6.08 VEDOLIZUMAB, Powder for injection 300 mg, Entyvio®, Takeda Pharmaceuticals Australia Pty Ltd

1 Purpose of Submission

1.1 The Category 3 submission sought to add a dose-escalation option to the current maintenance treatment listings of vedolizumab (Entyvio®) intravenous injection (IV) 300 mg for adults with moderate to severe ulcerative colitis (MSUC) and severe Crohn disease (CD), increasing the dose frequency from 8-weekly dosing (Q8W) to 4-weekly dosing (Q4W).

1.2 The submission proposed an amendment to the current Special Pricing Arrangement (SPA) to offset the net budget impact of doses additional to Q8W.

2 Background

2.1 At the time of consideration, vedolizumab 300 mg IV injection was the only IV form of vedolizumab on the PBS and was listed as an Authority Required (Telephone) S100 HSD listings for MSUC, severe CD and chronic pouchitis.

2.2 The PBS listings of vedolizumab included IV induction/maintenance and subcutaneous (SC) maintenance. The treatment algorithm was such that patients stable on Q8W IV maintenance could transition to 2-weekly (Q2W) SC maintenance. The submission sought Q4W maintenance as an escalation option to Q8W IV maintenance.

Registration status

2.3 Vedolizumab was Therapeutic Goods Administration (TGA) registered on 27 June 2014 for the:

- Treatment of adult patients with MSUC who have had an inadequate or lost response to, or are intolerant to, either conventional therapy or a tumour necrosis factor-alpha (TNF-alpha) antagonist.
- Treatment of adult patients with moderate to severe CD who have had an inadequate or response to, or are intolerant to, either conventional therapy or a tumour necrosis factor-alpha (TNF-alpha) antagonist.
- Treatment of adult patients with moderate to severe chronic pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis and have had an inadequate response with or lost response to antibiotic therapy.

2.4 The TGA registration stated that patients who experience a loss of clinical response on Q8W treatment may benefit from Q4W treatment, with the response to be reassessed after 12 to 14 weeks and treatment to be discontinued if no clinical benefit is seen.

Previous PBAC consideration

2.5 At its March 2015 meeting, the PBAC recommended listing vedolizumab IV for the treatment of MSUC and severe CD on the basis that maintenance treatment would be Q8W and that patients who did not respond to treatment during induction or maintenance would no longer be eligible for subsidy (Q8W ineligible patients). Vedolizumab IV was subsequently listed on 1 August 2015.

2.6 At its March 2024 meeting, the PBAC recommended listing an additional induction dose at week 10 of the induction phase for the treatment of CD on the basis that some patients required it to achieve an adequate response to induction and that it was made to be cost-neutral. The Department implemented the cost neutrality via an amendment to the SPA rebate to accommodate the uptake of the week 10 doses.

2.7 The PBAC has not previously considered Q4W maintenance for the treatment of MSUC or severe CD.

3 Requested listing

3.1 The submission requested new balance of supply restrictions to allow Q4W treatment to patients who, in the prescriber's opinion, would not be sufficiently maintained on Q8W dosing, and new continuing restrictions for patients who, in the prescriber's opinion, require ongoing Q4W treatment. The submission's proposed listings for Q4W dosing are provided below. Only the restriction wording that differed from the existing listing was included in this section. No changes were proposed to the program (s100 HSD), prescriber types, or authority level and type.

Moderate to severe ulcerative colitis - Balance of Supply (BoS)

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
VEDOLIZUMAB					
vedolizumab 300mg injection, 1 vial	NEW (public)	1	1	2	Entyvio
vedolizumab 300mg injection, 1 vial	NEW (private)	1	1	2	Entyvio
Indication: Moderate to severe ulcerative colitis					
Treatment Phase: Balance of supply (every 4 weeks)					
Clinical criteria:					
Patient must require therapy with this drug for this condition administered every 4 weeks					
AND					
Clinical criteria:					
Patient must have received insufficient therapy with this drug for this condition under the continuing treatment restriction (allowing for treatment every 8 weeks)					

