5.25 TEPROTUMUMAB, Powder for I.V. infusion 500 mg, Tepezza®, AMGEN AUSTRALIA PTY LTD.

1 Purpose of Submission

1.1 The Category 3 submission sought the PBAC's consideration of a revised proposal for the listing of teprotumumab for the treatment of active, moderate-to-severe (MS) thyroid eye disease (TED). The submission noted that the PBS listing for this population, recommended at the May 2025 PBAC meeting, could not be progressed, as the previously proposed price was no longer considered feasible by the sponsor.

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus standard of care (SoC) consisting of IV methylprednisolone (IVMP) with or without mycophenolate mofetil (MMF) in the first-line (1L) setting and tocilizumab in the second-line (2L) setting.

2 Background

Registration status

2.1 Teprotumumab was TGA registered on 27 March 2025 for the treatment of moderate to severe TED. The teprotumumab product information (PI) states that teprotumumab is subject to additional monitoring in Australia, with healthcare professionals encouraged to report any suspected adverse events.

Previous PBAC consideration

2.2 Teprotumumab was first considered by the PBAC and not recommended for PBS listing at the March 2025 meeting. At the meeting, the PBAC accepted that there was a high clinical need in the requested patient population, and the evidence presented demonstrated that teprotumumab was more effective in reducing proptosis and diplopia compared to the current SoC, which may lead to a reduced utilisation of eye surgery. However, the PBAC considered that due to the limited data available, the complexity of the economic model led to a high degree of uncertainty. The PBAC considered that revision to model inputs and a price reduction reflective of an incremental cost-effectiveness ratio (ICER) of less than $55,000 to < $75,000 per quality adjusted life year (QALY) gained would be required to address residual uncertainty and achieve a cost-effective listing, together with a risk sharing arrangement (RSA) (paragraphs 7.1 and 7.17, teprotumumab Public Summary Document [PSD], March 2025 PBAC Meeting).

2.3 An early resolution resubmission for teprotumumab was subsequently considered at the May 2025 PBAC meeting, with the PBAC recommending the listing of teprotumumab for the treatment of active MS TED.

2.4 The PBAC recommended additional changes to the restriction so that retreatment was not mistakenly initiated through the proposed continuing treatment phase and bypass the activity (clinical activity score [CAS] of ≥ 3) and severity criteria (2021 European Group on Graves' Orbitopathy [EUGOGO] guidelines) for retreatment (paragraph 11.2, teprotumumab PSD, May 2025 PBAC Meeting).

2.5 The PBAC maintained that the structure of the economic model remained a significant limitation for the consideration of the cost-effectiveness of teprotumumab. To address the uncertainty in the model, the PBAC noted that the resubmission proposed a re-specified base case with revised inputs. The PBAC noted that the changes to the model aligned with its previous advice and significant revision had been made to the utility weights in the economic model. The PBAC considered that while the revised utility weights were subject to some uncertainty, the values appeared to have greater face validity compared to the values applied to the economic model in the March 2025 submission. The PBAC also noted that a price reduction had been proposed which aligned with an ICER of less than $55,000 to < $75,000 per QALY gained. Overall, the PBAC considered that while uncertainty remained related to the structure and the data informing the economic model, that the changes made had reduced uncertainty, and in the context of a rare disease with a high and unmet clinical need, the ICER of $55,000 to < $75,000 per QALY gained based on the revised model was acceptable (paragraph 11.3, teprotumumab PSD, May 2025 PBAC Meeting).

2.6 The PBAC accepted that the resubmission largely addressed its concerns related to the financial estimates raised at the March 2025 consideration and considered that the revised financial estimates were reasonable (paragraph 11.4, teprotumumab PSD, May 2025 PBAC Meeting).

2.7 The resubmission proposed a 2-tier RSA with the second tier allowing for [redacted]% of patients who may be retreated with teprotumumab. The PBAC considered that this was reasonable. However, the PBAC considered that there was likely to be a delay between the listing of teprotumumab and the onset of retreatment and therefore considered that the incorporation of retreatment in the RSA should start from the second year of listing (paragraph 11.5, teprotumumab PSD, May 2025 PBAC Meeting).

3 Requested listing

3.1 The submission did not propose changes to the requested patient population or clinical intent of the PBS restriction or the intended dosing regimen (8 infusions per treatment course). The PBS listing recommended by the PBAC at its May 2025 meeting is shown below.

MEDICINAL PRODUCT medicinal product pack	DPMQ	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TEPROTUMUMAB					
Initial					
Teprotumumab 500 mg injection, 1 vial	Public $21,295.36 published price $[redacted] effective price Private $21,344.24 published price $[redacted] effective price	3	3	0	Tepezza
Continuing					
Teprotumumab 500 mg injection, 1 vial	Public $31,943.04 published price $[redacted] effective price Private $ 31,991.92 published price $[redacted] effective price	6	6	6	Tepezza

Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)

Prescriber type: ☒ Medical Practitioners

Restriction type: ☒ Authority Required (telephone/electronic) [new listing]

Authority type: ☒ Non-complex Authority Required (non-CAR)

Administrative Advice: No increase in the maximum number of repeats may be authorised.

