5.17 NIVOLUMAB, Solution for subcutaneous injection containing nivolumab 600 mg in 5 mL, Opdivo SC®, Bristol-Myers Squibb Australia Pty Ltd

1 Purpose of Submission

1.1 The Category 4 submission sought to list a new strength and form of nivolumab (solution for subcutaneous injection 600 mg in 5 mL) (hereafter referred to as NIVO SC) for the existing PBS-listed indications, except where nivolumab is administered 3-weekly or where nivolumab is used in combination with ipilimumab.

1.2 The Category 4 submission also requested that NIVO SC be available for all future PBS-listed indications as an alternative to the intravenous form of nivolumab (hereafter referred to as NIVO IV), where nivolumab is recommended at a flat dose on a 2- or 4-weekly dosing schedule either as monotherapy or in combination with other treatment(s), except ipilimumab.

1.3 Listing was requested on the basis of a cost-minimisation versus nivolumab 100 mg/10 mL injection, 10 mL vial (Opdivo).

2 Background and current situation

2.1 Currently, NIVO IV is available on the PBS as a weight-based or flat-dose 2-weekly (Q2W), 3-weekly (Q3W) or 4-weekly (Q4W), depending on the disease state.

2.2 Although the NIVO SC Product Information (PI) includes dosing at 900 mg every 3 weeks, the sponsor notes that this dosage form is not anticipated to be available in the Australian market for the foreseeable future due to manufacturing issues. Therefore, the current PBS reimbursement request is restricted to the 2- and 4-weekly dosing schedules only.

2.3 At the September 2025 meeting the PBAC considered a submission regarding nivolumab and ipilimumab and recommended an "expanded listing to facilitate broad access for the treatment of unresectable advanced and metastatic cancer", otherwise known as the 'broad listing'. This listing came into effect on 1 March 2026. With the implementation of 'broad listing', all nivolumab PBS listings consistent with the PBAC recommended indication 'immunotherapy sensitive advanced or metastatic cancer' collapse into a single PBS listing. Listings for earlier stage cancer (neoadjuvant, peri-adjuvant, adjuvant) remain unchanged.

2.4 The PBAC noted the recommended wording for the broad listing would allow clinicians to apply clinical judgment and discretion in using the medicines according to the best

available evidence at the time, including for retreatment, extended time on treatment and rare cancers for which regulatory submissions are unlikely. The listing would also remove the once in a lifetime limitation for these medicines when used for advanced or metastatic cancers (paragraph 20.2, nivolumab and ipilimumab Public Summary Document [PSD], July 2025).

Registration status

2.5 Nivolumab (solution for subcutaneous injection 600 mg in 5 mL) was TGA registered on 12 December 2025 for the following indications:

- Stage IIIB, IIIC, IIID, or Stage IV malignant melanoma
- Unresectable Stage III or Stage IV malignant melanoma
- Locally advanced or metastatic non-small cell lung cancer (NSCLC)
- Stage IV clear cell variant renal cell carcinoma (RCC)
- Recurrent or metastatic squamous cell carcinoma of the oral cavity, pharynx or larynx
- Urothelial carcinoma
- Unresectable or metastatic urothelial carcinoma
- Advanced or metastatic gastro-oesophageal cancers
- Adjuvant treatment of Stage II or III oesophageal cancer or gastro-oesophageal junction cancer

2.6 Notably, NIVO SC is not TGA registered for use in combination with ipilimumab. After completion of a maximum four doses of NIVO IV and ipilimumab combination therapy, patients may transition to NIVO SC as a single agent[1].

Previous PBAC consideration

2.7 Nivolumab (solution for subcutaneous injection 600 mg in 5 mL) has not been considered by the PBAC previously.

3 Requested listing

3.1 The submission requested listing NIVO SC under the same circumstances as the PBS-listed NIVO IV for the treatment of multiple PBS-listed indications. Specifically, the submission requested the addition of a dual Section 100 (Efficient Funding of Chemotherapy – Related Benefits) and Section 85 (General Schedule) PBS listings for NIVO SC. Section 100 (Efficient Funding of Chemotherapy Public/Private Hospital) listings require a single patient co-payment for each original prescription whereas both Section 85 (General Schedule) and Section 100 (Efficient Funding of

[1] OPDIVO SC (Nivolumab) Product Information

Chemotherapy – Related Benefits) listings require a patient co-payment each time the medicine is dispensed. The pre-PBAC Response indicated that the sponsor is not opposed to NIVO SC being listed on Section 100 (Efficient Funding of Chemotherapy – Public/Private Hospital). This position was based on consumer input, which highlighted that a dual General Schedule and Section 100 (CT) listings would result in additional co-payments for patients, and that Section 100 EFC Public/Private listings attract additional pharmacy fees to recognise the extra handling, preparation and dispensing requirements associated with hazardous cancer medicines. The submission noted that the request for dual listing is consistent with previous PBAC recommendations for subcutaneous formulations, including atezolizumab SC (March 2024 PBAC meeting), daratumumab (July 2021 PBAC meeting), trastuzumab SC (July 2015 PBAC meeting) and rituximab (November 2014 PBAC meeting).

3.2 The proposed restriction wording is based on the current PBS listings in the adjuvant setting and the PBAC recommended listing in the advanced or metastatic setting for NIVO IV with a maximum quantity of 480 mg. The requested restrictions are aligned with the current NIVO IV restrictions in terms of indication, Authority, treatment phase, clinical criteria, treatment criteria, population criteria, and number of repeats.

