

An addendum has been included at the end of the public summary document.

**6.16 BUDESONIDE,
Tablet 500 micrograms (orally disintegrating),
Tablet 1 mg (orally disintegrating),
Jorveza[®],
Dr Falk Pharma Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 3 submission requested changes to the current PBS listings of budesonide orally disintegrating tablets (BOT) 500 micrograms and 1 mg for the treatment of eosinophilic oesophagitis (EoE) to:
- remove the requirement for a histological assessment (endoscopy) to determine treatment response/eligibility for continuing treatment, and subsequently consolidate the first and subsequent continuing treatment phase listings.
 - expand the treatment criteria from ‘Must be treated by a gastroenterologist’ to include being treated by a physician or surgeon experienced in the diagnosis and management of EoE.
- 1.2 The submission also requested advice from the PBAC about the Prescribing Instruction on the optimal number of biopsies to increase diagnostic sensitivity in the Initial treatment – Induction of remission listing, and whether it should be removed (or a clarification included) to avoid it being enforced when determining patient eligibility under this PBS restriction.

2 Background

- 2.1 Budesonide 500 micrograms and 1 mg orally disintegrating tablets (BOT 0.5 mg and BOT 1 mg, respectively) are currently listed on the PBS as Authority Required (telephone/online) listings for the treatment of EoE. BOT 1 mg (90 tablets) is PBS listed for initial induction treatment, while BOT 0.5 mg and 1 mg (60 tablets) are PBS listed for continuing maintenance treatment.
- 2.2 The submission stated that Jorveza[®] is a novel mode of treatment and has been specifically designed to efficiently deliver the active drug to the oesophageal mucosa.¹

¹ Miehke S, Lucendo AJ, Straumann A, et al (2020) ‘Orodispersible budesonide tablets for the treatment of eosinophilic esophagitis: a review of the latest evidence’, *Therapeutic Advances in Gastroenterology*, 13:175628482092782, doi:10.1177/1756284820927282

Request to remove requirement for histological assessment (endoscopy) for continuing treatment

- 2.3 The current PBS criteria state ‘Applications for initial treatment with BOT must be received within 12 weeks of endoscopy/biopsy.... A histologic assessment of the oesophageal biopsy should be planned for approximately 8 weeks after the initiation of the first PBS-subsidised treatment with this drug under this restriction, and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to determine the patient’s eligibility for continuing therapy and to avoid an interruption to supply.’
- 2.4 The initial submission, considered by the PBAC in March 2021, proposed two listing options for BOT 1 mg: a ‘simple’ restriction that did not specify histological assessment criteria for continuing treatment, and ‘a more complex option comprising evaluation of response to initial treatment, first continuing treatment, and subsequent continuing treatment criteria. The PBAC agreed with the ESC² that the proposed ‘simple’ restriction was inconsistent with the clinical evidence presented and TGA³ dose recommendation in that it would allow all patients to continue treatment regardless of whether they achieved remission or not.’ (paragraph 3.1, budesonide, Public Summary Document (PSD), March 2021 PBAC meeting). The submission stated that feedback sought by the sponsor from local clinical experts following the PBAC’s March 2021 and November 2021 considerations indicated that a ‘complex’ restriction may be feasible/workable in clinical practice and therefore agreed to listing based on this advice.
- 2.5 The submission stated the following concerns had been raised by clinicians since PBS listing of BOT regarding the requirement for a follow-up endoscopy:
- some patients had difficulty obtaining follow-up endoscopies/biopsies 8-10 weeks after the initial endoscopy. This was especially prevalent in the public sector, with some hospitals unable to schedule endoscopies for up to 12 months or longer. This limited the treatment of patients who may be eligible and could benefit from treatment with BOT.
 - in other cases, patients were undergoing induction of remission treatment with BOT, but then were forced to cease treatment as they were unable to access a repeat endoscopy to confirm treatment response within the prescribed timeframe of the listing. The submission stated that this increases the risk of patients relapsing and experiencing adverse sequelae, such as becoming less responsive to pharmacologic treatment or requiring frequent and urgent endoscopic intervention for food bolus extraction and/or dilatation, increasing demand on public system resources.

² Economics Sub-Committee

³ Therapeutic Goods Administration

- 2.6 The submission concluded that it was too early to accurately identify limitations on patients transitioning to continuing treatment through PBS data. The submission provided available PBS data on the number of initial and continuing treatment prescriptions for BOT from initial listing in May 2022 until August 2022. It was assumed that the majority of continuing treatment reflected patients treated under the grandfather treatment listing as the PBS data reflected 4 months of BOT use on the PBS, consistent with the approximate treatment length during the initial treatment phase.
- 2.7 The submission stated that the majority of patients ($\geq 85\%$) with EoE are expected to achieve clinical and/or histological remission after 12 weeks of treatment with BOT, as supported by data from the pivotal induction of remission clinical trial (EOS-1). This trial found that treatment with BOT 1 mg twice daily induced histological remission in 93.2% of patients after 6 weeks, with clinical and clinicohistologic remission achieved in 86.4% and 84.7% of patients, respectively, after a total of 12 weeks of treatment (consistent with the duration of induction treatment in the current PBS listing). The submission therefore proposed that a resolution of clinical symptoms provides an alternative measure for treatment response in patients with EoE receiving BOT and anticipated a relatively low risk of use beyond the intended population if the requirement for follow-up endoscopy were removed. Specific criteria to evaluate clinical response were not provided, as the rating scale used in the clinical trials for BOT for the assessment of EoE symptom severity is not used in routine clinical practice.
- 2.8 The submission noted the following recommendations made by the PBAC for treatments for ulcerative colitis (UC), and stated that these recommendations differed from the primary endpoints in the associated clinical trials which included the endoscopy subscore:
- ‘With respect to the use of a partial Mayo score to identify eligible patients and/or to assess responders, the PBAC agreed that patients and clinicians are unlikely to use endoscopy on a regular basis in order to assess mucosal healing as required by the full Mayo score. The PBAC therefore accepted the use of a partial Mayo score in the PBS restriction.’ (Section 4, infliximab, PSD, March 2014 PBAC Meeting).
 - ‘The PBAC agreed with the Drug Utilisation Sub-Committee (DUSC) that there may be use of adalimumab beyond the restriction in patients who achieve a partial response but do not meet the specified continuation criteria, with use of the partial Mayo score (which does not require endoscopy) rather than the full Mayo score. The PBAC agreed with the Pre-Sub-Committee Response (PSCR) that it is not appropriate to undertake a second endoscopy to determine response to adalimumab.’ (Section 4, adalimumab, PSD, November 2013 PBAC Meeting).

Request to expand the list of eligible prescribers

- 2.9 The current treatment criteria for initial and first continuing treatment PBS listings for BOT state that patients must be treated by a gastroenterologist. The submission stated that the rationale for this requirement was based on the premise that endoscopic assessment is required to confirm eligibility for the initial and continuing treatment phases with BOT. The subsequent continuing treatment listing states that patients must be treated by a gastroenterologist or in consultation with a gastroenterologist.
- 2.10 The submission stated that the sponsor has been informed of situations where non-gastroenterologist physicians and/or surgeons (particularly in rural and remote locations) are accredited to perform endoscopies/biopsies and are experienced in the diagnosis and management of patients with EoE, however are currently unable to prescribe BOT through the PBS. The submission stated that this commonly occurs in areas where the closest gastroenterologist may be hundreds to thousands of kilometres away, and therefore inaccessible to most patients with EoE in that area.
- 2.11 The submission claimed that including non-gastroenterologist medical practitioners who are experienced in the diagnosis and management of EoE as prescribers is consistent with the information provided in the Jorveza Product Information (PI). The PI states ‘the treatment with this medicinal product should be initiated by a physician experienced in the diagnosis and treatment of eosinophilic oesophagitis.’
- 2.12 The submission stated that provisions are included in the PBS treatment criteria for medicines for other gastrointestinal conditions to allow treatment by non-gastroenterologist surgeons who specialise in the upper gastrointestinal tract/gastroenterology, and cited the following examples:
- pantoprazole 40 mg enteric tablets (PBS item code 12277E) for complex gastro-oesophageal reflux disease (GORD): the treatment criteria states ‘Must be treated by a gastroenterologist; OR Must be treated by a surgeon with expertise in the upper gastrointestinal tract; OR Must be treated by a medical practitioner who has consulted at least one of the above mentioned specialists in relation to this current PBS benefit being sought, with the specialist’s name documented in the patient’s medical records for auditing purposes....’
 - tofacitinib 5 mg tablets (PBS item code 12556W) for moderate to severe UC: the treatment criteria states ‘Must be treated by a gastroenterologist (code 87); OR Must be treated by a consultant physician [internal medicine specialising in gastroenterology (code 81)]; OR Must be treated by a consultant physician [general medicine specialising in gastroenterology (code 82)].’