Special Pricing Arrangements apply

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.

Severity: Moderate-to-severe

Condition: Thyroid eye disease

Indication: Active Moderate-to-severe thyroid eye disease

Treatment Phase: Initial treatment

Clinical criteria:

Patient must not have previously received PBS-subsidised treatment with this drug for this condition; OR

Patient must be both: (i) undergoing re-treatment with this drug for this condition (ii) have demonstrated response to previous PBS-subsidised treatment with this drug for this condition.

AND

Clinical criteria:

Patient must have a clinical activity score (CAS) of three or more for the most severely affected eye,

AND

Clinical criteria:

Patient must have two or more of the following: (i) Proptosis ≥3 mm above normal for race and gender, (ii) Lid retraction ≥2mm, (iii) Moderate to severe soft-tissue involvement, (iv) inconstant or constant diplopia

AND

Clinical criteria:

Patient must be at least 18 years of age

Treatment criteria:

Must be treated by a specialist physician experienced in the treatment of thyroid eye disease

Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records for the first prescription only:'

(i) Baseline clinical activity score (CAS)

(ii) Confirmation of the presence of Thyroid Eye Disease (this includes evidence of two or more of the following:

(i) Proptosis ≥3mm above normal for race and gender,

(ii) Lid retraction ≥2mm, (iii) Moderate to severe soft-tissue involvement, (iv) Inconstant or constant diplopia)
Prescribing Instructions: Increased maximum amounts may only be authorised where a patient's weight is greater than 150 kg.
Prescribing Instructions: After completing 8 doses in total of PBS subsidised treatment with teprotumumab, a patient may be eligible for re-treatment through the initial treatment phase only, if a response to treatment was previously demonstrated.
Caution: Assess patients' hearing before, and routinely during and after treatment, including use of audiograms where clinically warranted. If significant hearing loss is experienced while receiving treatment with this drug for this condition, treatment discontinuation is advised. See also TGA approved Product Information
Caution: Teprotumumab is contraindicated in pregnancy. Women of childbearing potential should have a negative pregnancy test before starting treatment with teprotumumab, and monthly during treatment and for 6 months after cessation of treatment. If the patient becomes pregnant during treatment teprotumumab should be discontinued. See also TGA approved Product Information.

Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
Prescriber type: ☒ Medical Practitioners
Restriction type: ☒ Authority Required (Streamlined) [new code]
Authority type: ☒ Non-complex Authority Required (non-CAR)
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Special Pricing Arrangements apply
Indication: Active Moderate-to-severe thyroid eye disease
Treatment Phase: Continuing treatment
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition
Treatment criteria:
Must be treated by a specialist physician experienced in the management of thyroid eye disease; or
Must be treated by a medical practitioner in consultation with a specialist physician experienced in the management of thyroid eye disease
Prescribing Instructions: Increased maximum amounts may only be authorised where a patient's weight is greater than 150 kg.
Prescribing Instructions: After completing 8 doses in total of PBS subsidised treatment with teprotumumab, a patient may be eligible for re-treatment through the initial treatment phase only, if a response to treatment was previously demonstrated.
Assess patients' hearing before, and routinely during and after treatment, including use of audiograms where clinically warranted. If significant hearing loss is experienced while receiving treatment with this drug for this condition, treatment discontinuation is advised. See also TGA approved Product Information
Teprotumumab is contraindicated in pregnancy. Women of childbearing potential should have a negative pregnancy test before starting treatment with teprotumumab, and monthly during treatment and for 6 months after cessation of treatment. If the patient becomes pregnant during treatment teprotumumab should be discontinued. See also TGA approved Product Information.

3.2 The submission requested a special pricing arrangement (SPA). The submission proposed an increase to the effective ex-manufacturer's price (EMP) previously proposed by the sponsor for the May 2025 PBAC meeting from $[redacted] to $[redacted] per vial. The submission also proposed an increase to the published EMP from $10,318.76 to $10,647.68. The Pre-PBAC Response proposed a reduced EMP of $[redacted] per vial.

3.3 The Pre-PBAC Response noted that the proposed PBS restriction specifies that patients 'must be treated by a specialist physician experienced in the treatment of thyroid eye disease'. The Response stated that recent clinical feedback suggested that the use of the word 'physician' could be misinterpreted by some surgeons who do not classify themselves as physicians. The Response therefore requested an alternate treatment criterion be considered; for example: 'Must be treated by a specialist medical practitioner experienced in the treatment of thyroid eye disease'.

4 Comparator

4.1 The previous submissions considered by the PBAC in March 2025 and May 2025 nominated SoC as the comparator consisting of IVMP with or without MMF in the 1L setting and tocilizumab in the 2L setting. The PBAC previously considered that this was appropriate, however noted that tocilizumab does not currently have registration by the TGA or PBS for this indication and considered that rituximab was also a relevant comparator in the 2L setting (paragraph 7.6, teprotumumab PSD, March 2025 PBAC Meeting).