Moderate to severe ulcerative colitis – Continuing Treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
VEDOLIZUMAB					
vedolizumab 300mg injection, 1 vial	NEW (public)	1	1	5	Entyvio
vedolizumab 300mg injection, 1 vial	NEW (private)	1	1	5	Entyvio
Indication: Moderate to severe ulcerative colitis					
Treatment Phase: Continuing treatment (every 4 weeks)					
Clinical criteria:					
Patient must require therapy with this drug for this condition administered every 4 weeks					
AND					
Clinical criteria:					
Patient must have received a balance of supply (every 4 weeks) as their most recent course of PBS-subsidised biological medicine treatment for this condition; OR					
Patient must have received this drug administered every 4 weeks as their most recent course of PBS-subsidised biological medicine for this condition under the vedolizumab 300 mg IV continuing restriction (Q4W),					
AND					
Clinical criteria:					
Patient must have demonstrated or sustained an adequate response to treatment by having a partial Mayo clinic score less than or equal to 2, with no sub score greater than 1 while receiving treatment with this drug.					
AND					
Clinical criteria:					
Patient must not receive more than 24 weeks of treatment under this restriction					

Severe Crohn disease - Balance of Supply (BoS)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
VEDOLIZUMAB					
vedolizumab 300mg IV	NEW	1	1	2	Entyvio
Indication: Severe Crohn disease					
Treatment Phase: Balance of supply (every 4 week)					
Clinical criteria:					
Patient must require therapy with this drug for this condition administered every 4 weeks					
AND					
Clinical criteria:					
Patient must have received insufficient therapy with this drug for this condition under the continuing treatment restriction (allowing for treatment every 8 weeks)					

Severe Crohn disease – Continuing Treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
VEDOLIZUMAB					
vedolizumab 300mg IV	NEW	1	1	5	Entyvio
Administrative Advice: At the time of the authority application, medical practitioners should request the appropriate number of vials, to provide sufficient for a single infusion of 300 mg vedolizumab per dose. Up to a maximum of 5 repeats will be authorised.					
Indication: Severe Crohn's disease					
Treatment Phase: Continuing treatment					
Clinical criteria:					
Patient must require therapy with this drug for this condition administered every 4 weeks					
AND					
Clinical criteria:					
Patient must have received a balance of supply (every 4 weeks) as their most recent course of PBS-subsidised biological medicine treatment for this condition; OR					
Patient must have received this drug administered every 4 weeks as their most recent course of PBS-subsidised biological medicine for this condition under the vedolizumab 300 mg IV continuing restriction (Q4W),					
AND					
Clinical criteria:					
Patient must have an adequate response to this drug defined as a reduction in Crohn Disease Activity Index (CDAI) Score to a level no greater than 150 if assessed by CDAI or if affected by extensive small intestine disease; OR					
Patient must have an adequate response to this drug defined as (a) an improvement of intestinal inflammation as demonstrated by: (i) blood: normalisation of the platelet count, or an erythrocyte sedimentation rate (ESR) level no greater than 25 mm per hour, or a C-reactive protein (CRP) level no greater than 15 mg per L; or (ii) faeces: normalisation of lactoferrin or calprotectin level; or (iii) evidence of mucosal healing, as demonstrated by diagnostic imaging findings, compared to the baseline assessment; or (b) reversal of high faecal output state; or (c) avoidance of the need for surgery or total parenteral nutrition (TPN), if affected by short gut syndrome, extensive small intestine or is an ostomy patient.					
AND					
Clinical criteria:					
Patient must not receive more than 24 weeks of treatment under this restriction					
Population criteria:					
Patient must be aged 18 years or older.					

