5.20 ATEZOLIZUMAB

Solution concentrate for I.V. infusion 840 mg in 14 mL, Tecentriq®, Roche Products Pty Ltd.

1 Purpose of Application

1.1 The minor submission requested a Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital) Authority Required (STREAMLINED) listing of a new form of atezolizumab (840 mg in 14 mL, atezolizumab 840 mg from herein) and the addition of a 1680 mg every four weeks (Q4W) flat dosing regimen to the current 1200 mg every three weeks (Q3W) dosing regimen.

1.2 The minor submission requested that atezolizumab 840 mg and the Q4W dosing regimen be made available for the atezolizumab PBS listed indications for second-line (2L) treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) and first-line (1L) treatment of stage IV metastatic non-squamous (NSQ) NSCLC (when administered as monotherapy in the maintenance phase after cessation of platinum doublet-chemotherapy and bevacizumab).

2 Requested listing

2.1 The minor submission requested the same listings for atezolizumab 840 mg as the existing atezolizumab listings except with:

- a maximum amount of 1680 mg in the initial and continuing treatment restrictions for 2L NSCLC.
- a maximum of three repeats in the initial treatment restriction for 2L NSCLC.
- addition of the criterion to restrict the use of the Q4W dosing regimen after cessation of bevacizumab and platinum-doublet chemotherapy (PDC) for 1L NSCLC.
- a continuing treatment listing for 1L NSCLC was only sought where atezolizumab is used as monotherapy.

2.2 The proposed restrictions are provided below with Secretariat suggested additions in italics and deletions in strikethrough.

Second-line treatment of locally advanced or metastatic NSCLC

Name, Restriction, Manner of administration and form	Max. amount	№.of Rpts	Dispensed Price for Max. amount	Proprietary Name and Manufacturer
ATEZOLIZUMAB 840 mg/14 mL injection, ~~1 x~~ 14 mL vial	1680 mg	3	$*10,551.88 (public)* *$10,738.18 (private)* *(Published)*	Tecentriq® Roche Products Pty Ltd

Category / Program:	Section 100 – Efficient Funding of Chemotherapy ~~Private Hospital/Private Clinic Authority Required (STREAMLINED)~~ ~~Public Hospital Authority Required (STREAMLINED)~~
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced or metastatic
Condition:	*n*~~N~~on-small cell lung cancer ~~(NSCLC)~~
PBS Indication:	Locally advanced or metastatic ~~NSCLC~~*non-small cell lung cancer*
Treatment phase:	Initial treatment
Restriction Level / Method:	☐Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☒Streamlined
Clinical criteria:	Patient must not have received prior treatment with a programmed cell death-1 (PD-1) inhibitor or a programmed cell death ligand-1 (PD-L1) inhibitor for this condition, AND Patient must have a WHO performance status of 0 or 1, AND The treatment must be the sole PBS subsidised therapy for this condition, AND The condition must have progressed on or after prior platinum based chemotherapy.
Administrative Advice:	No increase in the maximum number of repeats may be authorised. In the first few months after start of immunotherapy, some patients can have a transient tumour flare with subsequent disease response. When progression is suspected, this should be confirmed through a confirmatory scan, taken at least 4 weeks later. Special Pricing Arrangements apply.

Name, Restriction, Manner of administration and form	Max. amount	№.of Rpts	Dispensed Price for Max. amount	Proprietary Name and Manufacturer
ATEZOLIZUMAB 840 mg/14 mL injection, ~~1 x~~ 14 mL vial	1680 mg	5	$*10,551.88 (public)* *$10,738.18 (private)* *(Published)*	Tecentriq® Roche Products Pty Ltd

Category / Program:	Section 100 – Efficient Funding of Chemotherapy ~~Private Hospital/Private Clinic Authority Required (STREAMLINED)~~ ~~Public Hospital Authority Required (STREAMLINED)~~
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives

Severity:	Locally advanced or metastatic
Condition:	*n*~~N~~on-small cell lung cancer ~~(NSCLC)~~
PBS Indication:	Locally advanced or metastatic ~~NSCLC~~*non-small cell lung cancer*
Treatment phase:	Continuing treatment
Restriction Level / Method:	☐ Restricted benefit ☐ Authority Required – In Writing ☐ Authority Required – Telephone/Electronic/Emergency ☒ Streamlined
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND The treatment must be the sole PBS-subsidised treatment for this condition, AND Patient must have stable or responding disease.
Administrative Advice:	No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