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer inputs

5.2 The PBAC noted and welcomed the input from health care professionals (11), individuals who would like access to teprotumumab to treat their own condition (2) and the Orbital Plastics and Lacrimal (OPAL) and Ocular Rheumatology (EORC) units from the Royal Victorian Eye and Ear Hospital (RVEEH) via the Office of Health Technology Assessment Consultation Hub.

5.3 Input received from health care professionals (HCPs) noted an unmet clinical need for effective and disease specific therapies for patients living with TED in Australia. HCPs described current SoC to include corticosteroids, other immunosuppressive therapies, and radiotherapy, which were noted to target inflammation and symptoms, but had limited impact on key disease features such as proptosis and diplopia and were noted to be associated with a range of serious side effects. Surgical interventions were described as effective for specific indications, particularly for sight-threatening disease or structural correction, but were noted as invasive, associated with risks, and typically requiring multiple staged procedures. Teprotumumab was described as a targeted biological therapy acting on the underlying disease mechanism in TED. It was considered that treatment with teprotumumab would lead to clinically meaningful improvements during the active phase of disease, with potential to reduce or avoid the need for surgical intervention. Hearing impairment was identified as a key adverse

effect of teprotumumab, with HCPs highlighting the importance of careful patient selection and ongoing monitoring. The current cost of teprotumumab was identified as a significant barrier to access.

5.4 Individuals who would like access to teprotumumab to treat their own health condition described the significant burden that TED had on quality of life. Individuals noted experiencing pain, double vision, light sensitivity, fatigue, sleep disturbance, reduced ability to work, loss of confidence, and significant changes to daily activities and lifestyle. The condition was described as affecting personal identity, appearance, social participation, and future life decisions. Individuals with TED noted the limited treatment options currently available. Individuals also noted corrective surgery as an option but that it was associated with significant risks, including further vision loss. Individuals considered teprotumumab to offer potential benefits through reduction in proptosis, inflammation, double vision, pain and other symptoms, with the possibility of improving function, appearance, independence and overall quality of life. Concerns were noted about adverse effects, particularly hearing loss.

5.5 The PBAC noted advice from the OPAL and EORC units at the RVEEH supporting PBS listing of teprotumumab for active MS TED. The input stated that, in their experience, IVMP had shown limited effectiveness in reducing TED severity. The input noted that tocilizumab has been used in refractory cases but was not PBS-funded for TED and provided minimal reduction in proptosis. In contrast, the input highlighted the clinical benefits of teprotumumab observed in trials, which were considered to be substantially greater than those achieved with other TED treatments to date. The input also noted evidence supporting the use of teprotumumab for sight-threatening TED-dysthyroid optic neuropathy (DON)[1]. It also noted that patients with longer-standing TED may still respond favourably to teprotumumab, with studies demonstrating improvements in proptosis and diplopia in patients with chronic, low-activity TED[2,3,4].

Clinical evidence

5.6 The submission did not present new efficacy or safety data.

5.7 Overall, the PBAC previously considered that while there was significant uncertainty related to the indirect treatment comparisons (ITCs) presented, the totality of the available evidence suggested that the claim of superior efficacy of teprotumumab

[1] Tamhankar MA, Pradeep T, Chen Y, Briceno CA. Real-World Experience With Teprotumumab in Patients With Dysthyroid Optic Neuropathy. J Neuroophthalmol 2024;44(1):74-79.
[2] Ozzello DJ, Dallalzadeh LO, Liu CY. Teprotumumab for chronic thyroid eye disease. Orbit 2022;41(5):539-546
[3] Ugradar S, Kang J, Kossler AL, et al. Teprotumumab for the treatment of chronic thyroid eye disease. Eye (Lond) 2022;36(8):1553-1559
[4] Douglas RS, Couch S, Wester ST, et al. Efficacy and Safety of Teprotumumab in Patients With Thyroid Eye Disease of Long Duration and Low Disease Activity. J Clin Endocrinol Metab 2023;109(1):25-35.

versus IVMP in the 1L setting and versus tocilizumab in the 2L setting was likely reasonable. However, the PBAC considered that the magnitude of treatment effect of teprotumumab versus SoC was uncertain due to the substantial transitivity violations across the comparisons (paragraph 7.11, teprotumumab PSD, March 2025 PBAC Meeting).

5.8 The previous submissions did not present a formal comparison of safety for teprotumumab versus IVMP or tocilizumab. The PBAC previously noted that while there were significant safety concerns associated with teprotumumab, including permanent hearing impairment, as well as other common adverse events, that IVMP with or without MMF and tocilizumab were also associated with significant safety risks. The PBAC previously considered that overall, the claim of non-inferior comparative safety of teprotumumab versus the current SoC therapies to be uncertain, but likely reasonable (paragraph 7.12, teprotumumab PSD, March 2025 PBAC Meeting).

Economic analysis

5.9 The submission proposed two changes to the economic model previously accepted by the PBAC at the May 2025 meeting:

- Increasing the effective EMP from $[redacted] to $[redacted] per vial; and
- Reducing the assumed average vials per treatment course from 27.14 to 23.

