

5.10 BUDESONIDE

Enteric capsule 3 mg, Budenofalk®, Orphan Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission sought an Authority Required (STREAMLINED) listing for budesonide enteric capsules (Budenofalk from herein) for the treatment of mild to moderate Crohn’s disease (CD) affecting the ileum and/or the ascending colon.

2 Requested listing

- 2.1 The submission sought the same listing as budesonide (Entocort) (Entocort from herein) which the PBAC recommended for listing in July 2018. The submission did not provide proposed restrictions. The following restrictions were recommended by the PBAC in July 2018 for Entocort (budesonide (Entocort) Public Summary Document (PSD), p17).
- 2.2 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction Manner of administration and form	Max. Qty	№. of Rpts	Dispensed Price for Max. Qty (DPMQ)	Proprietary Name and Manufacturer
BUDESONIDE 3 mg enteric capsule	90	21	\$ [REDACTED]	Budenofalk® Orphan Australia Pty Ltd

Category/Program	Section 85 (general schedule)
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
Severity:	Mild to moderate
Condition:	Crohn disease
PBS Indication:	Mild to moderate Crohn disease
Restriction:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must affect the ileum, OR The condition must affect the ascending colon, OR The condition must affect the ileum and ascending colon.
Prescriber Instructions	The total duration of therapy should be no more than 42 10 weeks in any single course.

Administrative Advice	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.
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Secretariat comments on the restriction

- 2.3 The number of repeats for Budenofalk should be changed from two repeats to one repeat. The recommended dose for adults and the elderly is 9 mg budesonide once daily in the morning or 3 mg budesonide three times daily. A script with one repeat will allow sufficient treatment for eight weeks, the approved treatment duration for Budenofalk for acute CD. The pre-PBAC response noted that this calculation did not take into account the two-week tapering period. Based on the approved Product Information (PI) for Budenofalk, the treatment course would require 189 capsules altogether [(3 capsules x 8 weeks) + (2 capsules x 1 week) + (1 capsule x 1 week)]. The PBAC considered the maximum repeat should remain at two repeats as originally requested.
- 2.4 The approved PI for Budenofalk states that it should be used for acute CD for up to 10 weeks (8 weeks treatment + 2 weeks tapering), whereas Entocort should be used no more than 12 weeks in a single course. The prescribing instructions for Entocort states, “The total duration of therapy should be no more than 12 weeks in any single course.” The PBAC considered that, if both drugs are listed, each restriction should state the respective recommended maximum duration of therapy.
- 2.5 The PBAC previously recommended that Entocort be included as one of the prior systemic therapies that need to be failed prior to qualifying for subsidy of a biological medicine for severe CD. The PBAC noted that the flow-on restriction changes needed to be developed for this including the appropriate dose and duration of treatment with budesonide (paragraph 7.12, item 7.11 budesonide July 2018 PSD). The PBAC considered this flow-on should also be applied to Budenofalk.
- 2.6 The PBAC is asked to advise, under Section 101 (4AACD) of the *National Health Act*, if Budenofalk and Entocort should be considered equivalent for the purposes of substitution (i.e. ‘a’ flagged in the Schedule). The Secretariat noted that Budenofalk and Entocort have different capsule formulations. Budenofalk is described as an enteric capsule in the approved Product Information (PI) (p1). Entocort is described as a “hard gelatine capsule filled with gastric acid-resistant, prolonged release granules for oral use. The granules are practically insoluble in gastric juice and have prolonged release properties adjusted to release budesonide in the ileum and the ascending colon” (Entocort approved PI, p1). The submission noted that the different formulation of Budenofalk and Entocort resulted in the two drugs having different drug release profiles and surface area coverage. The submission claimed that Budenofalk was more specifically targeted and provided greater coverage in the distal small intestine, suggesting the budesonide concentration in the ileocecal region from Budenofalk would be higher than Entocort. However, the submission noted that there is no data available on the clinical effect resulting from these differences in

formulation. The submission did not indicate if Budenofalk and Entocort should be considered bioequivalent.

- 2.7 The Secretariat noted that the requested restriction is simple as it is based on an existing restriction.

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

3 Background

- 3.1 Budenofalk was TGA registered on 12 June 2012 for induction of remission in patients with mild to moderately active CD affecting the ileum and/or the ascending colon.
- 3.2 Budesonide in this presentation has not been considered by the PBAC previously.
- 3.3 Budenofalk is currently listed on the PBS in the presentation of a foam enema as an unrestricted benefit listing for ulcerative colitis.