First-line treatment of metastatic NSQ NSCLC

Name, Restriction, Manner of administration and form	Max. amount	№.of Rpts	Dispensed Price for Max. amount	Proprietary Name and Manufacturer
ATEZOLIZUMAB 840 mg/14 mL injection, ~~1 x~~ 14 mL vial	1680 mg	5	$*10,551.88 (public)* *$10,738.18 (private)* *(Published)*	Tecentriq® Roche Products Pty Ltd

Category / Program:	Section 100 – Efficient Funding of Chemotherapy ~~Private Hospital/Private Clinic Authority Required (STREAMLINED)~~ ~~Public Hospital Authority Required (STREAMLINED)~~
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Stage IV (metastatic)
Condition:	*n*~~N~~on-small cell lung cancer ~~(NSCLC)~~
PBS Indication:	Stage IV (metastatic) ~~NSCLC~~*non-small cell lung cancer*
Treatment phase:	Continuing treatment
Restriction Level / Method:	☐Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☒Streamlined
Treatment criteria:	~~Atezolizumab must be administered as monotherapy after cessation of bevacizumab and platinum-doublet chemotherapy.~~
Clinical criteria:	*Patient must have experienced intolerance to combination treatment with bevacizumab,* *AND* Patient must have previously received PBS-subsidised treatment with this drug in this line of treatment, AND Patient must have stable or responding disease, AND *The treatment must be the sole PBS subsidised treatment for this condition under this restriction.*
Administrative Advice:	No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Background

Registration status

3.1 Atezolizumab 840 mg in 14 mL injection is currently TGA registered for the following indications:

- First-line treatment of patients with metastatic NSQ NSCLC in combination with bevacizumab, paclitaxel and carboplatin. This treatment is indicated only after failure of appropriate targeted therapy in patients with EGFR mutant or ALK-positive NSCLC.

- Second-line treatment of patients with locally advanced or metastatic NSCLC as monotherapy after prior chemotherapy.
- First line treatment of patients with extensive-stage small cell lung cancer in combination with carboplatin and etoposide.
- Treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) who are considered cisplatin ineligible and whose tumours express PD-L1, as determined by a validated test, or are considered ineligible for any other platinum-containing chemotherapy regardless of the level of tumour PD-L1 expression.

Previous PBAC consideration

3.2 Atezolizumab was first considered and recommended by the PBAC at the November 2017 meeting for the treatment of locally advanced or metastatic NSCLC in patients who have disease progression on or after prior platinum-based chemotherapy. In making this recommendation, the PBAC considered that atezolizumab was non-inferior in effectiveness and safety compared with nivolumab, which is currently listed on the PBS for this population (paragraph 7.1, atezolizumab Public Summary Document (PSD), November 2017).

3.3 At its March 2019 meeting, the PBAC recommended the Section 100 (Efficient Funding of Chemotherapy - Public and Private Hospital) Authority Required (STREAMLINED) listing of atezolizumab and bevacizumab in combination with platinum-doublet chemotherapy (PDC) for first-line treatment of patients with stage IV metastatic non-squamous (NSQ) non-small cell lung cancer (NSCLC) (paragraph 7.1, atezolizumab and bevacizumab PSD, March 2019). Atezolizumab 1200 mg was PBS listed on 1 October 2019 for this indication. The PBAC considered that the appropriate main comparator for the submission was PDC followed by PD-(L)1 therapy, as this is the therapy most likely to be replaced in practice for patients with a PD-L1 TPS < 50%. The PBAC considered that for the EGFR mutant/ALK positive population, nivolumab and atezolizumab can be used in patients who have progressed on or after treatment with targeted therapies and therefore use of PDC followed by PD-(L)1 was also an appropriate comparator in this population. The PBAC considered pembrolizumab monotherapy followed by PDC was an appropriate comparator for the EGFR wild type/ALK negative PD-L1 ≥50% NSQ population (paragraph 7.5, atezolizumab and bevacizumab PSD, March 2019). The PBAC considered that on balance the cost-effectiveness of atezolizumab + bevacizumab + PDC is likely to be similar across the patient populations proposed in the submission. Therefore the PBAC was of the view that the cost of treatment with the atezolizumab + bevacizumab components of the quadruple therapy should not exceed the cost of pembrolizumab monotherapy for any patient group receiving treatment for stage IV metastatic non-squamous (NSQ) non-small cell lung cancer (NSCLC) (paragraph 7.13, atezolizumab and bevacizumab PSD, March 2019).