Request for advice about the Prescribing Instruction on the optimal number of biopsies in the PBS restriction criteria

- 2.13 The submission noted the Prescribing Instructions in the Initial treatment listing for BOT state, ‘Diagnostic sensitivity increases with the number of biopsies and is optimised after taking at least eight biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction).’
- 2.14 The submission stated that this criterion was based on advice from an Australian expert and is more stringent than the procedure used in the clinical development program for BOT^{4,5} and those outlined in international guidelines.^{6,7} The submission stated that 6-8 biopsies from 2-3 oesophageal segments is generally recommended to achieve optimal sensitivity in the determination of eosinophil count.
- 2.15 The submission stated that the sponsor had received clinician feedback stating that a minimum of eight biopsies taken from the mid and distal segments has been used as a mandatory requirement for authorisation from Services Australia to prescribe BOT under the PBS restrictions. The submission stated that this appears to be a misinterpretation, as the PBS clinical criteria states that eosinophil count of at least 15 from only one high power field (i.e. from a single biopsy) is required. The sponsor understood that the purpose of this Prescribing Instruction was to provide guidance to the clinician to increase the probability of confirming active EoE.
- 2.16 Services Australia advised that the number of biopsies obtained during endoscopy is not currently assessed during the telephone authority application from prescribers. Services Australia further noted that the current wording of the Prescribing Instruction does not mandate a minimum number of biopsies collected during the endoscopy.

Registration status

- 2.17 BOT was TGA registered on 15 September 2020 for the treatment of EoE in adults.

Previous PBAC consideration

- 2.18 BOT 1 mg was previously considered for EoE by the PBAC at its March 2021 meeting. The PBAC did not recommend BOT for the treatment of EoE, and ‘considered PBS

⁴ Lucendo AJ, Molina-Infante J, Arias Á, et al (2017) ‘Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults’, *United European gastroenterology journal*, 5(3):335-58, doi: 10.1177/2050640616689525.

⁵ Straumann A, Katzka DA (2018) ‘Diagnosis and Treatment of Eosinophilic Esophagitis’, *Gastroenterology*, 154(2):346-359, doi: 10.1053/j.gastro.2017.05.066.

⁶ Dellon ES, Liacouras CA, Molina-Infante J, et al (2018) ‘Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference’, *Gastroenterology*, 155(4):1022-1033.e10, doi: 10.1053/j.gastro.2018.07.009.

⁷ Dhar A, Haboubi HN, Attwood SE, et al (2022) ‘British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults’, *Gut*, 71(8):1459-1487, doi: 10.1136/gutjnl-2022-327326.

listing for use in the maintenance therapy setting is beyond the maximum duration of treatment reflected in the current approved product information (PI). The PBAC considered the cost-effectiveness of induction therapy alone to be uncertain and the incremental cost-effectiveness ratio (ICER) for both induction and maintenance therapy to be high and uncertain at the proposed price.’ (paragraph 7.1, budesonide, PSD, March 2021 PBAC meeting).

- 2.19 BOT 0.5 mg and 1 mg were considered for the treatment of EoE by the PBAC at its November 2021 meeting. The PBAC recommended the Authority Required (immediate assessment) listing of BOT for EoE (paragraph 5.1, budesonide, PSD, November 2021 PBAC meeting).

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

3 Requested listing

- 3.1 The submission requested the following changes to the existing listing:
- 3.2 Amend existing listings as follows. Suggested additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough:

MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack					
BUDESONIDE					
budesonide 1 mg orally disintegrating tablet, 90	12994X	1	90	1	Jorveza
Restriction Summary / Treatment of Concept:					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Administrative Advice: Special Pricing Arrangements apply.				
Indication: Eosinophilic oesophagitis					
Treatment Phase: Initial treatment - Induction of remission					
Clinical criteria:					
Patient must have a history of symptoms of oesophageal dysfunction					
AND					
Clinical criteria:					

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	Patient must have eosinophilic infiltration of the oesophagus, demonstrated by oesophageal biopsy specimens obtained by endoscopy confirming the presence of at least 15 eosinophils in at least one high power field (hpf); corresponding to approximately 60 eosinophils per mm ² hpf
	AND
	Clinical criteria:
	Patient must not receive more than 90 days of treatment under this restriction
	Treatment criteria:
	Must be treated by <i>at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis</i>
	Prescribing Instructions: Applications for treatment of this condition must be received within 12 weeks of biopsy.
	Prescribing Instructions: Symptoms of oesophageal dysfunction include at least one of the following: dysphasia, odynophagia, transient or self-cleared food impaction, chest pain, epigastric discomfort, vomiting/regurgitation.
	Prescribing Instructions: Diagnostic sensitivity increases with the number of biopsies and <i>is can be optimised, if necessary, after</i> by taking at least eight biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction).
	Prescribing Instructions: A histologic assessment of the oesophageal biopsy should be planned for approximately 8 weeks after the initiation of the first PBS-subsidised treatment with this drug under this restriction, and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to determine the patient's eligibility for continuing therapy and to avoid an interruption to supply.

MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack					
BUDESONIDE					
budesonide 500 microgram orally disintegrating tablet, 60	12987M	1	60	5	Jorveza
budesonide 1 mg orally disintegrating tablet, 60	12982G	1	60	5	Jorveza
Remove Restriction Summary / Treatment of Concept					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Administrative Advice: Special Pricing Arrangements apply.				
Indication: Eosinophilic oesophagitis					

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	Treatment Phase: First continuing treatment – Maintenance of remission Confirmation of remission
	Clinical criteria:
	Patient must have previously received PBS-subsidised initial treatment with this drug for this condition; or
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the – Transitioning from non-PBS to PBS-subsidised treatment – Grandfather treatment restriction
	AND
	Clinical criteria:
	Patient must have documented evidence of having achieved histologic remission while receiving initial PBS-subsidised treatment with this drug for this condition, defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf), corresponding to less than 16 eosinophils per mm ² hpf on oesophageal biopsy
	Patient must have both demonstrated and sustained an adequate response to this drug for this condition, based on the clinical assessment of the treating doctor
	AND
	Clinical criteria:
	Patient must not receive more than 26 weeks of treatment under this restriction
	Treatment criteria:
	Must be treated by at least one of: by a (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) a medical practitioner in consultation with one of these prescribers
	Prescribing Instructions: Histologic assessment should be based on the peak eosinophils count derived from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction). The histologic assessment should, where possible, be performed by the same physician who confirmed the diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should be conducted and submitted after the patient has completed 8 weeks of the initial treatment course and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to avoid an interruption to supply. Where a histologic assessment is not undertaken and the results submitted, the patient will be not be eligible for ongoing treatment.
	Prescribing Instructions: The assessment of treatment response should, where possible, be performed by or in consultation with the same physician or surgeon who confirmed the diagnosis of eosinophilic oesophagitis in the patient.
Remove Restriction Summary /Treatment of Concept:	
	Indication: Eosinophilic oesophagitis
	Treatment Phase: Subsequent continuing treatment – Maintenance of remission
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the First continuing treatment restriction; or
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the Transitioning from non-PBS to PBS-subsidised treatment – Grandfather treatment restriction
	AND
	Clinical criteria:

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	The condition must not have progressed while being treated with this drug
	Treatment criteria:
	Must be treated by a gastroenterologist or in consultation with a gastroenterologist
Restriction Summary / Treatment of Concept:	
	Indication: Eosinophilic oesophagitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised treatment - Grandfather treatment
	Clinical criteria:
	Patient must have previously received non-PBS-subsidised treatment with a corticosteroid for this condition prior to 1 May 2022
	AND
	Clinical criteria:
	Patient must be receiving non-PBS treatment with a corticosteroid for this condition at the time of application
	AND
	Clinical criteria:
	Patient must have had, prior to commencement of non-PBS-subsidised treatment with a corticosteroid, a history of symptoms of oesophageal dysfunction
	AND
	Clinical criteria:
	Patient must have had, prior to commencement of non-PBS-subsidised treatment with a corticosteroid, eosinophilic infiltration of the oesophagus, demonstrated by oesophageal biopsy specimens obtained by endoscopy confirming the presence of at least 15 eosinophils in at least one high power field (hpf); corresponding to approximately 60 eosinophils per mm ² hpf
	AND
	Clinical criteria:
	Patient must have documented evidence that they are currently in histologic remission, where remission is defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf); corresponding to less than 16 eosinophils per mm ² hpf on oesophageal biopsy
	Treatment criteria:
	Must be treated by <i>at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis</i>
	Prescribing Instructions: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.
	Prescribing Instructions: Symptoms of oesophageal dysfunction include at least one of the following: dysphasia, odynophagia, transient or self-cleared food impaction, chest pain, epigastric discomfort, vomiting/regurgitation.