5.10 The submission stated that the previously proposed price, accepted by the PBAC at its May 2025 meeting, could not be progressed, as it was no longer considered feasible by the sponsor. The proposed price increase led to a [redacted]% increase to the May 2025 ICER, from $55,000 to < $75,000 per QALY gained to $95,000 to < $115,000 per QALY gained. The Pre-PBAC Response proposed a revised price for teprotumumab of $[redacted] per vial, resulting in an ICER of $95,000 to < $115,000 per QALY gained.

5.11 The recommended dosing for teprotumumab is weight based with a lower dose (10 mg/kg) for the first infusion and a higher dose for the subsequent seven infusions (20 mg/kg). Teprotumumab is supplied as 500 mg vials, requiring dose preparation to be rounded to whole vials for dispensing and administration. For the previous submissions, the average vials per course was estimated using individual patient weight distribution from the pivotal trial population (OPTIC), with rounding to whole 500 mg vials, and allowing for wastage arising from fixed vial size. This resulted in an average vials per course (with wastage and compliance) of 27.14, comprising of an average of 2.10 vials for the first infusion and 3.58 vials for each of the subsequent 7 infusions.

5.12 The submission proposed to reduce the average vials per treatment course to 23, comprising of 2.0 vials for the first infusion and 3.0 vials for each of the subsequent 7 infusions. The submission stated that the revised values were based on updated real-world utilisation. The submission stated that the revised values reflect the differences

between the patient weight distribution observed in pivotal trials and routine clinical practice, where a lower average weight results in fewer vials required per infusion due to fixed 500 mg vial pack size and rounding. The submission noted that the revision does not change the recommended regimen, clinical benefit, or outcomes associated with teprotumumab; it is an update to the utilisation assumption only, based on the latest available evidence. However, the submission did not provide further detail or references related to the real-world data and therefore the updated data could not be verified by the Secretariat. The proposed change to the average vials per treatment course of teprotumumab reduced the ICER of the May 2025 submission by [redacted]%, from $55,000 to < $75,000 per QALY gained to $55,000 to < $75,000 per QALY gained. The Pre-PBAC Response provided clarification that the revised vial usage was based on weight data obtained from an Australian clinician. The Response noted that the clinician had treated 48 TED patients (71% women) over 15 years with weights recorded for 42 patients. The mean weight was reported to be 67.1 kg for women and 77.7 kg for men. Using the clinician-reported distribution of 71% women and 29% men results in a weighted mean of 70.2 kg, resulting in an average 23 vials per patient[5]. The Response also noted a Danish study reported a distribution of approximately 80% women and 20% men[6], resulting in a weighted average of 69.2 kg and an average of 23 vials per patient course. The Response acknowledged that the clinician-reported data may not be representative of the broader patient population. However, it argued that it was directly relevant to Australian TED patients managed in routine specialist practice. The Response also noted that an average utilisation of 23 vials per patient course was consistent with 'internal sponsor real-world utilisation data'. However, detail related to this data was not provided.

5.13 The economic evaluations of the submission and Pre-PBAC Response compared with the March and May 2025 economic models are presented in Table 1.

[5] For patients weighing more than 50 kg and up to 75 kg, the course requires 23 vials: 2 vials for the initial 10 mg/kg infusion and 3 vials for each of the seven subsequent 20 mg/kg infusions. Patients at or below 50 kg require fewer vials, while patients above 75 kg require more vials for continuing infusions.

[6] Peter Laurberg, Dalia C. Berman, Inge Bülow Pedersen, Stig Andersen, Allan Carlé, Incidence and Clinical Presentation of Moderate to Severe Graves' Orbitopathy in a Danish Population before and after Iodine Fortification of Salt, The Journal of Clinical Endocrinology & Metabolism, Volume 97, Issue 7, 1 July 2012, Pages 2325–2332.

Table 1: Results of the July 2026 submission model compared with the March and May 2025 economic models

	Teprotumumab	IVMP	Incremental	ICER
March 2025 submission				
Total cost	$[redacted]	$[redacted]	$[redacted]	-
LYs	16.13	16.13	0.00	-
QALYs	8.10	6.82	1.286	$[redacted][1]
May 2025 resubmission				
Total cost	$[redacted]	$[redacted]	$[redacted]	-
LYs	12.63	12.63	0.00	-
QALYs	9.74	8.77	0.967	$[redacted][1]
1. May 2025 resubmission + increasing the teprotumumab effective EMP from $[redacted] to $[redacted] per vial				
Total cost	$[redacted]	$[redacted]	$[redacted]	-
LYs	12.63	12.63	0.00	-
QALYs	9.74	8.77	0.967	$[redacted][2]
2. May 2025 resubmission + reducing the assumed average vials per treatment course from 27.14 to 23.00.				
Total cost	$[redacted]	$[redacted]	$[redacted]	-
LYs	12.63	12.63	0.00	-
QALYs	9.74	8.77	0.967	$[redacted][1]
July 2026 submission (1 + 2)				
Total cost	$[redacted]	$[redacted]	$[redacted]	-
LYs	12.63	12.63	0.00	-
QALYs	9.74	8.77	0.967	$[redacted][1]
Pre-PBAC Response (teprotumumab EMP = $[redacted]; and average vials per treatment course = 23.00)				
Total cost	$[redacted]	$[redacted]	$[redacted]	-
LYs	12.63	12.63	0.00	-
QALYs	9.74	8.77	0.967	$[redacted][1]