3.4 Atezolizumab 840 mg in 14 mL injection and the 1680 mg Q4W dosing regimen has not been previously considered by the PBAC.

4 Comparator

4.1 The minor submission nominated atezolizumab 1200 mg (Q3W) as the main comparator. The Secretariat considered this was appropriate as atezolizumab 1200 mg would most likely be replaced should atezolizumab 840 mg be listed on the PBS. The Secretariat also noted that nivolumab and pembrolizumab are potential comparators in the 2L and 1L NSCLC settings respectively, as atezolizumab was listed in 2L NSCLC on a cost-minimisation basis with nivolumab, and in 1L NSCLC on a cost comparison basis with pembrolizumab.

For more detail on PBAC's view, see section 6 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted and welcomed the input from individuals (1) and organisations (1) via the Consumer Comments facility on the PBS website. The comment described a range of benefits of treatment with atezolizumab for non-small cell lung cancer, including improved quality of life, slowing disease progression and manageable side effect profile, however, this comment was not specific to the proposed 1680 mg Q4W dosing regimen.

5.3 The Lung Foundation Australia indicated that the availability of atezolizumab 1680 mg Q4W would benefit patients and clinicians and it would provide the option of less frequent dosing, and therefore less frequent visits to hospital for treatment, without adversely impacting health outcomes.

Clinical trials

5.4 The minor submission stated that no clinical evidence for atezolizumab administered Q4W at a dose of 1680 mg was available.

5.5 The minor submission presented pharmacokinetics (PK) modelling data and an exposure-response analysis based on data from the clinical studies (PCD4989g, IMvigor211, OAK) as supporting evidence for the relative efficacy and safety compared to Q3W administration at 1200 mg.

5.6 The minor submission noted the results of the PK simulations (N=500 per dosing regimen) showed that dosing at 1680 mg Q4W has comparable overall exposure to the currently listed 1200 mg Q3W dosing regimen.

5.7 The minor submission noted that no statistically significant exposure-response relationships were identified for the efficacy endpoints; ORR (objective response rate) and OS (overall survival) with the atezolizumab exposure metrics investigated (Cmax[1], Cmin[2] and AUC[3] at first dose and steady state). The analysis of the incidence of all AE (adverse event) categories also did not show any statistically significant exposure-safety relationships.

5.8 As a minor submission, the analyses have not been independently evaluated.

Clinical claim

5.9 The minor submission claimed that based on the PK modelling and the exposure-response analysis, atezolizumab 1680 mg Q4W is non-inferior to atezolizumab 1200 mg Q3W in terms of efficacy and safety.

5.10 The PBAC considered the claims of non-inferior efficacy and safety compared to atezolizumab 1200 mg Q3W to be reasonable overall based on the available data.

Economic analysis

5.11 The minor submission presented two cost-minimisation analyses against atezolizumab 1200 mg Q3W over an average calendar month (30.4375 days) for 2L NSCLC and 1L NSCLC indications. The cost minimisation-analyses are presented in Table 1 and Table 2.

[1] maximum of simulated concentrations
[2] minimum of simulated concentrations
[3] area under the serum concentration-time curve

Table 1: Cost-minimisation for 2L NSCLC using cost of atezolizumab at effective DPMA

	Atezolizumab 1200mg Q3W	Atezolizumab 1680mg Q4W
EEMP per administration[a]	$[redacted]	$[redacted]
EEMP per month[b]	$[redacted]	$[redacted]
Weighted[c] DPMA per administration[d]	$[redacted]	$[redacted]
Weighted DPMA per month	$[redacted]	$[redacted]
Cost of administration (IV infusion)[e]	$66.10	$66.10
Cost of administration per month	$95.81	$71.85
Total cost per administration	$[redacted]	$[redacted]
Total cost per month (cost-minimised)	**$[redacted]**	**$[redacted]**