	<p>Prescribing Instructions:</p> <p>Histologic assessment should be based on the peak eosinophils count derived from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction).</p> <p>The histologic assessment should, where possible, be performed by the same physician who confirmed the diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should have been conducted after the patient has completed 8 weeks of the initial treatment course and no later than 2 weeks prior to the patient completing the initial treatment course, to avoid an interruption to supply. Where a histologic assessment is not undertaken and the results submitted, the patient will not be eligible for ongoing treatment.</p>
	<p>Prescribing Instructions:</p> <p><i>The assessment of treatment response should, where possible, be performed by or in consultation with the same physician or surgeon who confirmed the diagnosis of eosinophilic oesophagitis in the patient.</i></p>
	<p>Administrative Advice:</p> <p>This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>

- 3.3 The sponsor’s pre-PBAC response agreed with the suggested revised wording for the Prescribing Instruction on the optimal number of biopsies, stating that it provided additional clarity on this matter.

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

4 Consideration of the evidence

- 4.1 The submission provided 2 testimonials from clinicians to support the request for expansion of eligible prescribers to include physicians or surgeons experienced in the diagnosis and management of EoE. The submission further stated that the sponsor has received confirmation from the Gastroenterological Society of Australia that there are a number of non-gastroenterologist physicians/surgeons who have successfully completed endoscopy accreditation in Australia.
- 4.2 The submission provided one testimonial from a clinician expressing concern that the current PBS restriction criteria for BOT could result in potentially unnecessary endoscopic procedures.

Sponsor hearing

- 4.3 There was no hearing for this item.

Consumer comments

- 4.4 The PBAC noted and welcomed the input from health care professionals (19) and organisations (3) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with BOT for EoE, including that it is a highly effective medication, has greater efficacy and ease of use compared to alternative treatments, and that it is well tolerated and has a good safety profile.

Comments were also received about the current requirement for a follow-up endoscopy, including that it is difficult to schedule a repeat endoscopy in the public sector, with several comments suggesting a longer timeframe for a follow-up endoscopy (e.g. within 6 to 12 months of commencing treatment) would be appropriate. Other comments cited concerns about the proposal to remove the requirement for a follow-up endoscopy to confirm response to treatment, stating that it is poor clinical practice to allow long-term treatment without confirming effectiveness. One comment stated that while a follow-up histological assessment is best practice and should occur in the majority of patients, it is not appropriate for certain patients (e.g. those with a high anaesthetic risk or under palliative management), and therefore the decision for a repeat endoscopy should lie with the treating gastroenterologist.

- 4.5 The PBAC noted the advice received from the Australasian Society of Clinical Immunology and Allergy (ASCIA) and Allergy & Anaphylaxis Australia that specialists other than gastroenterologists are commonly responsible for the care of patients with EoE.

Clinical trials

- 4.6 The submission cited the pivotal induction of remission trial (study EOS-1), a Phase III, prospective, randomised, double blind study comparing the efficacy and tolerability of BOT versus placebo (Table 1).
- 4.7 The PBAC had previously considered that there is a risk of use in non-responding patients, both following induction (with 15.3% of patients not achieving clinicohistologic remission over 12 weeks) (Table 4, budesonide, PSD, March 2021 PBAC Meeting) and in the longer term (15% of patients failed to maintain histological remission at 48 weeks) (paragraph 6.38, budesonide, PSD, March 2021 PBAC Meeting). This submission's clinical data included one extra respondent reaching the primary endpoint at 12 weeks (51/59) compared to 6 weeks (50/59).

Table 1: Results for histological and clinical remission endpoints in the EOS-1 study

Outcome measure	BOT 1 mg BID N=59	Placebo N=29	Treatment difference (95%RCI); p-values ^a
Primary endpoint			
Clinicohistologic remission ^b at 6 weeks (LOCF; FAS-DB): n/N (%)	34/59 (57.6%)	0/29 (0.0%)	57.63% (38.22%, 71.97%); p<0.0001
Cumulative clinicohistologic remission ^c after 6 weeks DB treatment + additional 6 weeks OLI treatment for those not in clinicohistologic remission at the end of the DB phase: n/N (%)	50/59 (84.7%)	-	-
Secondary endpoints			
Histological remission ^d at 6 weeks (LOCF; FAS-DB): n/N (%)	55/59 (93.2%)	0/29 (0.0%)	93.22% (86.81%, 99.64%); p<0.0001
Resolution of clinical symptoms ^e at 6 weeks (LOCF; FAS-DB): n/N (%)	35/59 (59.3%)	4/29 (13.8%)	45.53% (27.79%, 63.27%); p<0.0001
Clinical remission after 12 weeks (DB + OLI treatment): n/N (%)	51/59 (86.4%)	-	-

Source: Submission main body, Table 4, p.9.

BID = twice daily, BOT = budesonide orally disintegrating tablets, CI = confidence interval, DB = double-blind, FAS = full analysis set, LOCF = last observation carried forward, OLI = open-label induction, PBO = placebo, RCI = repeated confidence interval

^aOne-sided p-value from Fisher's exact test as reported in the CSR.

^bDefined as histological remission, i.e., peak of <16 eos/mm² hpf (< 5 eos/hpf) at week 6 (LOCF), AND resolution of symptoms (i.e., no or only minimal problems) defined as a severity of ≤2 points on 0 to 10-point (0-10) Numerical Rating Scale (NRS) for dysphagia AND a severity of ≤2 points on 0-10 NRS for pain during swallowing (odynophagia) on each day in the week prior to week 6 (LOCF).

^cIncludes 16/23 patients who were not in clinicohistologic remission at 6 weeks, who achieved this outcome by week 12 after an additional 6 weeks of treatment with BOT 1.0 mg BID in a protocol-defined open-label extension phase.

^dDefined as peak of <16 eos/mm² hpf (<5 eos/hpf) at week 6 (LOCF)

^eResolution of symptoms on each day in the week prior to week 6, based on the NRS score of ≤ 2 for dysphagia and odynophagia on the respective 0-10

4.8 As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

Drug cost/patient/year: \$ [REDACTED]

4.9 The estimated drug cost/patient per year would be \$ [REDACTED], based on an initial treatment course of BOT 1 mg twice daily for 45 days (effective price of \$ [REDACTED]), and then ongoing treatment of either BOT 0.5 mg or BOT 1 mg twice daily (effective price of \$ [REDACTED]).

Estimated PBS usage and financial implications

4.10 The submission estimated additional costs to the PBS/RPBS of approximately \$0 to < \$10 million over 6 years of listing if the requirement for histological assessment (endoscopy) for continuing treatment was removed. This assumed a 100% treatment continuation rate (a treatment continuation of 93.2% was applied in the original estimates). The submission stated that these costs would be offset by savings to the healthcare system of >\$5.5 million over 6 years by endoscopies no longer being performed to assess for response in this patient cohort.

4.11 There is currently limited PBS data available to estimate the proportion of patients initiating treatment with BOT who transition to continuing treatment. The PBAC considered a review of the use of BOT by the Drug Utilisation Sub-Committee (DUSC) would be appropriate.