Source: March 2025 PBAC minutes with May 2025 Addendum, Table 30 and current submission's economic model: 'Attachment 1 Tepezza Economic model.xlsb' and the Pre-PBAC Response's economic model: '5.25 - Attachment 1 Tepezza Economic model pre-PBAC response.xlsb'

The redacted values correspond to the following ranges:

[1] *$75,000 to < $95,000*

[2] *$95,000 to < $115,000*

5.14 The Pre-PBAC Response noted that teprotumumab is a fixed-course treatment given as eight infusions over 24 weeks, and therefore drug costs incur almost entirely in the first six months of the economic model. In contrast, the modelled clinical benefits from improved proptosis and diplopia, reduced long-term disease burden, and avoided or reduced rehabilitative surgery accrue over a 20-year time horizon. The Response noted that a discount rate of [redacted]% for costs and outcomes had limited impact on upfront treatment costs but reduced the present value of future health gains. The Response noted that this issue was recognised in the Review of the Discount Rate in the PBAC Guidelines Report (2022)[7] and the recent HTA Policy and Methods Review[8]. The

[7] University of Technology Sydney (2022). Review of the Discount Rate in the PBAC Guidelines Report. Centre for Health Economics Research and Evaluation (CHERE). Available at: https://opus.lib.uts.edu.au/bitstream/10453/181863/2/Viney%20et%20al%20%282022%29%20Review%20of%20the%20Discount%20Rate.pdf

[8] Australian Government Department of Health and Aged Care (2024) Health Technology Assessment Policy and Methods Review – Final report. Australian Government. Available at: https://www.health.gov.au/sites/default/files/2024-09/health-technology-assessment-policy-and-methods-review-final-report_0.pdf

Response noted that Recommendation 39 of the HTA Policy and Methods Review supports a lower discount rate of [redacted]% for technologies with upfront costs and benefits claimed over a long period. For these reasons, the Response considered that a discount rate of [redacted]% was appropriate for consideration by the PBAC. At a [redacted]% discount rate, the ICER is $55,000 to < $75,000 per QALY gained, and at [redacted]%, the ICER is $45,000 to < $55,000 per QALY gained (assuming teprotumumab EMP = $[redacted]; and average vials per treatment course = [redacted]).

Drug cost/patient/course

5.15 The per patient cost of teprotumumab based on use in clinical evidence, the economic model and in the financial estimates are presented in Table 2.

Table 2: Drug cost per patient for proposed drug

	Teprotumumab		
	Trial dose and duration	**Economic model**	**Financial estimates**
Mean dose	Initial: 2.11 vials [a] Continuing: 3.60 vials [a]	Initial: 2.00 vials Continuing: 3.00 vials	Initial: 2.00 vials Continuing: 3.00 vials
Mean no. doses per patient	7.7 (OPTIC)	8.0 with treatment discontinuation applied (2.18% per 6-week cycle). Compliance assumed to be 100%.	8.0 No treatment discontinuation applied. Compliance assumed to be 100%.
Cost per dose	Submission: Initial: $[redacted] Continuing: $[redacted] Pre-PBAC Response: Initial: $[redacted] Continuing: $[redacted]	Submission: Initial: $[redacted] [c] Continuing: $[redacted] [c] Pre-PBAC Response: Initial: $[redacted] [c] Continuing: $[redacted] [c]	Submission: Initial: $[redacted] Continuing: $[redacted] Pre-PBAC Response: Initial: $[redacted] Continuing: $[redacted]
Cost per course	Submission: $[redacted] [b] Pre-PBAC Response: $[redacted] [b]	Submission: $[redacted] Pre-PBAC Response: $[redacted]	Submission: $[redacted] Pre-PBAC Response: $[redacted]

Source: March 2025 PBAC minutes with May 2025 Addendum, the current submission's economic model: 'Attachment 1 Tepezza Economic model.xlsb', and the current submission's financial model: 'Attachment 2 - Tepezza TED Financial Model 20 Feb 2026 - with summary table.xlsx'

[a] Based on individual patient data of patient weight in teprotumumab-treated patients across the pooled analysis.

[b] Assuming 1 initial script and 6.7 continuing scripts.

[c] Treatment discontinuation not applied.

Estimated PBS usage and financial implications

5.16 As a Category 3 submission, the estimated utilisation and financial implications have not been independently evaluated.

5.17 The submission provided revised estimated usage and financial implications of listing teprotumumab. The May 2025 submission estimated the total cost to the PBS/RPBS

of listing teprotumumab was $40 million to < $50 million in year 6 and $200 million to < $300 million over the first 6 years of listing, assuming a EMP of $[redacted] per vial.