4 Population and disease

- 4.1 The clinical place of Budenofalk in mild to moderate CD is likely to be in the first or second line treatment of mild to moderate CD. This is the same clinical place in therapy that was accepted in the consideration of Entocort in November 2017.

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

5 Comparator

- 5.1 The minor submission nominated Entocort as the main comparator. The PBAC considered this to be appropriate as it is a near market competitor.
- 5.2 Entocort, in the form of a modified release capsule, was considered by the PBAC at its November 2017 meeting and July 2018 meeting. The PBAC recommended the listing of Entocort in July 2018 on a cost-minimisation basis against a weighted mixed comparator of mesalazine and prednisolone. The PBAC did not agree that the calculation of the weighted price presented in the minor resubmission was appropriate. The PBAC considered that, unless more robust current data becomes available, a weighting that allows for one-fifth to one quarter, but closer to one-fifth, of use in which mesalazine is the alternative therapy may be more appropriate, with the corresponding weighting for prednisolone applied accordingly (paragraph 7.4, budesonide (Entocort) Public Summary Document (PSD), July 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 an individual (1) via the Consumer Comments facility on the PBS website. The comment described that the condition had a significantly large impact on their life when it advanced from mild to moderate disease including more hospital stays and day procedure visits. The comment described benefits with being treated with budesonide including it being able to control flare-ups and it had less side effects compared to prednisolone. Cost was also identified in the comment as a significant factor for this condition.
- 6.3 The PBAC noted the consumer comment highlighted the clinical need for treatment options in mild to moderate CD.

Clinical trials

- 6.4 As a minor submission, no clinical trials were presented in the submission.

Economic analysis

- 6.5 The minor presented a cost-minimisation approach against Entocort.
- 6.6 The submission could not take into account the pricing arrangement for Entocort, as the information is not publicly available. Therefore, the submission based its projections for Entocort on the budesonide (Entocort) PSD from the July 2018 meeting.
- 6.7 The submission proposed an AEMP of \$ [REDACTED] for Budenofalk. The prices of the mixed comparators for Entocort, mesalazine and prednisolone, were used to estimate the price for Budenofalk. The submission expressed the sponsor's willingness to consider an alternative pricing offer if a positive PBAC recommendation was received.
- 6.8 No equi-effective dose was nominated by the submission. The PBAC considered that Budenofalk was non-inferior in terms of comparative effectiveness and safety to Entocort and therefore considered that the equi-effective doses to be:
- Budenofalk® brand of budesonide 9 mg/day for 8 weeks followed by 6 mg/day for 1 week, and then 3 mg/day for 1 week;
 - Entocort® brand of budesonide 9 mg/day for 9 weeks followed by 4.5 mg/day for 3 weeks;
 - Pentasa® brands of mesalazine 4 g/day for 12 weeks;
 - Salofalk® brands of mesalazine 4.5 g/day for 8 weeks followed by a 3 g/day for 4 weeks; and
 - prednisolone 25 mg/day for 8 weeks followed by 5 mg/day for 4 weeks.

Drug cost/patient/course

6.9 The estimated drug cost/patient/course would be \$ [REDACTED], based on a 10 week course of Budenofalk which includes 2 weeks of tapering treatment and also accounts for wastage (DPMQ= \$ [REDACTED] * 3 packs).

Estimated PBS usage & financial implications

6.10 Table 3 presents the estimated use and financial implications of Budenofalk. The submission stated that there would be no financial implications to the PBS given that Budenofalk and Entocort had the same indication and dosing. The total patient estimates in the submission were based on assumptions used in the Entocort consideration from July 2018 and the estimated patient growth rate was from ABS data.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated script volume - PBS	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Estimated script volume - RPBS	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Estimated volume of proposed medicine	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Less co-payments	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Cost to RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Less co-payments	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net cost to RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

Source: Sheet 3c. Impact – EFF of Budesonide (BUDENOFALK) Utilisation and Cost Model.xlsx provided in the submission.

The redacted table shows that at Year 6, the estimated number of prescriptions was 10,000 to 50,000 and the net cost to the PBS/RPBS would be less than \$10 million.

6.11 The treatment duration of Budenofalk did not appear to have been taken into account when calculating the financial estimates. The financial implication of Budenofalk may be less than Entocort given the approved treatment duration of Budenofalk (10 weeks) is shorter than Entocort (12 weeks). The financial implication provided in the submission showed a net cost to the PBS/RPBS.