Source: Table 5.1, p15 of the submission
Abbreviations: EEMP: effective ex-manufacturer price; DPMA: dispensed price for maximum amount
[a] Based on effective prices.
[b] Based on 1.45 administrations per month for Q3W dosing and 1.09 for Q4W dosing
[c] The weightings across private (66.1%) and public (33.9%) hospital settings were derived based on PBS statistics from July 2018 to June 2019.
[d] DPMA was calculated using EEMP and applicable fees and mark-ups under the Efficient Funding of Chemotherapy (EFC) initiative in the public and private hospital settings, which included the preparation fee ($85.06) in the public and private settings, and the ready prepared dispensing fee ($7.39), distribution fee ($27.02), diluent fee ($5.35) and mark ups at 1.4% of the drug cost ($[redacted]) in the private hospital setting only
[e] Administration/infusion costs based on MBS item 13915

Table 2: Cost-minimisation for 1L NSCLC using cost of atezolizumab at effective DPMA

	Atezolizumab 1200mg Q3W	Atezolizumab 1680mg Q4W
EEMP per administration[a]	$[redacted]	$[redacted]
EEMP per month[b]	$[redacted]	$[redacted]
Weighted[c] DPMA per administration[d]	$[redacted]	$[redacted]
Weighted DPMA per month	$[redacted]	$[redacted]
Cost of administration (IV infusion)[e]	$66.10	$66.10
Cost of administration per month	$95.81	$71.85
Total cost per administration	$[redacted]	$[redacted]
Total cost per month (cost-minimised)	**$[redacted]**	**$[redacted]**

Source: Table 5.2, p16 of the submission
Abbreviations: EEMP: effective ex-manufacturer price; DPMA: dispensed price for maximum amount
[a] Based on effective prices.
[b] Based on 1.45 administrations per month for Q3W dosing and 1.09 for Q4W dosing
[c] The weightings across private (66.1%) and public (33.9%) hospital settings were derived based on PBS statistics from July 2018 to June 2019.
[d] DPMA was calculated using EEMP and applicable fees and mark-ups under the Efficient Funding of Chemotherapy (EFC) initiative in the public and private hospital settings, which included the preparation fee ($85.06) in the public and private settings, and the ready prepared dispensing fee ($7.39), distribution fee ($27.02), diluent fee ($5.35) and mark ups at 1.4% of the drug cost ($[redacted]) in the private hospital setting only
[e] Administration/infusion costs based on MBS item 13915

5.12 The cost-minimisation analyses were conducted on a cost per month basis. This approach assumed that duration of treatment of atezolizumab would be the same with the different dosing regimens. The weighted DPMA per 840 mg vial for 2L NSCLC

was $[redacted] and 1L NSCLC was $[redacted]. The cost-minimisation analyses were calculated using the DPMA per month (i.e. incorporating public/private hospital fees and private hospital mark-up) and the administration cost (based on MBS item 13915). The alternative cost-minimisation analyses calculated at the ex-manufacturer level with the administration cost and a comparison of the costs per 4 weeks are presented below in Table 3.

Table 3: A comparison of the costs per month using the effective ex-manufacturer price of atezolizumab

	2L NSCLC		1L NSCLC	
Strength and dose	**1200 mg Q3W**	**1680 mg Q4W**	**1200 mg Q3W**	**1680 mg Q4W**
EEMP per administration	$[redacted]	$[redacted]	$[redacted]	$[redacted]
EEMP per 4 weeks	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost of administration – 85% benefit (IV infusion)[b]	$56.20		$56.20	
Cost of administration per 4 weeks	*$74.93*	*$56.20*	*$74.93*	*$56.20*
Total cost per 4 weeks (cost-minimised)	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**

Source: Table 5.1, Table 5.2, pp15-16 of the submission, compiled by the Secretariat
Abbreviations: EEMP: effective ex-manufacturer price; DPMA: dispensed price for maximum amount
[a] Estimated effective ex-manufacturer price for atezolizumab 840 mg x 2 vials
[b] Administration/infusion costs based on MBS item 13915.

5.13 The alternative calculations resulted in the cost-minimised effective ex-manufacturer price per 840 mg vial of $[redacted] for 2L NSCLC and $[redacted] for 1L NSCLC. The pre-PBAC response argued that basing the cost-minimisation analyses on ex-manufacturer prices and the MBS administration fee at 85% of the item cost were not in accordance with PBAC recommended methodology for economic evaluations. The pre-PBAC response indicated that the Manual of resource items and their associated unit costs (version 5.0) infers that the full MBS schedule fee should be used when there is no explicit reference to the rebate amount and that the price applied to the proposed medicine should be based on the DPMA when a Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital) is being sought. The Secretariat noted that the guidance in the Manual of resource items and their associated unit costs is in the context of costs applied to economic models, which differs from the basis upon which prices for PBS listings are agreed. The Secretariat noted that pricing agreements are made under *the National Health Act 1953* at the ex-manufacturer level.