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- 4.12 The submission stated that the use of BOT beyond the current restriction will be managed through the Risk Share Arrangements currently in place for BOT and proposed no changes to the subsidisation caps.
- 4.13 Table 2 presents the estimated extent of use, cost of BOT to the PBS/RPBS and the net financial implications to the PBS/RPBS and MBS.
- 4.14 The submission estimated that 500 to < 5,000 patients would be supplied BOT initial treatment over the first six years of listing (500 to < 5,000 in Year 1 to 500 to < 5,000 in Year 6), and 10,000 to < 20,000 patients would be supplied BOT continuing treatment over the first six years of listing (500 to < 5,000 in Year 1 to 500 to < 5,000 in Year 6).
- 4.15 The submission claimed that the cost of BOT to the PBS/RPBS is expected to be \$40 million to < \$50 million over six years (Year 1 \$0 to < \$10 million to Year 6 \$10 million to < \$20 million).
- 4.16 The submission stated that the estimated net financial impact to the PBS/RPBS for the listing of BOT is \$40 million to < \$50 million over six years (Year 1 \$0 to < \$10 million to Year 6 \$0 to < \$10 million).
- 4.17 The submission stated that the estimated net financial impact of BOT to the healthcare system is a cost saving of \$0 to < \$10 million over six years (Year 1 -\$0 to < \$10 million to Year 6 -\$0 to < \$10 million).

Table 2: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use (number of patients treated), revised^a						
Initiators	1	1	1	1	1	1
Continuers	1	1	1	1	1	1
Estimated extent of use (number of scripts dispensed), revised^a						
BOT initiation scripts	1	1	1	1	1	1
BOT continuation scripts	2	2	3	3	4	4
Total BOT scripts	2	3	3	3	4	4
Estimated financial implications of BOT, revised^a						
Cost to PBS/RPBS less co-payment	5	5	5	5	5	5
Hypothetical additional drug costs due to removal of endoscopy criteria	5	5	5	5	5	5
Costs to MBS of endoscopies avoided	6	6	6	6	6	6
Net financial implications						
Net impact	6	6	6	6	6	6

Source: Submission main body, Table 6, p.12

Note: These estimates are based on the latest budget impact model spreadsheet from post-PBAC discussions following the November 2021 submission and vary slightly to those in the final deed

BOT = budesonide orally disintegrating tablets, MBS = Medicare Benefits Schedule, PBS = Pharmaceutical Benefits Scheme, RPBS = Repatriation Pharmaceutical Benefits Scheme.

^aRevised from estimates in the previous submission

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² 10,000 to < 20,000

³ 20,000 to < 30,000

⁴ 30,000 to < 40,000; ⁵ \$0 to < \$10 million

⁶ net cost saving

4.18 As a Category 3 submission, the financial estimates analysis was not independently evaluated.

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

5 PBAC Outcome

Request to remove requirement for histological assessment (endoscopy) for continuing treatment

5.1 The PBAC deferred making a recommendation regarding the request to remove the PBS criteria requiring a histological assessment (endoscopy) to determine treatment response/eligibility for continuing treating for budesonide orally disintegrating tablets (BOT) 500 micrograms and 1 mg for the treatment of eosinophilic oesophagitis (EoE). The PBAC deferred making a recommendation to seek further advice from relevant experts and for the DUSC to conduct a utilisation review of BOT.

5.2 The PBAC noted the submission's concerns that patients who were unable to obtain a second endoscopy within the required timeframe could not meet the PBS criteria for continuing treatment and subsequently needed to cease treatment.

5.3 The PBAC noted concerns raised by healthcare professionals about the difficulty in scheduling a repeat endoscopy within a short timeframe, particularly in the public system. It also noted concerns raised by several healthcare professionals that

removing the requirement for a second histological assessment increased the risk of patients continuing on an ineffective treatment.

- 5.4 The PBAC noted the submission's claim that the use of BOT beyond the current restriction would be managed through the Risk Share Arrangements currently in place for BOT and that there were no proposed changes to the subsidisation caps. The PBAC further noted the submission's claim of a cost saving to the healthcare system overall from fewer endoscopies being performed if the requirement for a second histological assessment was removed.
- 5.5 However, the PBAC remained concerned that removing the requirement for a histological assessment to determine treatment response could lead to patients continuing treatment that was ineffective and therefore using a treatment unnecessarily.
- 5.6 The PBAC requested that further advice be sought from relevant experts on the appropriateness and safety of the removal of this restriction criteria.
- 5.7 The PBAC also referred the matter to the DUSC to review the utilisation of BOT after 12 months of listing, noting that BOT for the treatment of EoE was listed on the PBS in May 2022.
- 5.8 The PBAC requested that this additional information be available for its July 2023 meeting.

Outcome:

Deferred

Request to expand the list of eligible prescribers

- 5.9 The PBAC recommended expanding the list of eligible prescribers in the PBS treatment criteria for BOT to include physicians or surgeons experienced in the diagnosis and management of EoE.
- 5.10 The PBAC noted the submission's concerns that the current PBS treatment criteria for eligible prescribers may disadvantage patients living in rural and remote areas if there is a lack of access to gastroenterologists, and that there are non-gastroenterologist physicians and surgeons who are accredited to perform endoscopies/biopsies and are experienced in the diagnosis and management of EoE.
- 5.11 The PBAC noted input received from the Australasian Society of Clinical Immunology and Allergy and Allergy & Anaphylaxis Australia that non-gastroenterologist specialists are commonly responsible for caring for patients with EoE.

Outcome:

Recommended

Request for advice about the Prescribing Instruction on the optimal number of biopsies in the PBS restriction criteria

- 5.12 The PBAC recommended a change to wording of the Prescribing Instruction on the optimal number of biopsies in the PBS restriction criteria to provide additional clarity around this matter for prescribers.
- 5.13 The PBAC noted the submission’s concerns about confusion caused by the Prescribing Instruction regarding the optimal number of biopsies in the PBS restriction criteria for BOT.
- 5.14 The PBAC noted the advice received from Services Australia that the number of biopsies obtained during endoscopy is not assessed during the telephone authority application from prescribers, and that the current wording of the Prescribing Instruction does not mandate a minimum number of biopsies collected during the endoscopy.
- 5.15 The PBAC agreed with the change to wording of the Prescribing Instruction as suggested by the Secretariat in Section 3, and noted that the sponsor had also supported this wording change in its pre-PBAC response.

Outcome:

Recommended

- 5.16 The PBAC noted that this submission is not eligible for an Independent Review as the requested change to expand the list of eligible prescribers and requested advice about the Prescribing Instruction on the optimal number of biopsies received positive recommendations.

6 Recommended listing

- 6.1 Amend existing listing as follows:

MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack					
BUDESONIDE					
budesonide 1 mg orally disintegrating tablet, 90	12994X	1	90	1	Jorveza
Restriction Summary [New1] / Treatment of Concept: [New2]					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Administrative Advice:				

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	Special Pricing Arrangements apply.
	Indication: Eosinophilic oesophagitis
	Treatment Phase: Initial treatment - Induction of remission
	Clinical criteria:
	Patient must have a history of symptoms of oesophageal dysfunction
	AND
	Clinical criteria:
	Patient must have eosinophilic infiltration of the oesophagus, demonstrated by oesophageal biopsy specimens obtained by endoscopy confirming the presence of at least 15 eosinophils in at least one high power field (hpf); corresponding to approximately 60 eosinophils per mm ² hpf
	AND
	Clinical criteria:
	Patient must not receive more than 90 days of treatment under this restriction
	Treatment criteria:
	Must be treated by <i>at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis.</i>
	Prescribing Instructions: Applications for treatment of this condition must be received within 12 weeks of biopsy.
	Prescribing Instructions: Symptoms of oesophageal dysfunction include at least one of the following: dysphasia, odynophagia, transient or self-cleared food impaction, chest pain, epigastric discomfort, vomiting/regurgitation.
	Prescribing Instructions: Diagnostic sensitivity increases with the number of biopsies and <i>is can be optimised, where necessary, after</i> by taking at least eight biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction).
	Prescribing Instructions: A histologic assessment of the oesophageal biopsy should be planned for approximately 8 weeks after the initiation of the first PBS-subsidised treatment with this drug under this restriction, and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to determine the patient's eligibility for continuing therapy and to avoid an interruption to supply.

MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack					
BUDESONIDE					
budesonide 500 microgram orally disintegrating tablet, 60	12987M	1	60	5	Jorveza
budesonide 1 mg orally disintegrating tablet, 60	12982G	1	60	5	Jorveza
Remove Restriction Summary [New3] / Treatment of Concept: [New4]					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice:				

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	No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Eosinophilic oesophagitis
	Treatment Phase: First continuing treatment – Confirmation of remission
	Clinical criteria:
	Patient must have previously received PBS-subsidised initial treatment with this drug for this condition;
	AND
	Clinical criteria:
	Patient must have documented evidence of having achieved histologic remission while receiving initial PBS-subsidised treatment with this drug for this condition, defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf), corresponding to less than 16 eosinophils per mm ² hpf on oesophageal biopsy
	AND
	Clinical criteria:
	Patient must not receive more than 26 weeks of treatment under this restriction
	Treatment criteria:
	Must be treated by <i>at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) medical practitioner in consultation with one of these prescribers</i>
	Prescribing Instructions: Histologic assessment should be based on the peak eosinophils count derived, <i>where necessary</i> , from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction). The histologic assessment should, where possible, be performed by <i>or in consultation with</i> the same physician <i>or surgeon</i> who confirmed the diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should be conducted and submitted after the patient has completed 8 weeks of the initial treatment course and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to avoid an interruption to supply. Where a histologic assessment is not undertaken and the results submitted, the patient will be not be eligible for ongoing treatment.
Remove Restriction Summary [New5] / Treatment of Concept: [New6]	
	Indication: Eosinophilic oesophagitis
	Treatment Phase: Subsequent continuing treatment - Maintenance of remission
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the First continuing treatment restriction; or
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the - Transitioning from non-PBS to PBS-subsidised treatment - Grandfather treatment restriction

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	AND
	Clinical criteria:
	The condition must not have progressed while being treated with this drug
	Treatment criteria:
	Must be treated by <i>at least one of: by a(i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) medical practitioner in consultation with one of these prescribers.</i>
Restriction Summary [New7] / Treatment of Concept: [New8]	
	Indication: Eosinophilic oesophagitis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised treatment - Grandfather treatment
	Clinical criteria:
	Patient must have previously received non-PBS-subsidised treatment with a corticosteroid for this condition prior to 1 May 2022
	AND
	Clinical criteria:
	Patient must be receiving non-PBS treatment with a corticosteroid for this condition at the time of application
	AND
	Clinical criteria:
	Patient must have had, prior to commencement of non-PBS-subsidised treatment with a corticosteroid, a history of symptoms of oesophageal dysfunction
	AND
	Clinical criteria:
	Patient must have had, prior to commencement of non-PBS-subsidised treatment with a corticosteroid, eosinophilic infiltration of the oesophagus, demonstrated by oesophageal biopsy specimens obtained by endoscopy confirming the presence of at least 15 eosinophils in at least one high power field (hpf); corresponding to approximately 60 eosinophils per mm ² hpf
	AND
	Clinical criteria:
	Patient must have documented evidence that they are currently in histologic remission, where remission is defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf); corresponding to less than 16 eosinophils per mm ² hpf on oesophageal biopsy
	Treatment criteria:
	Must be treated by <i>at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis</i>
	Prescribing Instructions: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.
	Prescribing Instructions: Symptoms of oesophageal dysfunction include at least one of the following: dysphasia, odynophagia, transient or self-cleared food impaction, chest pain, epigastric discomfort, vomiting/regurgitation.

	<p>Prescribing Instructions:</p> <p>Histologic assessment should be based on the peak eosinophils count derived, <i>where necessary</i>, from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastrooesophageal junction).</p> <p>The histologic assessment should, where possible, be performed by <i>or in consultation with</i> the same physician <i>or surgeon</i> who confirmed the diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should have been conducted after the patient has completed 8 weeks of the initial treatment course and no later than 2 weeks prior to the patient completing the initial treatment course, to avoid an interruption to supply. Where a histologic assessment is not undertaken and the results submitted, the patient will not be eligible for ongoing treatment.</p>
	<p>Administrative Advice:</p> <p>This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>

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

7 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.

8 Sponsor’s Comment

Dr Falk Pharma Australia acknowledges the outcome of this submission and notes that two of the three requested changes received positive recommendations, and hopes these changes will be implemented in a timely manner. For the remaining item, the Sponsor looks forward to working with the PBAC and DUSC to resolve any ongoing questions ahead of the July PBAC meeting. All three of the requested changes are intended to assure equity of ongoing supply of JORVEZA within the public health system to appropriate patients with eosinophilic oesophagitis, a chronic inflammatory/fibrostenotic disease.

**4.04 BUDESONIDE,
Tablet 500 micrograms (orally disintegrating),
Tablet 1 mg (orally disintegrating),
Jorveza[®],
Dr Falk Pharma Australia Pty Ltd**

9 Purpose of Submission

- 9.1 For the Pharmaceutical Benefits Advisory Committee (PBAC) to consider expert advice from the Gastroenterological Society of Australia (GESA) regarding the appropriateness of the requirement for a histological assessment (endoscopy) to determine treatment response/eligibility for continuing treatment with budesonide orally disintegrating tablets (BOT) 500 micrograms and 1 mg for eosinophilic oesophagitis (EoE).
- 9.2 For the PBAC to provide advice on GESA's request to change the authority type for continuing treatment from Authority Required (telephone/online) to Authority Required (STREAMLINED).
- 9.3 For the PBAC to note the results of the Drug Utilisation Sub-Committee (DUSC) review on the utilisation of BOT.

10 Background

- 10.1 At its March 2023 meeting, the PBAC considered a request from the sponsor of BOT, Dr Falk Pharma Australia, to remove the requirement for a histological assessment (endoscopy) to determine treatment response/eligibility for continuing treatment, and subsequently consolidate the first and subsequent continuing treatment phase listings, for the current PBS listings of BOT 500 micrograms and 1 mg for the treatment of EoE.
- 10.2 The current PBS listings for BOT for EoE state 'Applications for initial treatment with BOT must be received within 12 weeks of endoscopy/biopsy.... A histologic assessment of the oesophageal biopsy should be planned for approximately 8 weeks after the initiation of the first PBS-subsidised treatment with this drug under this restriction, and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to determine the patient's eligibility for continuing therapy and to avoid an interruption to supply.'
- 10.3 The submission considered by the PBAC at its March 2023 meeting stated that concerns had been raised by clinicians since the PBS listing of BOT in May 2022 regarding the requirement for a follow-up endoscopy. The submission claimed that clinicians had reported that because of the challenges in obtaining a follow-up endoscopy, patients who would have otherwise benefited from treatment with BOT

were either not being started on this treatment or started the initial induction of remission treatment but then were forced to cease as they were unable to access a repeat endoscopy to confirm treatment response (see Section 2).

- 10.4 At its March 2023 meeting, the PBAC considered concerns raised by health professionals via the Consumer Comments facility on the PBS website. The PBAC noted the concerns raised, such as difficulty scheduling a repeat endoscopy in the public sector, and noted that there were several comments suggesting a longer timeframe for a follow-endoscopy (e.g. within 6 to 12 months of commencing treatment). The PBAC also noted other comments that raised concerns about the proposal to remove the requirement for a follow-up endoscopy to confirm response to treatment, stating that it is poor clinical practice to allow long-term treatment without confirming effectiveness. A suggestion was also raised that repeat endoscopy may not be appropriate for certain patients (e.g. those with high anaesthetic risk) (paragraph 4.4).
- 10.5 The PBAC remained concerned that removing the requirement for a histological assessment to determine treatment response could lead to patients continuing treatment that was ineffective and therefore using a treatment unnecessarily. This was also raised by the PBAC at its March 2021 meeting when it considered the initial PBS listing of BOT. At that time, the PBAC considered that a restriction that did not specify histological assessment criteria for continuing treatment ‘was inconsistent with the clinical evidence presented and Therapeutic Goods Administration dose recommendation in that it would allow all patients to continue treatment regardless of whether they achieved remission or not.’ (paragraph 3.1, budesonide, PSD, March 2021 PBAC meeting).
- 10.6 The PBAC deferred making a recommendation to the requirement for a histological assessment in March 2023 to seek further advice from relevant experts on the appropriateness of this Prescribing Instruction and any potential impacts on patient safety and care should these criteria be removed. The PBAC also referred the matter to DUSC to conduct a utilisation review of BOT.