5.18 Aligned with the economic evaluation, the financial estimates were amended to include an increase to the EMP of teprotumumab (from $[redacted] to $[redacted] per vial) and a reduced average vials per treatment course (from 27.14 to 23). The Pre-PBAC Response provided updated financial estimates with an EMP of $[redacted] per vial of teprotumumab.

5.19 The revised estimated financial implications of listing teprotumumab compared with the May 2025 submission estimates are presented in Table 3. Based on the estimates provided in the Pre-PBAC Response, the estimated total cost to the PBS/RPBS of listing teprotumumab was $40 million to < $50 million in year 6 and $200 million to < $300 million over the first 6 years of listing.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
May 2025 submission						
Estimated extent of use of teprotumumab						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Total script numbers	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of teprotumumab						
Cost to PBS less copayments	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]
Cost to RPBS less copayments	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Net cost PBS/RPBS	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]
Cost to MBS	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]
Net cost PBS/RPBS/MBS	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]
July 2026 submission						
Estimated extent of use of teprotumumab						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Total script numbers	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of teprotumumab						
Cost to PBS less copayments ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Cost to RPBS less copayments ($)	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Net cost PBS/RPBS ($)	—	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Cost to MBS	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]
Net cost PBS/RPBS/MBS ($)	[redacted][4]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Pre-PBAC Response						
Cost to PBS less copayments ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]
Cost to RPBS less copayments ($)	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Net cost PBS/RPBS ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Cost to MBS	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]
Net cost PBS/RPBS/MBS ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]

Source: March 2025 PBAC minutes with May 2025 Addendum, Pre-PBAC Response financial model: 5.25 - Attachment 2 - Tepezza TED Financial Model pre-PBAC response July 2026.xlsx

The redacted values correspond to the following ranges:

[1] *< 500*

[2] *500 to < 5,000*

[3] *$30 million to < $40 million*

[4] *$40 million to < $50 million*

[5] *$0 to < $10 million*

[6] *net cost saving*

Risk-sharing arrangements

5.20 The submission proposed a revised RSA, updated for the revised financial estimates. The revised RSA compared with the RSA accepted by the PBAC at its May 2025 meeting is presented in Table 4. The Pre-PBAC Response updated the proposed RSA to include an EMP of $[redacted] per vial of teprotumumab and a 23 vial usage assumption per patient.

Table 4: Proposed risk-sharing arrangement

	Year 1	Year 2	Year 3	Year 4	Year 5
May 2025 PBAC meeting[a]					
Tier 1 ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Tier 2 ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
July 2026 submission					
Tier 1 ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Tier 2 ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Pre-PBAC Response					
Tier 1 ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Tier 2 ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: March 2025 PBAC minutes with May 2025 Addendum and the current submission, Table 4. The Pre-PBAC Response (p3).
[a] The PBAC previously considered that a [redacted]% rebate for use above tier 1 should apply to the first year of listing and the resubmission's proposal for a [redacted]% rebate for use above the tier 1 expenditure cap and a [redacted]% rebate for use above the tier 2 expenditure cap should apply from the second year of listing.

6 PBAC Outcome

6.1 The PBAC recommended the listing of teprotumumab (Tepezza®), sponsored by Amgen Australia Pty Ltd, for the treatment of active, moderate-to-severe (MS) thyroid eye disease (TED). The PBAC reaffirmed its previous view that there is a high clinical need in the requested patient population. The PBAC noted the PBS listing for this population, recommended at its May 2025 meeting, could not be progressed, as the previously proposed price was no longer considered feasible by the sponsor. The PBAC considered that the assumed reduction in average vial use per treatment course was highly uncertain. The PBAC considered that a price reduction would be required to achieve a cost-effective listing, together with additional amendments to the risk sharing arrangement (RSA) to manage uncertainty related to the assumed average vial use per patient.

6.2 The PBAC noted the consumer comments received from health care professionals, individuals who would like access to teprotumumab to treat their own condition and the Orbital Plastics and Lacrimal (OPAL) and Ocular Rheumatology (EORC) units from the Royal Victorian Eye and Ear Hospital (RVEEH) emphasising the high clinical need for effective treatment options for patients living with active MS TED. The PBAC noted comments emphasising the substantial burden of disease associated with TED, which included significant impacts on daily activities and lifestyle. The PBAC noted that comments highlighted the limited effectiveness of current therapies in reducing disease severity. These therapies were described as primarily managing symptoms and inflammation rather than targeting the underlying disease mechanism, and as being associated with a range of serious side effects. Teprotumumab was described

as a targeted biological therapy that acts on the underlying disease mechanism in TED. The comments highlighted the clinical benefits of teprotumumab observed in clinical trials. Hearing impairment was identified as a key adverse effect, with input highlighting the importance of careful patient selection and ongoing monitoring.