3.2 While the proposed balance of supply restriction only referred to insufficient therapy, the submission stated that escalation to Q4W treatment is to maintain an adequate response to vedolizumab IV maintenance therapy, and the proposed continuing restriction outlines the clinical endpoints for adequate response to Q4W treatment. The submission did not present any direct randomised trial to support escalation specifically in patients who have had an inadequate response on Q8W treatment but instead drew its justification from observed equivalence in outcomes at week 52 in the GEMINI I/II trial maintenance arms and observed clinical practice from its access program. The submission noted that the Intention-to-Treat (ITT) population from the trials are those who may otherwise have lost response if returned to Q8W treatment (Q8W ineligible). The TGA Product Information (PI) states that patients may clinically benefit from Q4W treatment and that patients reassessed after 12-14 weeks of Q4W treatment should not continue treatment if clinical benefit is not demonstrated. While

dose escalation may be clinically reasonable in this population, the balance of supply restriction was not explicit about what the definition of insufficient therapy is, nor the clinical parameters for escalation. The pre-PBAC response clarified that the proposed restrictions aim to exclude Q8W-ineligible patients, shifting away from the submission's suggestion that these are the intended population. It explains that escalation is for patients at risk of losing response to Q8W therapy and would occur before they no longer meet the adequate response criteria. However, the pre-PBAC response did not specify what would constitute a sufficient loss of response to justify escalation.

3.3 The submission did not specify if ongoing eligibility for Q4W treatment should be contingent on demonstrating response to therapy at a fixed interval after escalation, or only at the end of the 24-week maintenance course in which dose escalation occurred. The TGA PI requires reassessment 12-14 weeks after dose escalation takes place. The restriction wording could be amended such that the balance of supply restriction for dose escalation only allows supply sufficient to 14 weeks.

3.4 The submission did not specify how to handle the cancellation of remaining Q8W scripts when a patient transitions to Q4W treatment nor did the proposed restrictions address patients not transitioning back to Q8W treatment despite indicating that the intended population would be those who would become Q8W ineligible. Patients who dose escalate early in the maintenance period may have 1-2 Q8W repeats remaining, and having these dispensed in addition to the new Q4W prescription may be outside the cost-effective use of the Q8W restriction.

3.5 The submission stated that vedolizumab SC 108 mg, administered every two weeks (Q2W) as another maintenance regimen, is not being proposed as an option for patients who escalate to vedolizumab Q4W treatment. Only patients who are well controlled after vedolizumab IV induction or vedolizumab Q8W are candidates for switching to the vedolizumab SC regimen. While the pre-PBAC response stated that the sponsor was not opposed to SC maintenance after Q4W maintenance, no evidence was provided to support the clinical effectiveness or the equi-effective dosing in the submission nor the pre-PBAC response. Flow-on changes to the vedolizumab SC 108 mg listing for 'Continuing treatment with subcutaneous form or switching from intravenous form to subcutaneous form' might be required to limit access to stable IV induction responders or IV Q8W maintenance responders.

3.6 The submission proposed new separate restrictions for Q4W dose escalation and maintenance/continuing treatment; however, the Secretariat's review noted the dose escalation logic can be achieved by amending the existing Q8W restrictions to include Q4W dosing, and new restrictions may not be necessary. It was noted that administratively it is better for prescribers to be able to use the one restriction, however, to implement the SPA effectively, a separate listing would be required. Further discussion in the economic analysis, estimated usage and financial implications section may inform how the restriction would need to be structured to

ensure cost-neutrality. At the time of consideration, the Secretariat had proposed amendments to the existing restrictions to include Q4W dosing (shown below). Only the restriction wording that would differ from the existing restrictions has been included in this section.

Moderate to severe ulcerative colitis – Balance of Supply (BOS) – 10384M & 10198G

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
VEDOLIZUMAB					
vedolizumab 300mg injection, 1 vial	10384M (public)	1	1	0	Entyvio
vedolizumab 300mg injection, 1 vial	10398G (private)	1	1	0	Entyvio
Restriction Summary 15842 / Treatment of Concept: 15909: Authority Required					
[New]	***Prescribing Instructions**: At the time of the authority application, medical practitioners should request the appropriate maximum number of repeats to complete 24 weeks treatment:* • *Where dosing is to be administered every 8 weeks for continuing treatment following the induction/initial doses – up to a maximum of 2 repeats may be requested* • *Where a patient is dose escalating from 8 weekly to 4 weekly dosing during continuing treatment, a maximum of 3 repeats may be requested to complete 24 weeks treatment for the first course of continuing treatment.*				
[33089]	***Prescribing Instructions:** Where there is a current, approved PBS prescription with valid repeat prescriptions specified (i.e. where the dose is changing), mark the prescription that is intended for no further supply as 'Cancelled'.*				