11 Advice from GESA

- 11.1 In its response to the PBAC Chair’s request for advice, GESA noted that BOT is well tolerated, has a favourable adverse effect profile, and appropriate use will result in potential cost savings due to reduced procedural interventions.
- 11.2 GESA stated that the current requirement for a second endoscopy to confirm remission within 8-10 weeks is difficult to schedule not only for patients in the public sector, but also for patients in general due to their own time constraints and for patients who live in rural and remote areas. GESA also noted that COVID infection of both procedural staff and patients can make it difficult to schedule a repeat endoscopy due to cancellations and the management of procedural lists.

- 11.3 GESA noted that histological follow-up is still best practice in the majority of situations and is also used to reinforce long term compliance with the medicine. It was also noted that there are a number of new pharmacological agents that have been shown to be efficacious in situations of treatment failure, and histological assessment will therefore be essential to guide future therapies.
- 11.4 GESA suggested that increasing the time for a follow-up endoscopy would increase the flexibility of scheduling this assessment, and it was suggested to allow patients to access 6 months of treatment with the first PBS prescription of BOT, with a requirement for a follow-up endoscopy within 3-6 months of initiating BOT. An alternative time for requiring a follow-up endoscopy could be 4 months if the 3-6 month timeframe was considered too long. The PBAC noted that the Product Information (PI) for BOT states ‘the usual duration of induction treatment is 6 weeks. For patients who are not appropriately responding during 6 weeks the treatment can be extended for up to 12 weeks.’ Therefore, for PBS listings to be consistent with the dosage recommendations in the PI, the induction phase should last for a maximum of 12 weeks.
- 11.5 It was suggested that a specialist follow-up should be required at least annually for the ongoing use of BOT to support compliance with treatment, and due to EoE being a long-term condition where the natural history is not fully understood and treatment guidelines will continue to evolve and change.
- 11.6 GESA also suggested the following changes to the PBS restrictions for BOT for EoE:
- extending the prescriber eligibility to include surgical and physician Conjoint Committee for Recognition in Gastrointestinal Endoscopy (CCRTGE) approved endoscopy colleagues to manage rural and remote patients and ensure equitable access. The PBAC noted that at its March 2023 meeting it recommended expanding the list of eligible prescribers in the PBS treatment criteria for BOT to include physicians or surgeons experienced in the diagnosis and management of EoE and noted that this recommendation has not yet been implemented.
 - Changing the authority level for continuing treatment from Authority Required (telephone/online) to Authority Required (STREAMLINED) to improve efficiency of prescribing. The PBAC noted that changing the authority level has not been proposed by the sponsor.

12 Requested listing

- 12.1 Suggested additions proposed by the Secretariat are in italics and suggested deletions are crossed out with strikethrough.

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MEDICINAL PRODUCT Medicinal Product Pack		PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BUDESONIDE						
budesonide 1 mg orally disintegrating tablet, 90		12994X	1	90	1	Jorveza
Restriction Summary / Treatment of Concept:						
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)					
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.					
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.					
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.					
	Administrative Advice: Special Pricing Arrangements apply.					
Indication: Eosinophilic oesophagitis						
Treatment Phase: Initial treatment - Induction of remission						
Clinical criteria:						
Patient must have a history of symptoms of oesophageal dysfunction						
AND						
Clinical criteria:						
Patient must have eosinophilic infiltration of the oesophagus, demonstrated by oesophageal biopsy specimens obtained by endoscopy confirming the presence of at least 15 eosinophils in at least one high power field (hpf); corresponding to approximately 60 eosinophils per mm ² hpf						
AND						
Clinical criteria:						
Patient must not receive more than 90 days of treatment under this restriction						
Treatment criteria:						
Must be treated by at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis.						
Prescribing Instructions: Applications for treatment of this condition must be received within 12 weeks of biopsy.						
Prescribing Instructions: Symptoms of oesophageal dysfunction include at least one of the following: dysphasia, odynophagia, transient or self-cleared food impaction, chest pain, epigastric discomfort, vomiting/regurgitation.						
Prescribing Instructions: Diagnostic sensitivity increases with the number of biopsies and can be optimised, where necessary, by taking at least eight biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction).						

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	<p>Prescribing Instructions: A histologic assessment of the oesophageal biopsy should be planned for approximately 8 weeks after the initiation of the first PBS-subsidised treatment with this drug under this restriction, and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to determine the patient's eligibility for continuing therapy and to avoid an interruption to supply.</p>
	<p>Prescribing Instructions: After prescribing the initial induction treatment with budesonide, a histologic assessment must be conducted between 12-24 weeks of treatment to determine the patient's eligibility for continuing therapy. The histologic assessment should be conducted no later than 2 weeks prior to completing the PBS subsidised first continuing maintenance treatment course to avoid an interruption of supply for continuing therapy.</p>

MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack					
BUDESONIDE					
budesonide 500 microgram orally disintegrating tablet, 60	New	1	60	5-2	Jorveza
budesonide 1 mg orally disintegrating tablet, 60	New	1	60	5-2	Jorveza

Remove Restriction Summary / Treatment of Concept:

Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Eosinophilic oesophagitis
	Treatment Phase: First continuing treatment – Confirmation of remission
	Clinical criteria:
	Patient must have previously received PBS-subsidised initial treatment with this drug for this condition;
	AND
	Clinical criteria:
	Patient must have demonstrated an adequate response to treatment with this drug for this condition.
	Clinical criteria:
	Patient must have documented evidence of having achieved histologic remission while receiving initial PBS-subsidised treatment with this drug for this condition, defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf), corresponding to less than 16 eosinophils per mm ² hpf on oesophageal biopsy
	AND
	Clinical criteria:
	Patient must not receive more than 26 weeks 12 weeks of treatment under this restriction

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	Treatment criteria:
	Must be treated by at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) medical practitioner in consultation with one of these prescribers
	Prescribing Instructions: Histologic assessment should be based on the peak eosinophils count derived, where necessary, from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction). The histologic assessment should, where possible, be performed by <i>or in consultation with</i> the same physician <i>or surgeon</i> who confirmed the diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should be conducted and submitted after the patient has completed 8 weeks of the initial treatment course and between 12-24 weeks of initiating therapy and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to avoid an interruption to supply. <i>The histologic assessment should be conducted no later than 2 weeks prior to the patient completing the PBS subsidised first continuing maintenance treatment course to avoid an interruption of supply for continuing therapy.</i> Where a histologic assessment is not undertaken and the results submitted , the patient will be not be eligible for ongoing treatment. <i>The result of the histological assessment must be documented in the patient's medical records.</i>

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BUDESONIDE					
budesonide 500 microgram orally disintegrating tablet, 60	12987M	1	60	5	Jorveza
budesonide 1 mg orally disintegrating tablet, 60	12982G	1	60	5	Jorveza
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Administrative Advice: Special Pricing Arrangements apply.				
Restriction Summary / Treatment of Concept:					
	Indication: Eosinophilic oesophagitis				
	Treatment Phase: Subsequent continuing treatment - Maintenance of remission				
	Clinical criteria:				
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the First continuing treatment restriction;				
	AND				
	Clinical criteria:				

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	<i>Patient must have documented evidence of having achieved histologic remission while receiving initial and first continuing PBS-subsidised treatment with this drug for this condition, defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf), corresponding to less than 16 eosinophils per mm² hpf on oesophageal biopsy</i>
	AND
	Clinical criteria:
	The condition must not have progressed while being treated with this drug
	Patient must have demonstrated or sustained an adequate response to treatment with this drug.
	Treatment criteria:
	Must be treated by at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) medical practitioner in consultation with one of these prescribers.
	Prescribing Instructions: Histologic assessment should be based on the peak eosinophils count derived, where necessary, from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction). The histologic assessment should, where possible, be performed by <i>or in consultation with</i> the same physician <i>or surgeon</i> who confirmed the diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should be conducted and submitted after the patient has completed 8 weeks of the initial treatment course and between 12-24 weeks of initiating therapy and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to avoid an interruption to supply. <i>The histologic assessment should be conducted no later than 2 weeks prior to the patient completing the PBS subsidised first continuing maintenance treatment course to avoid an interruption of supply for continuing therapy.</i> Where a histologic assessment is not undertaken and the results submitted, the patient will be not be eligible for ongoing treatment. <i>The result of the histological assessment must be documented in the patient's medical records.</i>