5.14 The Secretariat noted that the Q4W dosing regimen of nivolumab was available on the PBS from 1 September 2019 and it may be appropriate that atezolizumab 1680 mg Q4W for 2L NSCLC be cost-minimised to nivolumab 480 mg Q4W, noting that atezolizumab was listed for 2L NSCLC on a cost-minimisation basis with nivolumab.

5.15 The Secretariat also noted that pembrolizumab in combination with cisplatin/carboplatin and pemetrexed was recommended for 1L NSCLC at the July 2019 PBAC meeting and a reduction in the pembrolizumab monotherapy price for 1L

NSCLC at its March 2019 meeting. Therefore, these pembrolizumab listings, if implemented, are also relevant for the purpose of the cost-minimisation basis of the proposed Q4W dosing regimen of atezolizumab in the 1L NSCLC setting.

5.16 The requested published price of the 840 mg vial is consistent with the price per mg of the currently listed 1200 mg form for all existing indications.

Estimated PBS usage & financial implications

5.17 The minor submission used a market share approach to estimate the extent of use and financial impact of listing atezolizumab 840 mg on the PBS/RPBS. The estimated utilisation and financial implications for 1L NSCLC and 2L NSCLC indications, based on both published and effective DPMA are presented in Table 4 and Table 5.

5.18 The minor submission assumed that atezolizumab 840 mg Q4W would only substitute for atezolizumab 1200 mg in the 2L setting, estimating that 100% of eligible patients for 2L NSCLC would use the 1680 mg Q4W dosing regimen if recommended for listing. The minor submission did not consider the proportion of nivolumab that may be replaced. However, the Secretariat considered that substitution of nivolumab, associated with the reduced dosing frequency would most likely be minor as nivolumab is PBS listed for the same condition under a Q4W flat dosing regimen.

5.19 The minor submission also assumed that the use of atezolizumab in the 2L setting is expected to decline significantly over time following the PBS listing for 1L NSCLC given that patients may receive a PD-1 or PD-L1 inhibitor once only under the PBS restrictions. Decrease in the use of the 2L atezolizumab was predicted to be 20% each year.

5.20 The estimated financial implications to the Government of the addition of atezolizumab 840 mg for 2L treatment is presented in Table 4 below.

Table 4: Estimated use and financial implications for 2L NSCLC

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed[a]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimated financial implications of atezolizumab 1680 mg Q4W						
Cost to PBS/RPBS[b]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Less Copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost to PBS/RPBS less copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Estimated financial implications for atezolizumab 1200 mg Q3W						
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Less Copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost to PBS/RPBS less copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net financial implications						
Net cost to PBS/RPBS (Published)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to PBS/RPBS (Effective)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to MBS	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Net cost to Government (Published)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to Government (Effective)	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]

[a] Assuming number of scripts dispensed for a calendar year based on the PBS dataset from 2019 as estimated by the submission; note that the submission did not specify the period that PBS data was collected.

[b] The financial estimates incorporated the weighted DPMA of $10,675.02, derived from the AEMP (published) of $5,233.41 per 840 mg vial for public hospital ($10,551.88 weighted at 33.9%) and private hospital ($10,738.18 weighted at 66.1%) in the first-line and second-line settings.

Source: Section 4 workbook 2L NSCLC supplied with the submission.

5.21 The minor submission assumed that 100% of eligible patients would receive combination therapy with bevacizumab for continuing treatment in the 1L setting, and that 10% of these patients would use atezolizumab 1680 mg Q4W as monotherapy after cessation of bevacizumab and PDC. The Secretariat considered the estimated proportion of patients who would use atezolizumab 1680 mg Q4W as monotherapy was uncertain.

5.22 The estimated financial implications to the Government of the addition of atezolizumab 840 mg for the 1L treatment is presented in Table 5 below.