6.3 The PBAC noted that the proposed restriction aligned with the restriction previously recommended at its May 2025 meeting. The PBAC noted that the Pre-PBAC Response requested an amendment to the treatment criteria to remove the word 'physician' and considered this change reasonable.

6.4 The PBAC noted that the PBS listing for the requested population had been recommended at its May 2025 meeting, however, could not be progressed as the previously proposed price was no longer considered feasible by the sponsor. The PBAC noted that the submission increased the effective ex-manufacturer (EMP) price of teprotumumab from $[redacted] to $[redacted] per vial. The PBAC noted that the Pre-PBAC Response proposed a revised price of $[redacted] per vial of teprotumumab, resulting in an increase to the May 2025 incremental cost-effectiveness ratio (ICER) from $55,000 to < $75,000 to $75,000 to < $95,000 per quality adjusted life year (QALY) gained.

6.5 The PBAC noted that the submission also proposed reducing the assumed average number of vials per treatment course of teprotumumab from 27.14 to 23.00. The PBAC noted that this reduction offset the proposed increase in price of teprotumumab, resulting in an ICER of $75,000 to < $95,000 per QALY gained. The PBAC noted that the submission stated that the revised values were based on updated real-world utilisation and reflected the differences between the patient weight distribution observed in pivotal trials and routine clinical practice, where a lower average weight results in fewer vials required per infusion. The PBAC noted that the Pre-PBAC Response provided clarification that the revised vial usage was based on weight data obtained from an Australian clinician. The Response stated that revised vial use was based on weight data from an Australian clinician's TED patient cohort and was supported by a Danish study, with both sources indicating an average of 23 vials per treatment course. The Response also noted that an average utilisation of 23 vials per patient course was consistent with 'internal sponsor real-world utilisation data'. The PBAC noted that detail related to this data was not provided in the submission or Pre-PBAC Response.

6.6 The PBAC noted that vial use varies substantially with patient weight, and would typically range from approximately 15 to 45 vials per treatment course, with women requiring 23 vials on average (based on a weight of >50–75 kg) and men requiring 30 vials on average (based on a weight of >75–100 kg). The PBAC therefore considered that the proportion of men and women in the Australian TED population would be a key determinant of whether 23 vials was a reasonable overall average. However, the PBAC noted that an average of 23 vials would not represent approximately 20–30% of the TED population who were men requiring 30 vials on average. The PBAC noted that the previous estimate of 27.14 vials per course was based on weight data from the

pivotal OPTIC trial, which recruited patients from the United States, Germany and Italy in 2017–2018. The PBAC considered it unclear whether patients in Australian clinical practice would differ substantially from the trial population. It also considered that weight data from a single clinician's TED cohort over 15 years may not be representative of the current Australian TED population. Overall, the PBAC considered the revised vial-use assumption to be highly uncertain and was likely to be underestimated.

6.7 The PBAC recalled it had previously considered that the economic model was associated with a high degree of uncertainty due to the limited data available and the complexity of the economic model. While noting the high unmet clinical need for individuals with MS TED, the PBAC recalled it had previously considered a respecified model would be appropriate, which included a price reduction reflective of an ICER of less than $55,000 to < $75,000 per QALY gained (paragraphs 7.1, 7.17, and 11.1, teprotumumab PSD, March and May 2025 PBAC Meetings). The PBAC noted that the ICER presented in the Pre-PBAC Response remained above $55,000 to < $75,000 per QALY gained. The PBAC acknowledged the impact of lower discount rate on the ICER, given that teprotumumab is a fixed-course treatment with benefits modelled over a 20-year time horizon. However, it also noted that the modelled benefits (both short-term and long-term) remained highly uncertain. For this reason, the PBAC advised that a price reduction reflecting an ICER below $55,000 to < $75,000 per QALY gained was required to achieve a cost-effective listing for teprotumumab.

6.8 The PBAC noted that the submission revised the financial estimates and the Risk Sharing Arrangement to include the increased price of teprotumumab and the reduced average vial use assumption. The PBAC noted that the two-tier RSA structure (rebate of [redacted]% for tier 1 followed by [redacted]% for tier 2) accepted at its May 2025 meeting had been maintained by the submission. However, given the uncertainty and likely underestimated vial use per patient, the PBAC considered that further revisions to the RSA were required. These included a price reduction to achieve an ICER below $55,000 to < $75,000 per QALY gained, and an increase in the rebate between tiers 1 and 2 from [redacted]% to [redacted]%. The PBAC also considered that a review of the utilisation of teprotumumab should be conducted by the DUSC after 2 years of PBS listing. The PBAC advised that teprotumumab would no longer be considered cost-effective if the average vial use was found to exceed 23 vials per treatment course.

6.9 The PBAC maintained that teprotumumab should not be treated as interchangeable with any other drugs under Section 101 (3BA) of the *National Health Act 1953*.

6.10 The PBAC maintained that teprotumumab is not suitable for prescribing by nurse practitioners. The PBAC advised that teprotumumab is suitable for prescribing by medical practitioners only.