Moderate to severe ulcerative colitis – Continuing Treatment – 10384M & 10398G

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
VEDOLIZUMAB					
vedolizumab 300mg injection, 1 vial	10384M (public)	1	1	0	Entyvio
vedolizumab 300mg injection, 1 vial	10398G (private)	1	1	0	Entyvio
Restriction Summary 15841 / Treatment of Concept: 15923: Authority Required					
~~17047~~ *[New]*	**Prescribing Instructions:** Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain a response*, with either the 4 weekly or 8 weekly dosing regimen.*				
~~15040~~ *[New]*	**Prescribing Instructions:** Up to a maximum of 2 repeats will be authorised *where dosing is administered every 8 weeks. OR Up to a maximum of 5 repeats will be authorised where dosing is administered every 4 weeks.*				
[New]	***Prescribing Instructions:** If fewer than 2 repeats (for 8 weekly dosing), or fewer than 5 repeats (for 4 weekly dosing) are requested at the time of the application, authority approvals for sufficient repeats to complete 24 weeks treatment may be requested through the Balance of Supply treatment phase PBS restriction.*				

Severe Crohn disease – Balance of Supply (BoS) – 10390W & 10415E

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
VEDOLIZUMAB					
vedolizumab 300mg injection, 1 vial	10390W (public)	1	1	0	Entyvio
vedolizumab 300mg injection, 1 vial	10415E (private)	1	1	0	Entyvio
Restriction Summary 15868 / Treatment of Concept: 15840: Authority Required					
[New]	***Prescribing Instructions**: At the time of the authority application, medical practitioners should request the appropriate maximum number of repeats to complete 24 weeks treatment:* • *Where dosing is to be administered every 8 weeks for continuing treatment following the induction/initial doses – up to a maximum of 2 repeats may be requested* • *Where a patient is dose escalating from 8 weekly to 4 weekly dosing during continuing treatment, a maximum of 3 repeats may be requested to complete 24 weeks treatment for the first course of continuing treatment.*				
[33089]	***Prescribing Instructions:** Where there is a current, approved PBS prescription with valid repeat prescriptions specified (i.e. where the dose is changing), mark the prescription that is intended for no further supply as 'Cancelled'.*				

Severe Crohn disease – Continuing Treatment – 10390W & 10415E

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
VEDOLIZUMAB					
vedolizumab 300mg injection, 1 vial	10390W (public)	1	1	0	Entyvio
vedolizumab 300mg injection, 1 vial	10415E (private)	1	1	0	Entyvio
Restriction Summary 15881 / Treatment of Concept: 15839: Authority Required					
~~17047~~ *[New]*	**Prescribing Instructions:** Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain a response*, with either the 4 weekly or 8 weekly dosing regimen.*				
~~17145~~ *[New]*	**Prescribing Instructions:** At the time of the authority application, medical practitioners should request the appropriate number of vials, to provide sufficient for a single infusion of 300 mg vedolizumab per dose. Up to a maximum of 2 repeats will be authorised, *where dosing is administered every 8 weeks. OR Up to a maximum of 5 repeats will be authorised where dosing is administered every 4 weeks.*				
~~15152~~ *[New]*	**Prescribing Instructions:** If fewer than 2 repeats *(for 8 weekly dosing), or fewer than 5 repeats (for 4 weekly dosing)* are requested at the time of the application, authority approvals for sufficient repeats to complete 24 weeks treatment may be requested by telephone and authorised through the Balance of Supply treatment phase PBS restriction. Under no circumstances will telephone approvals be granted for continuing authority applications, or for treatment that would otherwise extend the continuing treatment period.				