Table 5: Estimated use and financial implications for 1L NSCLC

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of scripts dispensed[a]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimated financial implications of atezolizumab 1680 mg Q4W						
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Less Copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost to PBS/RPBS less copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Estimated financial implications for atezolizumab 1200 mg Q3W						
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Less Copayments	$[redacted]	[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost to PBS/RPBS less copayments	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net financial implications						
Net cost to PBS/RPBS (Published price)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to PBS/RPBS (Effective price)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to MBS[b]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Net cost to Government (Published)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost to Government (Effective)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

[a] Assuming that number of scripts per patient was 7.88 based on the treatment duration of 31.50 weeks as estimated by the submission.
[b] A minor calculation error in 'net cost to MBS' in Section 4 workbook 1L NSCLC. The corrected estimates are presented.
Source: Section 4 workbook 1L NSCLC supplied with the submission.

The redacted table shows that at year 6, the estimated number of patients was less than 10,000 per year and the net cost to the PBS would be less than $10 million per year.

5.23 Overall, the minor submission claimed that the addition of atezolizumab 840 mg injection for Q4W dosing regimen would have no net financial impact to the Government.

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

Financial Management – Risk Sharing Arrangement

5.25 Atezolizumab is currently subject to Deeds of Agreement for both 1L and 2L NSCLC indications, which encompass Special Pricing Arrangements (SPA) and subsidisation caps, and that it would be appropriate that the new form and the requested listing be managed under the same RSAs.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

6.1 The PBAC recommended the Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital) Authority Required (STREAMLINED) listing of a new form of atezolizumab (840 mg in 14 mL) and addition of the 1680 mg every four weeks (Q4W) dosing regimen to the existing 1200 mg every three weeks (Q3W) dosing regimen for the PBS indications for second-line (2L) treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) and first-line (1L) treatment of stage IV metastatic non-squamous (NSQ) NSCLC. The PBAC recommended 1680 mg Q4W dosing of atezolizumab when administered as monotherapy in 2L NSCLC and for continuing treatment, after cessation of platinum doublet-chemotherapy (PDC) and bevacizumab, in 1L NSCLC.

6.2 The PBAC noted that no clinical data was provided to support the claim of non-inferiority in terms of efficacy and safety compared to the 1200 mg Q3W dosing regimen. However, the PBAC considered that based on the evidence presented, the 1680 mg Q4W dosing regimen was likely comparable to the 1200 mg Q3W dosing regimen.

6.3 The PBAC considered that atezolizumab 1200 mg Q3W was the appropriate main comparator as it would most likely to be replaced if atezolizumab 1680 mg Q4W dosing was available on the PBS. The PBAC also considered nivolumab to be an appropriate comparator in 2L NSCLC, noting that atezolizumab was recommended for 2L NSCLC on a cost-minimisation basis against nivolumab. The PBAC considered the argument in the pre-PBAC response, that nivolumab is not a relevant comparator as it is unlikely to be substituted by atezolizumab 1680 mg Q4W dosing. However, the PBAC maintained its consideration that nivolumab is also an appropriate comparator given it is an alternative therapy in this treatment setting. The PBAC considered it would be appropriate for atezolizumab 840 mg injection to be cost-minimised to the lowest cost alternative therapy in the 2L NSCLC setting. The PBAC recalled it considered pembrolizumab monotherapy followed by PDC to be an appropriate comparator for the EGFR wild type/ALK negative population in its consideration of atezolizumab for 1L NSCLC in November 2017. The PBAC further recalled that it considered on balance, the cost-effectiveness of atezolizumab + bevacizumab + PDC is likely to be similar across the patient populations proposed and therefore, was of the view that the cost of treatment with the atezolizumab + bevacizumab components of the quadruple therapy should not exceed the cost of pembrolizumab monotherapy for any patient group receiving treatment for NSQ NSCLC. In this regard, the PBAC considered that in the absence of evidence demonstrating that atezolizumab 1680 mg Q4W monotherapy dosing is superior in terms of efficacy and safety compared to pembrolizumab monotherapy in patients treated for 1L NSCLC, the cost of 1680 mg Q4W dosing should not exceed that of pembrolizumab monotherapy in this treatment setting.

6.4 The PBAC noted the uncertainty around the estimated uptake and utilisation of the 1680 mg Q4W dosing regimen however, the PBAC considered there may be some cost-savings to Government associated with the addition of the Q4W dosing regimen due to reduced infusion administrations.

6.5 The PBAC considered that atezolizumab 840 mg injection would need to be included within the existing financial caps of the risk share arrangement (RSA) in place for the currently listed indications.