13 DUSC review

- 13.1 PBS prescription data for BOT for EoE (PBS item codes 12982G, 12987M & 12994X) were extracted from the PBS data maintained by the Department of Health and Aged Care and processed by Services Australia. Data were extracted for dates of supply from the date of listing for EoE (1 May 2022) up to and including the end of March 2023. It was noted that the Grandfather treatment phase listing ceased on 1 May 2023.
- 13.2 While the PBAC had requested a review after 12 months of listing to be available for its consideration in July 2023, only 11 months of complete prescription supply data were available at the time of data extraction. Thus, to compare actual to predicted utilisation for Year 1 post listing, the actual utilisation was projected to 12 months.
- 13.3 DUSC considered this utilisation analysis at its June 2023 meeting.

Predicted versus Actual

- 13.4 The predicted values used in this comparison are from Table 5 in the submission to the PBAC for its March 2023 meeting which were based on the latest utilisation and cost model spreadsheet from post-PBAC discussions following the November 2021 submission and vary slightly to those in the final deed. These estimates are shown in Table 3 below. They are not the updated estimates from the submission (i.e. Table 6)

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as these are estimates of future utilisation if the proposed changes are approved by the PBAC.

Table 3: Estimated use and financial implications – previous submission/post-PBAC

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total
Estimated extent of use (number of patients treated)							
Initiators	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	
Continuers	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	
Estimated extent of use (number of scripts dispensed)							
BOT initiation scripts	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	
BOT continuation scripts, first	█ ²	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	
BOT continuation scripts, subsequent	█ ¹	█ ³	█ ³	█ ⁴	█ ⁴	█ ⁴	
Total BOT scripts	█ ³	█ ³	█ ⁴	█ ⁴	█ ⁵	█ ⁵	
Estimated financial implications of BOT							
Cost to PBS/RPBS less co-payments	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁷
Cost to MBS of endoscopy for efficacy assessment	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶	█ ⁶

Source: Submission main body, Table 5, p.12

Note: These estimates are based on the latest budget impact model spreadsheet from post-PBAC discussions following the November 2021 submission and vary slightly to those in the final deed

BOT = budesonide orally disintegrating tablets, MBS = Medicare Benefits Schedule, PBS = Pharmaceutical Benefits Scheme, RPBS = Repatriation Pharmaceutical Benefits Scheme.

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² 5,000 to < 10,000

³ 10,000 to < 20,000

⁴ 20,000 to < 30,000

⁵ 30,000 to < 40,000

⁶ \$0 to < \$10 million

⁷ \$40 million to < \$50 million

Table 4: Predicted vs Actual analysis

Budesonide for EoE	Year 1 (May 2022 - April 2023)		
	Predicted	Actual*	% Difference
Patients - initial treatment	1	1	+72%
Patients - continuing treatment	1	1	-14%
Patients - grandfather treatment	2	2	n.a.
Prescriptions - initial treatment	1	1	+36%
Prescriptions - continuing treatment	3	1	-75%
Prescriptions - grandfather treatment	2	1	n.a.
Prescriptions - total	3	4	%
Government Expenditure - published	\$ 5 **	\$ 5	%
Government Expenditure - effective	\$ 5	\$ 5 **	%

* Actuals are based on 11 months of data (May 2022 to the end of March 2023) plus an extrapolated estimate of the 12th month (see Appendix A).

**Estimated based on a ratio of published to effective expenditure of 1.43 in the March 2023 submission.

Note that "continuing treatment" includes both "First continuing treatment" and "Subsequent continuing treatment".

EoE = eosinophilic oesophagitis

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² < 500

³ 10,000 to < 20,000

⁴ 5,000 to < 10,000

⁵ \$0 to < \$10 million

- 13.5 The submission assumed two prescriptions per patient in the initial treatment phase. This is because initial treatment is 90 days and the PBS item for initial treatment (12994X) contains 90 x 1 mg tablets which are intended to last 45 days (one tablet in the morning and one in the evening). Therefore, two prescriptions (the original prescription and one repeat) are required.
- 13.6 Table 4 shows that the number of initial treatment patients was 72% more than predicted and the number of continuing patients was 14% less than predicted. The prescriptions for initial treatment were only 36% more than expected. That is 1.6 prescriptions per patient instead of the predicted 2 prescriptions.
- 13.7 This is partially due to early discontinuation (i.e. prior to their 2nd prescription) and also the fact that not all initiating patients had the opportunity to have their 2nd prescription filled in the period (i.e. they initiated in the last 45 days of the period). The PBAC noted this could also be due to patients only requiring 6 weeks of induction treatment, which is consistent with the recommended dose for Jorveza in the PI.
- 13.8 This is likely to be an underestimate as it takes time (i.e. 90 days) for patients to progress from initial to continuing treatment, so patients that initiated in the last 3 months of the period will not have had the opportunity to show continuation.
- 13.9 Overall, prescription utilisation was [redacted] % less than predicted and Government expenditure was [redacted] % less than expected. DUSC considered that the number of patients receiving continuing treatment was likely to be underestimated due to immature data.
- 13.10 The estimated continuation rate of 53.1% calculated in the analysis is considerably less than the [redacted] % assumed in the November 2021 submission. It is not possible to determine

from the data if the low continuation rate is due to difficulty in obtaining a follow-up endoscopy, a low remission rate, or immature data.

- 13.11 It was also noted that 5.4% of patients only received continuation phase prescriptions and other unexpected sequences were also present. This suggests that the allocation of Authority restriction codes was not always accurate.
- 13.12 DUSC considered that there appears to be some prescribing outside the restriction where non-gastroenterology and hepatology specialists are prescribing in treatment phases that are only intended to be prescribed by a gastroenterologist.
- 13.13 DUSC noted that there is an upwards rise in the use of BOT, however costs are less than what was expected in the first 12 months of listing. DUSC also considered that due to the COVID pandemic some patients may have had delays in receiving endoscopies.
- 13.14 DUSC suggested that patients could be given more time to receive a second endoscopy, particularly given the issues with access and backlog following COVID.

14 PBAC Outcome

- 14.1 The PBAC recommended extending the required timeframe for a histological assessment (endoscopy) following initiation of treatment to determine treatment response/eligibility for continuing treatment with BOT 500 micrograms and 1 mg for EoE. The PBAC considered that the timeframe could be extended from within 8-10 weeks to within 12 months from starting treatment. The PBAC recommended patients could continue to access BOT through the PBS until they have the repeat endoscopy (the histological assessment), subject to advice provided by their treating clinician.
- 14.2 The PBAC recalled the concerns raised in the March 2023 submission regarding the challenges for clinicians and patients in obtaining a follow-up endoscopy within the 8-10 week timeframe. The PBAC recalled the submission's claim that patients who would have otherwise benefited from treatment with BOT were either not being started on this treatment or were started on initial induction of remission treatment but then were forced to cease as they were unable to access a repeat endoscopy to confirm treatment response. The PBAC also recalled concerns raised by health professionals via the Consumer Comments facility on the PBS website that there was difficulty in scheduling a repeat endoscopy, particularly in the public sector.
- 14.3 The PBAC noted advice received from the Gastroenterological Society of Australia (GESA) that the current requirement for a second endoscopy within 8-10 weeks was difficult to meet, but a histological follow-up is still best practice. The PBAC noted GESA's suggestion to extend the time for a follow-up endoscopy.
- 14.4 The PBAC noted the advice from GESA that BOT is well tolerated and has a favourable adverse effect profile and considered the risk to patients of extending the time for a follow-up endoscopy would be low.

