQ of \$142.55 less copay ^a)	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²
If BUF is the only product substituted						
BUF scripts substituted (1:1)	-■ ¹	-■ ¹	-■ ¹	-■ ¹	-■ ¹	-■ ¹
BUF expenditure substituted (\$123.69 per script net of copay)	■ ³	■ ³	■ ³	■ ³	■ ³	■ ³
Net financial implications of BUS	■ ³	■ ³	■ ³	■ ³	■ ³	■ ³
If prednisolone enema is the only product substituted						
Prednisolone enema scripts substituted (1:1)	-■ ¹	-■ ¹	-■ ¹	-■ ¹	-■ ¹	-■ ¹
Prednisolone enema expenditure substituted (\$154.28 per script net of copay)	■ ³	■ ³	■ ³	■ ³	■ ³	■ ³
Net financial implications of BUS	■ ³	■ ³	■ ³	■ ³	■ ³	■ ³
If prednisolone suppository is the only product substituted						
Prednisolone suppository scripts substituted (2:1)	-■ ¹	-■ ¹	-■ ¹	-■ ¹	-■ ¹	-■ ¹
Prednisolone suppository expenditure substituted (\$12.54 per script net of copay)	■ ³	■ ³	■ ³	■ ³	■ ³	■ ³
Net financial implications of BUS	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²

Source: Table 4 of pre-PBAC response

Abbreviations: BUF, budesonide foam; BUS, budesonide suppository; PBS, Pharmaceutical Benefits Scheme; RPBS, Repatriation Pharmaceutical Benefits Scheme; DPMQ = dispensed price for maximum quantity

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² \$0 to < \$10 million

³ net cost saving

5.28 As a Category 4 submission, the financial estimates have not been independently evaluated.

6 PBAC Outcome

6.1 The PBAC recommended the General Schedule unrestricted benefit listing of budesonide 4 mg suppository (BUS) under the same circumstances as the PBS-listed budesonide foam (rectal foam 2 mg per application, 14 applications, aerosol 16.8 g, 2; BUF). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of BUS would be acceptable if it were cost-minimised to the lowest cost comparator on a cost per day basis.

6.2 The PBAC noted the submission requested the listing of BUS under the same conditions as the existing listing for BUF, with a maximum number of 3 repeats. The PBAC considered that this was appropriate.

6.3 The PBAC noted the submission nominated BUF as the main comparator. The PBAC also noted other PBS-listed rectal corticosteroids (prednisolone (as sodium phosphate) 20 mg/100 mL enema, 7 x 100 mL, prednisolone (as sodium phosphate)

5 mg suppository, 10, and hydrocortisone acetate 10% enema, 21.1) and considered these were also relevant comparators.

- 6.4 The PBAC advised the equi-effective daily doses were:
- BUS 4 mg: BUF 2 mg: prednisolone enema 20 mg: prednisolone suppository 10 mg
- 6.5 The PBAC noted that the TGA Clinical Evaluation Report (CER) stated that the results from study BUS-4/UCA overall demonstrated non-inferiority of BUS to BUF, and secondary endpoints were supportive of this result. The PBAC therefore considered that the submission’s claim of non-inferior comparative effectiveness and safety was appropriate.
- 6.6 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because BUS is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over BUF, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
BUDESONIDE					
budesonide 2 mg/application foam, 2 x 14 applications	10034D	1	1	3	Budenofalk
budesonide 4 mg suppository, 30	NEW	1	30	3	
Benefit Type: Unrestricted					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners				
	Restriction Type: Unrestricted				
	Administrative Advice: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				

*Pending the PBAC outcome of its November 2024 review of PBS items for prescribing by nurse practitioners and endorsed midwives; the subset of PBS listings for Nurse Practitioner prescribing – Continuing Therapy Only review.

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor welcomes the PBAC's recommendation, however, is unable to pursue a PBS listing at this time due to the PBAC's nominated comparator (prednisolone suppositories) being only one of the several identified by DUSC as currently approved and prescribed products by Australian doctors and used in the treatment of ulcerative proctitis. This has resulted in a proposed price for BUS, based on the associated cost effectiveness calculation, which is not commercially viable.