6.6 The PBAC considered that the change from atezolizumab 1200 mg Q3W dosing in combination with bevacizumab and PDC to atezolizumab monotherapy at 1680 mg Q4W for patients who experience intolerance to combination treatment with bevacizumab was potentially complex and could cause confusion.

6.7 The PBAC considered it would be appropriate to include a criterion specifying that the "Patient must have experienced intolerance to combination treatment with bevacizumab" to the continuing treatment restriction for 1L NSCLC to restrict use of the 1680 mg Q4W dosing regimen to patients who have ceased treatment with bevacizumab and PDC.

6.8 The PBAC considered that the proposed number of repeats (3) for initial treatment of 2L NSCLC which would provide 16 weeks of therapy, was appropriate.

6.9 The PBAC advised that, because atezolizumab 840 mg is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over currently listed form of atezolizumab 1200 mg, or address a high and urgent unmet clinical need, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.

6.10 The PBAC advised that under Section 101(3BA) of the *National Health Act 1953* atezolizumab should not be treated as interchangeable with any other drugs on an individual patient basis.

6.11 The PBAC advised that atezolizumab is not suitable for prescribing by nurse practitioners.

6.12 The PBAC recommended that the Early Supply Rule should not apply as this is a Section 100 listing.

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

Outcome:

Recommended

7 Recommended listing

7.1 Add new item:

Second-line treatment of locally advanced or metastatic NSCLC

Name, Restriction, Manner of administration and form	Max. amount	№.of Rpts	Proprietary Name and Manufacturer
ATEZOLIZUMAB 840 mg/14 mL injection, 14 mL vial	1680 mg	3	Tecentriq® Roche Products Pty Ltd

Category / Program:	Section 100 – Efficient Funding of Chemotherapy
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced or metastatic
Condition:	non-small cell lung cancer
PBS Indication:	Locally advanced or metastatic non-small cell lung cancer
Treatment phase:	Initial treatment
Restriction Level / Method:	☐Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☒Streamlined
Clinical criteria:	Patient must not have received prior treatment with a programmed cell death-1 (PD-1) inhibitor or a programmed cell death ligand-1 (PD-L1) inhibitor for this condition, AND Patient must have a WHO performance status of 0 or 1, AND The treatment must be the sole PBS subsidised therapy for this condition, AND The condition must have progressed on or after prior platinum based chemotherapy.
Administrative Advice:	No increase in the maximum number of repeats may be authorised. In the first few months after start of immunotherapy, some patients can have a transient tumour flare with subsequent disease response. When progression is suspected, this should be confirmed through a confirmatory scan, taken at least 4 weeks later. Special Pricing Arrangements apply.

Name, Restriction, Manner of administration and form	Max. amount	№.of Rpts	Proprietary Name and Manufacturer
ATEZOLIZUMAB 840 mg/14 mL injection, 14 mL vial	1680 mg	5	Tecentriq® Roche Products Pty Ltd

Category / Program:	Section 100 – Efficient Funding of Chemotherapy
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives

Severity:	Locally advanced or metastatic
Condition:	non-small cell lung cancer
PBS Indication:	Locally advanced or metastatic non-small cell lung cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	☐Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☒Streamlined
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND The treatment must be the sole PBS-subsidised treatment for this condition, AND Patient must have stable or responding disease.
Administrative Advice:	No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

First-line treatment of metastatic NSQ NSCLC

Name, Restriction, Manner of administration and form	Max. amount	№.of Rpts	Proprietary Name and Manufacturer
ATEZOLIZUMAB			Tecentriq® Roche Products Pty Ltd
840 mg/14 mL injection, 14 mL vial	1680 mg	5	

Category / Program:	Section 100 – Efficient Funding of Chemotherapy
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Stage IV (metastatic)
Condition:	non-small cell lung cancer
PBS Indication:	Stage IV (metastatic) non-small cell lung cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	☐Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☒Streamlined
Clinical criteria:	Patient must have experienced intolerance to combination treatment with bevacizumab, AND Patient must have previously received PBS-subsidised treatment with this drug in this line of treatment, AND Patient must have stable or responding disease, AND The treatment must be the sole PBS subsidised treatment for this condition under this restriction.

Administrative Advice:	No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

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

8 Context for Decision

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

9 Sponsor's Comment

The sponsor had no comment.