4 Comparator

4.1 The submission nominated Q8W maintenance treatment as the main comparator with a claim of non-inferiority with respect to efficacy based on the outcome of clinical remission at Week 52 in the clinical trials, stating this was the basis of the March 2015

recommendation for vedolizumab IV Q8W maintenance treatment. However, the ITT population of the trials includes Q8W ineligible patients for whom Q4W treatment would be clinically superior.

4.2 The submission did not include other biologic disease-modifying antirheumatic drugs (bDMARDs) as relevant comparators for each indication. Patients who become Q8W ineligible must discontinue vedolizumab and may commence treatment with an alternative bDMARD. Since the target population are those likely to have stopped responding to Q8W treatment, alternative bDMARDs would be relevant comparators.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

5.2 The PBAC noted and welcomed input from Crohn's and Colitis Australia (CCA). They described how compassionate access programs are unsustainable, create direct relationships between patients and pharmaceutical companies, and do not promote equitable access. Additional comments from CCA identified a practical need for follow on changes to dosing and restrictions, noting that Q4W should be accompanied by access to weekly (Q1W) subcutaneous formulations. They claim that subcutaneous dosing is better for the environment, with reduced travel and intravenous infusions, both of which reduce the impact of treatment on patient lives. The PBAC would welcome a resubmission with evidence to support transitioning from IV Q4W to SC Q1W.

Clinical evidence

5.3 The submission was primarily based on an access program that the sponsor has implemented in Australia since September 2018 to provide additional vedolizumab 300 mg IV doses to enable Q4W maintenance dosing for eligible patients. Real-world utilisation data from the access program, spanning August 2021 to September 2023, demonstrated that Q4W treatment is already being used in clinical practice for patients who require dose escalation to maintain disease control.

5.4 The submission also referenced clinical trial findings from the GEMINI I and GEMINI II phase 3, randomised, placebo-controlled, blinded, multicentre studies (see Table 1). The submission claimed that both the trial and program highlight the unmet need for a PBS-listed Q4W option to ensure equitable access and alignment with the TGA-approved PI.

Table 1: Clinical trials presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
GEMINI I NCT00783718	Vedolizumab as induction and maintenance therapy for ulcerative colitis. Sandborn, W J et al.	22 August 2013 New England Journal of Medicine, 2013; 369(8): 699-710
GEMINI II NCT00783692	Vedolizumab as Induction and Maintenance Therapy for Crohn's Disease Sandborn, W J et al.	22 August 2013 New England Journal of Medicine, 2013; 369(8): 711-721

Source: Table 2-4, p38 of the submission and Table 2-42, p 68 of the submission.

Comparative effectiveness & harms

5.5 The submission claimed that both the GEMINI I and II trials found no statistically significant difference between Q4W and Q8W maintenance treatment for clinical remission at week 52 in terms of clinical response, mucosal healing, clinical remission and corticosteroid-free remission. These trials were designed to compare active treatment with placebo; they were not powered to formally test superiority or equivalence between Q4W and Q8W treatment, nor to evaluate dose escalation in patients not showing an adequate response to Q8W treatment. The justification for escalation therefore relies on the observed parity of Q4W and Q8W in maintenance responders and on the clinical practice demonstrated via the Access Program, rather than on a dedicated randomised trial of escalation.

5.6 The submission stated that both the GEMINI I and GEMINI II trials concluded that there were no statistically significant differences between Q4W and Q8W maintenance in the occurrence of adverse events (AEs), drug related AEs, serious infectious AEs (SAEs) and drug-related SAEs.

Clinical claim

5.7 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Q4W maintenance compared with Q8W maintenance for patients who achieved a clinical response to induction therapy.

5.8 The PBAC considered the claim of non-inferior comparative effectiveness was adequately supported by data for patients who have responded to induction therapy (induction responders) and were not or would not be Q8W ineligible. The PBAC noted that evidence comparing Q8W treatment to Q4W treatment in induction responders who have demonstrated a loss of adequate response to Q8W treatment has not been presented.