- 14.5 The PBAC noted the findings from the utilisation review of BOT by the DUSC and the projected use of BOT for 12 months since initial listing in May 2022. The PBAC noted the number of patients accessing continuing treatment was lower than was predicted. The PBAC asked DUSC to continue to monitor the use of BOT and undertake a repeat review of its utilisation in 12 months' time.
- 14.6 The PBAC noted the request by GESA to change the authority level for continuing treatment from Authority Required (telephone/online) to Authority Required (STREAMLINED) to improve efficiency of prescribing, however noted that this change had not been requested by the sponsor. Furthermore, no concerns had been raised by either the sponsor or other health professionals about the current authority levels. The PBAC considered the current authority levels for BOT were appropriate.
- 14.7 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

15 Recommended listing

15.1 Amend existing listing as follows:

MEDICINAL PRODUCT		PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack						
BUDESONIDE						
budesonide 1 mg orally disintegrating tablet, 90		12994X	1	90	1	Jorveza
Restriction Summary / Treatment of Concept:						
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)					
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
	Administrative Advice: No increase in the maximum number of repeats may be authorised.					
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.					
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.					
	Administrative Advice: Special Pricing Arrangements apply.					
Indication: Eosinophilic oesophagitis						
Treatment Phase: Initial treatment - Induction of remission						
Clinical criteria:						

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	Patient must have a history of symptoms of oesophageal dysfunction
	AND
	Clinical criteria:
	Patient must have eosinophilic infiltration of the oesophagus, demonstrated by oesophageal biopsy specimens obtained by endoscopy confirming the presence of at least 15 eosinophils in at least one high power field (hpf); corresponding to approximately 60 eosinophils per mm ² hpf
	AND
	Clinical criteria:
	Patient must not receive more than 90 days of treatment under this restriction
	Treatment criteria:
	<i>Must be treated by at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis.</i>
	Prescribing Instructions: Applications for treatment of this condition must be received within 12 weeks of biopsy.
	Prescribing Instructions: Symptoms of oesophageal dysfunction include at least one of the following: dysphasia, odynophagia, transient or self-cleared food impaction, chest pain, epigastric discomfort, vomiting/regurgitation.
	Prescribing Instructions: Diagnostic sensitivity increases with the number of biopsies and <i>can be optimised, where necessary</i> , by taking at least eight biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction).
	Prescribing Instructions: A histologic assessment of the oesophageal biopsy should be planned for approximately 8 weeks after the initiation of the first PBS-subsidised treatment with this drug under this restriction, and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to determine the patient's eligibility for continuing therapy and to avoid an interruption to supply.
	Prescribing Instructions: <i>After prescribing the initial induction treatment with budesonide, a histologic assessment must be conducted within 48 weeks of initiating treatment to determine the patient's eligibility for continuing therapy.</i> <i>The histologic assessment should be conducted no later than 2 weeks prior to completing the PBS subsidised first continuing maintenance treatment course to avoid an interruption of supply for continuing therapy.</i>

MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product Pack					
BUDESONIDE					
budesonide 500 microgram orally disintegrating tablet, 60	New	1	60	5 8	Jorveza
budesonide 1 mg orally disintegrating tablet, 60	New	1	60	5 8	Jorveza
Remove Restriction Summary / Treatment of Concept:					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				

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	<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
	<p>Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.</p>
	<p>Administrative Advice: Special Pricing Arrangements apply.</p>
	<p>Indication: Eosinophilic oesophagitis</p>
	<p>Treatment Phase: First continuing treatment – until confirmation of remission is confirmed</p>
	<p>Clinical criteria:</p>
	<p>Patient must have previously received PBS-subsidised initial treatment with this drug for this condition;</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p><i>Patient must have demonstrated an adequate response to treatment with this drug for this condition.</i></p>
	<p>Clinical criteria:</p>
	<p>Patient must have documented evidence of having achieved histologic remission while receiving initial PBS-subsidised treatment with this drug for this condition, defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf), corresponding to less than 16 eosinophils per mm² hpf on oesophageal biopsy</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p>Patient must not receive more than 26 weeks 36 weeks of treatment under this restriction</p>
	<p>Treatment criteria:</p>
	<p><i>Must be treated by at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) medical practitioner in consultation with one of these prescribers</i></p>
	<p>Prescribing Instructions: Histologic assessment should be based on the peak eosinophils count derived, <i>where necessary</i>, from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction). The histologic assessment should, where possible, be performed by <i>or in consultation with</i> the same physician <i>or surgeon</i> who confirmed the <i>patient's</i> diagnosis of eosinophilic oesophagitis. in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should must be conducted and submitted after the patient has completed 8 weeks of the initial treatment course and within 48 weeks of initiating treatment, to determine the patient's eligibility for continuing treatment. and no later than 2 weeks prior to the patient completing the PBS-subsidised initial treatment course, to avoid an interruption to supply. The histologic assessment should be conducted no later than 2 weeks prior to the patient completing the PBS subsidised first continuing treatment course to avoid an interruption of supply for continuing therapy. Where a histologic assessment is not undertaken and the results submitted, the patient will be not be eligible for ongoing treatment. <i>The result of the histological assessment must be documented in the patient's medical records.</i></p>
	<p>Prescribing Instructions: <i>First applications for the subsequent continuing treatment of this condition, must be received within 12 weeks of the histologic assessment.</i></p>

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MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
BUDESONIDE					
budesonide 500 microgram orally disintegrating tablet, 60	12987M	1	60	5	Jorveza
budesonide 1 mg orally disintegrating tablet, 60	12982G	1	60	5	Jorveza
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Administrative Advice: Special Pricing Arrangements apply.				
Restriction Summary / Treatment of Concept:					
	Indication: Eosinophilic oesophagitis				
	Treatment Phase: Subsequent continuing treatment - Maintenance of remission				
	Clinical criteria:				
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the First continuing treatment restriction				
	AND				
	Clinical criteria:				
	<i>Patient must have documented evidence of having achieved histologic remission while receiving initial and first continuing PBS-subsidised treatment with this drug for this condition, defined as a peak eosinophil count of less than 5 eosinophils per high power field (hpf), corresponding to less than 16 eosinophils per mm² hpf on oesophageal biopsy</i>				
	AND				
	Clinical criteria:				
	The condition must not have progressed while being treated with this drug.				
	Treatment criteria:				
	<i>Must be treated by at least one of: (i) gastroenterologist, (ii) surgeon experienced in the management of patients with eosinophilic oesophagitis, (iii) physician experienced in the management of patients with eosinophilic oesophagitis, (iv) medical practitioner in consultation with one of these prescribers.</i>				

	<p>Prescribing Instructions: Histologic assessment should be based on the peak eosinophils count derived, <i>where necessary</i>, from the evaluation of at least eight oesophageal biopsies (minimum of four collected from each of the mid and distal segments, with the distal segment biopsies taken at least 5 cm above the gastroesophageal junction). The histologic assessment should, where possible, be performed by <i>or in consultation with</i> the same physician <i>or surgeon</i> who confirmed the patient’s diagnosis of eosinophilic oesophagitis in the patient. This assessment, which will be used to determine eligibility for continuing treatment, should <i>must</i> be conducted and submitted after the patient has completed 8 weeks of the initial treatment course and <i>within 48 weeks of initiating treatment, to determine the patient’s eligibility for continuing treatment. and no later than 2 weeks prior to the patient completing the PBS subsidised initial treatment course, to avoid an interruption to supply. The histologic assessment should be conducted no later than 2 weeks prior to the patient completing the PBS subsidised first continuing treatment course to avoid an interruption of supply for continuing therapy.</i> Where a histologic assessment is not undertaken and the results submitted, the patient will be not be eligible for ongoing treatment. <i>The result of the histological assessment must be documented in the patient’s medical records.</i></p>
	<p>Prescribing Instructions: <i>First applications for the subsequent continuing treatment of this condition, must be received within 12 weeks of the histologic assessment.</i></p>

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

16 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.

17 Sponsor’s Comment

The Sponsor welcomes the PBAC positive recommendation to extend the time allowed for the repeat endoscopy/ histologic assessment to confirm treatment response. This change recognises the difficulties faced by some Doctors and their patients in scheduling the repeat endoscopy and now increases the probability that patients with confirmed eosinophilic oesophagitis (EoE) will have continuing access to treatment with Jorveza – the only TGA approved, and PBS reimbursed, treatment for this condition.