6.12 As a minor submission, the financial estimates have not been independently evaluated.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of budesonide (Budenofalk) for treatment of mild to moderate CD affecting the ileum and/or the ascending colon. The PBAC recommended the listing on a cost minimisation basis against budesonide (Entocort), which was recommended for listing in July 2018 based on the mixed comparator of mesalazine and prednisolone.
- 7.2 The PBAC noted the consumer comment from an individual that highlighted the clinical need for treatment options in mild to moderate CD.
- 7.3 The PBAC accepted the clinical place of Budenofalk in mild to moderate CD is likely to be in the first or second line treatment of mild to moderate CD, which was accepted in the consideration of Entocort in November 2017.
- 7.4 The PBAC accepted the nomination of Entocort as the main comparator as it is clinically considered a near market competitor.
- 7.5 The PBAC considered that Budenofalk was non-inferior in terms of comparative effectiveness and safety to Entocort. Therefore, the PBAC considered the equi-effective doses to be:
- Budenofalk® brand of budesonide 9 mg/day for 8 weeks followed by 6 mg/day for 1 week, and then 3 mg/day for 1 week;
 - Entocort® brand of budesonide 9 mg/day for 9 weeks followed by 4.5 mg/day for 3 weeks;
 - Pentasa® brands of mesalazine 4 g/day for 12 weeks;
 - Salofalk® brands of mesalazine 4.5 g/day for 8 weeks followed by a 3 g/day for 4 weeks; and
 - prednisolone 25 mg/day for 8 weeks followed by 5 mg/day for 4 weeks.
- 7.6 The PBAC recalled its recommendation for Entocort from its July 2018 meeting where it recommended the weighted average price of Entocort to be calculated as one-fifth to one quarter, but closer to one-fifth of use in which mesalazine is the alternative therapy, with the corresponding weighting for prednisolone applied accordingly. Therefore, the PBAC considered that the price of Budenofalk should be calculated using the same methodology.
- 7.7 The PBAC considered the requested maximum repeats of 2 and maximum quantity of 90 capsules to be appropriate.
- 7.8 The PBAC noted that Budenofalk has a 10-week treatment duration (which includes a 2-week tapering period) which is different to Entocort that has a 12-week treatment duration (which includes a 2-4 week tapering period). Therefore, the PBAC considered that, if both drugs were listed, each restriction should state the respective recommended maximum duration of therapy in the prescriber instructions.
- 7.9 The PBAC recalled that there were significant uncertainties in the likely use of budesonide or lower levels of mesalazine substitution than predicted when it

considered the listing of Entocort in July 2018. The PBAC was of the view that a risk sharing agreement is required to manage these uncertainties, set at the level of the projected utilisation of budesonide. The PBAC was therefore of the view that listing Budenofalk would attract the same uncertainty.

- 7.10 The PBAC recommended that budesonide should be included as one of the prior systemic therapies that need to be failed prior to qualifying for subsidy of a biological medicine for severe CD (paragraph 7.12, item 7.11 budesonide July 2018 PSD). The PBAC noted that the flow-on restriction changes need to be developed for this including the appropriate dose and duration of treatment with the Budenofalk and Entocort brands of budesonide.
- 7.11 The PBAC advised the Minister that it considered under Section 101 (4AACD) of the *National Health Act*, that Budenofalk and Entocort brands of budesonide could be considered equivalent for the purposes of substitution by the pharmacist at the point of dispensing (i.e. 'a' flagged in the Schedule), as the active ingredient is designed to work locally in the small intestine and colon so the formulation differences are not expected to result in differences in outcomes.
- 7.12 The PBAC advised that budesonide is suitable for prescribing by nurse practitioners, which is consistent with its advice for Entocort.
- 7.13 The PBAC recommended that the Early Supply Rule should not apply, which is consistent with its recommendation for Entocort.
- 7.14 The submission is not eligible for an Independent Review, because the PBAC has 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
BUDESONIDE 3 mg enteric capsule	90	2	Budenofalk® Orphan Australia Pty Ltd

Category/Program	Section 85 (general schedule)
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
Severity:	Mild to moderate
Condition:	Crohn disease
PBS Indication:	Mild to moderate Crohn disease

Restriction:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must affect the ileum, OR The condition must affect the ascending colon, OR The condition must affect the ileum and ascending colon.
Prescriber Instructions	The total duration of therapy should be no more than 10 weeks in any single course.
Administrative Advice	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.

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 acknowledges the positive recommendation of PBAC and its acceptance of the clinical place for Budenofalk as a first line treatment for mild to moderate Crohns Disease, to improve the Quality of Life outcomes for patients affected by this condition.