5.9 The PBAC noted that it was unclear whether the proposed population in the submission aligned with the GEMINI I and GEMINI II trials. The PBAC identified that the response criteria in the trials did not align with PBS response criteria, and added that, in clinical practice, there is a high risk of Q8W non-responders escalating to Q4W treatment.

5.10 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

5.11 As a Category 3 submission, the economic analysis was not independently evaluated.

5.12 The submission presented a cost-minimisation approach (CMA) (see Table 2) that includes a SPA rebate of [redacted]% of the cost of additional Q4W doses minus co-payments, administration costs and MBS costs, claiming that this would make the PBS listing cost neutral to the PBS/RPBS. The submission claimed this was consistent with their proposal for the additional dose of vedolizumab 300 mg IV at Week 10 for severe CD, considered at the March 2024 PBAC meeting.

Table 2: Cost-minimisation approach

	Vedolizumab Q8W	Vedolizumab Q4W	Incremental
Severe CD			
Vedolizumab powder for injection, 300 mg			
PBS subsidised	13	13	0
Rebated	0	13	13
AEMP per vedolizumab powder for injection, 300 mg			
PBS subsidised	$[redacted]	$[redacted]	[redacted]
Rebated	$[redacted]	$[redacted]	[redacted]
Cost of treatment			
PBS subsidised	$[redacted]	$[redacted]	$[redacted]
MSUC			
Vedolizumab powder for injection, 300 mg			
PBS subsidised	13	13	0
Rebated	0	13	13
AEMP per vedolizumab powder for injection, 300 mg			
PBS subsidised	$[redacted]	$[redacted]	[redacted]
Rebated	$[redacted]	$[redacted]	[redacted]
Cost of treatment			
PBS subsidised	$[redacted]	$[redacted]	$[redacted]

Source: Table 3-3 of the submission main body.
Abbreviations: AEMP = Approved ex-manufacturer price; CD = Crohn disease; MSUC = moderate to severe ulcerative colitis; PBS = Pharmaceutical benefits Scheme; Q4W = every 4 weeks; Q8W = every 8 weeks.

5.13 The cost-minimisation table shows 13 Q8W doses being supplied over 24 months, and 26 Q4W doses being supplied over the same period, of which [redacted]% are rebated.

5.14 The submission proposed CMA:

- assumes all the patients eligible for escalation to Q4W would otherwise continue to access Q8W dosing in the absence of a Q4W listing (i.e. are/would be Q8W responders),
- assumes all patients requiring dose escalation were captured by the sponsor's Access Program at the time the data sample was taken, and
- defines patients requiring escalation to Q4W as those who have "insufficient therapy" under the Q8W listing and such patients would be required to "demonstrate an adequate response to treatment" to continue Q4W treatment.

5.15 While not explicit in the proposed restrictions, the submission stated that patients would require escalation if they no longer maintained an adequate treatment response to Q8W, however, the pre-PBAC response stated that patients who escalated would still be Q8W eligible. In the absence of a Q4W listing and the access program, patients who become Q8W ineligible must discontinue vedolizumab, and therefore such patients who accessed Q4W treatment via the access program reflect a population that was not anticipated under the 2015 PBAC recommendation. If all the above assumptions hold true, vedolizumab usage in this population would only be cost neutral if the sponsor rebates the full cost of all Q4W doses (i.e., 26 doses over 2 years) for Q8W ineligible patients rather than just the incremental 13 doses over Q8W.

5.16 The submission excluded MBS costs from the CMA on the basis that prescribers have utilised MBS item 14245 for the IV administration of the Q4W doses for patients on the access program for the last 7 years, and that this cost has been accepted by the Commonwealth. MBS item 14245 is restricted to infusions of agents provided under section 100 of the PBS. The administration of non-PBS vedolizumab doses provided via an access program should not have been claimed under this item, and doing so is outside the scope of the MBS and constitutes non-compliance. The additional MBS expenditure and administration expenses of the additional doses must be included in the CMA as per the PBAC Guidelines. Furthermore, this MBS item should not be used for the administration of non-PBS supplies of vedolizumab.