6.11 The PBAC maintained the Early Supply Rule should not apply.

6.12 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals*

and Vaccines – Cost Recovery) Regulations 2022 for Pricing Pathway A were met. Specifically, the PBAC found that in the circumstances of its recommendation for teprotumumab:

a) The treatment is expected to provide a substantial and clinically relevant improvement in efficacy over alternative therapies on the basis of superior comparative effectiveness to standard of care;

b) The treatment is expected to address a high and urgent unmet clinical need due to the lack of treatment options for patients with active MS TED;

c) It would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A on the basis of the preceding findings.

6.13 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

Add new item:

Initial Restriction

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TEPROTUMUMAB					
Teprotumumab 500 mg injection, 1 vial	NEW (public) NEW (private)	3	3	0	Tepezza
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (telephone/electronic)				
	Authority type: ☒ Non-complex Authority Required (non-CAR)				
Prescribing rule level	**Administrative Advice:** No increase in the maximum number of repeats may be authorised.				
Prescribing rule level	**Administrative Advice:** Special Pricing Arrangements apply				
Prescribing rule level	**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.				
	Severity: Moderate-to-severe				
	Condition: Thyroid eye disease				
	Indication: Active Moderate-to-severe thyroid eye disease				
	Treatment Phase: Initial treatment				

	Clinical criteria:
	Patient must not have previously received PBS-subsidised treatment with this drug for this condition; OR
	Patient must be both: (i) undergoing re-treatment with this drug for this condition (ii) have demonstrated response to previous PBS-subsidised treatment with this drug for this condition.
	AND
	Clinical criteria:
	Patient must have a clinical activity score (CAS) of at least three for the most severely affected eye,
	AND
	Clinical criteria:
	Patient must have two or more of the following: (i) Proptosis at least 3 mm above normal for race and gender, (ii) Lid retraction of at least2mm, (iii) Moderate to severe soft-tissue involvement, (iv) inconstant or constant diplopia
	AND
	Clinical criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by a specialist medical practitioner experienced in the treatment of thyroid eye disease
	Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records for the first prescription only: (1) Baseline clinical activity score (CAS); and (2) Confirmation of the presence of Thyroid Eye Disease (this includes evidence of two or more of the following: (iv) Proptosis at least 3mm above normal for race and gender, (v) Lid retraction of at least 2mm, (vi) Moderate to severe soft-tissue involvement, (vii) Inconstant or constant diplopia)
	Prescribing Instructions: Increased quantities may only be authorised where a patient's weight is greater than 150 kg.
	Prescribing Instructions: After completing 8 doses in total of PBS-subsidised treatment with teprotumumab, a patient may be eligible for re-treatment through the initial treatment phase only, if a response to treatment was previously demonstrated.
	Caution: Assess patients' hearing before, and routinely during and after treatment, including use of audiograms where clinically warranted. If significant hearing loss is experienced while receiving treatment with this drug for this condition, treatment discontinuation is advised. See also TGA approved Product Information
	Caution: Teprotumumab is contraindicated in pregnancy. Women of childbearing potential should have a negative pregnancy test before starting treatment with teprotumumab, and monthly during treatment and for 6 months after cessation of treatment. If the patient becomes pregnant during treatment, teprotumumab should be discontinued. See also TGA approved Product Information.

Continuing Restriction

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TEPROTUMUMAB					
Teprotumumab 500 mg injection, 1 vial	NEW (public) NEW (private)	6	6	6	Tepezza

Restriction Summary / Treatment of Concept		
		Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
		Prescriber type: ☒ Medical Practitioners
		Restriction type: ☒ Authority Required (Streamlined) [new code]
		Authority type: ☒ Non-complex Authority Required (non-CAR)
Prescribing rule level		**Administrative Advice:** No increase in the maximum number of repeats may be authorised.
Prescribing rule level		**Administrative Advice:** Special Pricing Arrangements apply
		Indication: Active Moderate-to-severe thyroid eye disease
		Treatment Phase: Continuing treatment
		Clinical criteria:
		Patient must have previously received PBS-subsidised treatment with this drug for this condition
		Treatment criteria:
		Must be treated by or in consultation with a specialist medical practitioner experienced in the management of thyroid eye disease
		Prescribing Instructions: Increased quantities may only be authorised where a patient's weight is greater than 150 kg.
		Prescribing Instructions: After completing 8 doses in total of PBS-subsidised treatment with teprotumumab, a patient may be eligible for re-treatment through the initial treatment phase only, if a response to treatment was previously demonstrated.
		Caution: Assess patients' hearing before, and routinely during and after treatment, including use of audiograms where clinically warranted. If significant hearing loss is experienced while receiving treatment with this drug for this condition, treatment discontinuation is advised. See also TGA approved Product Information
		Caution: Teprotumumab is contraindicated in pregnancy. Women of childbearing potential should have a negative pregnancy test before starting treatment with teprotumumab, and monthly during treatment and for 6 months after cessation of treatment. If the patient becomes pregnant during treatment, teprotumumab should be discontinued. See also TGA approved Product Information.

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

8 Context for Decision

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

9 Sponsor's Comment

The sponsor had no comment.