5.17 If the SPA rebate is calculated based on the estimated uptake of Q4W dosing (whether just the additional doses to Q8W or all Q4W doses), with no adjustment post-listing based on actual PBS utilisation, the accuracy of the weighted AEMP will be critically dependent on the reliability of the estimated Q4W uptake. The Department advised that the rebate can be based on the actual uptake if the Q4W listing is separate to the Q8W listing.

5.18 The published AEMP of vedolizumab 300 mg IV used in the submission remains current as of 1 November 2025.

Drug cost/patient/year: $[redacted] - $[redacted]

5.19 The drug cost/patient/year of MSUC maintenance Q4W would be $[redacted], based on 13 doses per year at a weighted AEMP of $[redacted].

5.20 The drug cost/patient/year of severe Crohn disease maintenance Q4W would be $[redacted], based on 13 doses per year at a weighted AEMP of $[redacted].

Estimated PBS usage and financial implications

5.21 Table 3 presents the estimated extent of use and cost of the additional doses of vedolizumab 300mg IV Q4W to the PBS/RPBS and the net financial implications to the MBS and PBS/RPBS as proposed in the submission. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

Table 3: Revised estimates with effective pricing showing only additional Q4W usage and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use – severe Crohn disease						
Number of Q4W scripts dispensed	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of Q8W scripts impacted	-[redacted][2]	-[redacted][2]	-[redacted][2]	-[redacted][2]	-[redacted][2]	-[redacted][2]
Estimated Impact (Scripts x DPMQ[a] - Co-Payment) – severe Crohn disease						
Q4W cost to PBS/RPBS less co-payment ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]
Q8W cost to PBS/RPBS less co-payment ($)	-[redacted][3]	-[redacted][3]	-[redacted][3]	-[redacted][3]	-[redacted][3]	-[redacted][3]
Net cost to the PBS/RPBS ($)	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Estimated extent of use – moderate to severe ulcerative colitis						
Number of Q4W scripts dispensed	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]
Number of Q8W scripts impacted	-[redacted][7]	-[redacted][7]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]
Estimated Impact (Scripts x DPMQ[a] - Co-Payment) – moderate to severe ulcerative colitis						
Q4W cost to PBS/RPBS less co-payment ($)	[redacted][9]	[redacted][9]	[redacted][9]	[redacted][10]	[redacted][10]	[redacted][10]
Q8W cost to PBS/RPBS less co-payment ($)	-[redacted][4]	-$[redacted][4]	-[redacted][9]	-[redacted][9]	-[redacted][9]	-[redacted][9]
Net cost to the PBS/RPBS ($)	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Combined impact (MSUC + CD)						
MBS cost	$0	$0	$0	$0	$0	$0
Net cost to the PBS/RPBS (pre-rebate)	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][3]	[redacted][3]
Rebate	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][3]	-[redacted][3]
Net cost to the PBS/RPBS	$0	$0	$0	$0	$0	$0

[a] based on current effective prices

Abbreviations: MBS = Medical Benefits Scheme; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; MSUC = moderate to severe ulcerative colitis; CD = severe Chron disease.

The redacted values correspond to the following ranges:

[1] 500 to < 5,000
[2] 10,000 to < 20,000
[3] $10 million to < $20 million
[4] $20 million to < $30 million
[5] $0 to < $10 million
[6] 5,000 to < 10,000
[7] 20,000 to < 30,000
[8] 30,000 to < 40,000
[9] $30 million to < $40 million
[10] $40 million to < $50 million

5.22 The submission estimated that 50,000 to < 60,000 additional doses (every 2nd Q4W supply; 5,000 to < 10,000 in Year 1 and 10,000 to < 20,000 in Year 6) would be supplied over the first six years of listing and this would result in a 200,000 to < 300,000 reduction in Q8W scripts and a net financial impact of $50 million to < $60 million ($0 to < $10 million in Year 1 to $10 million to < $20 million in Year 6). The submission offered to rebate this amount via a SPA to result in a $0 net cost to the PBS/RPBS.

5.23 The estimates assumed all Australians eligible for the Q4W treatment had already been included in the sponsor's access program and therefore the continuing scripts were projected to increase annually by a fixed rate of [redacted]% for CD and [redacted]% for MSUC based on the proportion of Q8W patients who required escalation in the access program. This may not reflect the actual PBS usage of Q4W treatment in practice.

5.24 The submission estimated there to be no financial implications to the PBS/RPBS as the submission proposed that any additional cost of Q4W minus co-payments would be reimbursed as a rebate to the Commonwealth. The submission outlined that during the access program, patients were receiving Q8W dosing via the PBS and the additional Q4W doses from the sponsor. As such, the access program may have already increased PBS utilisation over the last 7 years by retaining patients who would have otherwise discontinued Q8W therapy.

5.25 The proposed restriction wording did not include the cancellation of Q8W scripts when a patient dose escalates, yet the submission assumed patients would not return to Q8W treatment. The model did not account for the risk of overlapping Q8W and Q4W scripts during the transition, which could lead to double-counting or wastage. Without explicit protocols for script cancellation or transition management, there is a risk of overestimating the drug utilisation and rebate requirements.

6 PBAC Outcome

6.1 The PBAC did not recommend vedolizumab 300mg IV Q4W for the treatment of patients with MSUC or severe CD. The submission suggested that the requested listings would be cost neutral, however, costs to the MBS and Services Australia incurred by providing additional infusions for Q4W dosing were not included in the usage estimates and financial implications should be accounted for to be considered truly cost neutral. The PBAC highlighted a previous submission for vedolizumab in the March 2024 PBAC meeting, which outlined that a cost neutral listing should be inclusive of MBS costs associated with additional testing and specialist visits.

6.2 The secondary reason for the PBAC not recommending vedolizumab Q4W was due to a poorly defined clinical need for dose escalation. The clinical trial populations were defined as patients who had a clinical response to induction treatment. The population proposed by the submission was requested for patients who responded to induction treatment and require a dose escalation to maintain an adequate response to treatment. The PBAC noted that dose optimisation may benefit some patients,

however, considered there was a high risk of use outside of the intended population, and a risk of high Q4W uptake following inadequate treatment response to Q8W maintenance. The PBAC considered that clearer eligibility for dose escalation needed to be defined, and that modelling to account for the high likelihood of increased uptake outside of intended indications should be provided.

6.3 The PBAC acknowledged the need for effective disease modifying treatments to manage MSUC and CD, including personalised dosing regimens, noting there is no clear hierarchy and limited alternatives.

6.4 The PBAC highlighted that providing dose escalation via a sponsor access program to patients who would otherwise not respond to Q8W maintenance therapy, retaining access to PBS-subsidised vedolizumab therapy instead of transitioning to another therapy, is not appropriate in the absence of a PBAC recommendation that vedolizumab is cost-effective in this population. The PBAC likewise highlighted that usage of the MBS for the infusion of non-PBS doses of vedolizumab is not appropriate and is considered non-compliance.

6.5 The PBAC considered a resubmission for vedolizumab 300mg IV Q4W should address the following issues:

- Estimated usage and financial implications calculations should include the costs incurred by the MBS and Services Australia involved in all additional infusions.
- Definition of the clinical place for dose escalation and clear guidelines for Q8W non-responders who should permanently discontinue therapy and would not be eligible for Q4W treatment.
- Outline timing and criteria for clinical reassessment post dose escalation to determine effectiveness of Q4W.
- Clarify flow on consequences of Q4W dosing such as if patients become ineligible to return to Q8W or if they can transition to SC maintenance and SC dosing frequency.
- Identify script transition management to avoid overlap between transition from Q8W to Q4W and ensure accurate tracking of Q4W uptake.
- Include modelling that accounts for increased uptake of Q4W dosing within and outside of intended indications.

6.6 The resubmission may be lodged for any future PBAC meeting via the standard re-entry pathway.

6.7 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

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

The sponsor had no comment.