3.3 The submission proposed different Prescribing Instructions to reflect the different dosing schedule between SC and IV administration. The main difference across all indications is to explicitly require a choice between 2- or 4-weekly SC doses, i.e. “Patients must only receive a maximum of 600 mg every two weeks or 1200 mg every four weeks under a weight based or flat dosing regimen” vs “Patients must only receive a maximum of 240 mg every two weeks, or 480 mg every four weeks under a weight based or flat dosing regimen” for NIVO IV.

3.4 As the submission requested that NIVO SC be listed for multiple indications, the full restrictions have not been reproduced here. An outline of the proposed NIVO SC restrictions with the Secretariat suggested amendments (in italics and strikethrough) is presented as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
NIVOLUMAB					
nivolumab 600 mg/5 mL *injection*, *5 mL vial* solution ~~for subcutaneous injection~~	NEW (CT)	2	2	Consistent with current listings	Opdivo *SC*
nivolumab 600 mg/5 mL *injection*, *5 mL vial* solution ~~for subcutaneous injection~~	NEW (GE)	2	2	Consistent with current listings	Opdivo *SC*
Concept ID (for internal Dept. use)	Category / Program: ☒ GENERAL – General Schedule (Code GE) ☒ Section 100 – Efficient Funding of Chemotherapy – Related Benefits (Code CT)				
	Prescriber type: ☒Medical Practitioners				
	Restriction type: ☒Authority Required (Telephone/Online) • Stage IIIB, IIIC, IIID or Stage IV malignant melanoma • Adjuvant treatment of stage II or III oesophageal cancer or gastro-oesophageal junction cancer • Urothelial carcinoma ☒Authority Required (STREAMLINED) • All other PBS indications				
Restrictions criteria and wording consistent with existing NIVO IV listings with the inclusion of the following:					
New	**Prescribing instructions:** Patients must only receive a maximum of 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen.				

An example of the listing follows:

Category/Program: Section 100 – Chemotherapy Related Benefits (CT) and General Schedule (GE)					
MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№. of Rpts**	**Available brands**
NIVOLUMAB					
nivolumab 600 mg/5 mL *injection, 5 mL vial* ~~solution for subcutaneous injection~~	NEW (CT)	2	2	8	Opdivo *SC*
nivolumab 600 mg/5 mL *injection, 5 mL vial* ~~solution for subcutaneous injection~~	NEW (GE)	2	2	8	Opdivo *SC*
Restriction Summary [New] / Treatment of Concept: [New]: Authority Required [STREAMLINED]					
	Indication: Stage III or Stage IV malignant melanoma				
	Treatment Phase: Initial treatment				
	Clinical criteria:				
	Patient must not have received prior treatment with nivolumab plus relatlimab, ipilimumab or a PD-1 (programmed cell death-1) inhibitor for the treatment of unresectable Stage III or Stage IV malignant melanoma,				
	AND				
	Patient must not have experienced disease progression whilst on either: (i) PD-1 inhibitor treatment, (ii) CTLA-4 inhibitor treatment, if previously treated for resected or resectable melanoma, **OR**				
	Patient must not have experienced disease recurrence within 6 months of completing either: (i) PD-1 inhibitor treatment, (ii) CTLA-4 inhibitor treatment, if previously treated for resected or resectable melanoma,				
	AND				

	The treatment must be the sole PBS-subsidised therapy for this condition.
	Prescribing instructions: Patients must only receive a maximum of 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№. of Rpts**	**Available brands**
NIVOLUMAB					
nivolumab 600 mg/5 mL *injection*, *5 mL vial* ~~solution for subcutaneous injection~~	NEW (CT)	2	2	11	Opdivo *SC*
nivolumab 600 mg/5 mL *injection*, *5 mL vial* ~~solution for subcutaneous injection~~	NEW (GE)	2	2	11	Opdivo *SC*

Restriction Summary [New] / Treatment of Concept: [New] / Authority Required [STREAMLINED]	
	Unresectable Stage III or Stage IV malignant melanoma
	Treatment Phase: Continuing treatment
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition,
	AND
	Patient must have previously been issued with an authority prescription for this drug for this condition,
	AND
	Patient must have stable or responding disease.
	Prescribing instructions: Patients must only receive a maximum of 600 mg every two weeks or ~~480~~ *1200* mg every four weeks under a flat dosing regimen.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
Restriction Summary [New] / Treatment of Concept: [New] / Authority Required [STREAMLINED]	
	Unresectable Stage III or Stage IV malignant melanoma
	Treatment Phase: Maintenance treatment
	Clinical criteria:
	Patient must have previously received of up to maximum 4 doses of PBS-subsidised combined therapy with nivolumab and ipilimumab as induction for this condition,
	AND
	The treatment must be as monotherapy for this condition,
	AND
	Patient must not have developed disease progression while receiving PBS-subsidised treatment with this drug for this PBS indication.

	Prescribing instructions: Patients must only receive a maximum of 600 mg every two weeks or ~~480~~ *1200* mg every four weeks under a flat dosing regimen.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.

3.5 The PBS indications requested in the submission for NIVO SC are:

- Stage IIIB, IIIC, IIID, or Stage IV malignant melanoma
- Unresectable Stage III or Stage IV malignant melanoma
- Locally advanced or metastatic non-small cell lung cancer (NSCLC)
- Stage IV clear cell variant renal cell carcinoma (RCC)
- Recurrent or metastatic squamous cell carcinoma of the oral cavity, pharynx or larynx
- Urothelial carcinoma
- Unresectable or metastatic urothelial carcinoma
- Advanced or metastatic gastro-oesophageal cancers
- Adjuvant treatment of Stage II or III oesophageal cancer or gastro-oesophageal junction cancer

3.6 Noting that the 'broad listing' was anticipated to be implemented in early 2026, the submission also requested 'broad listing' restrictions for NIVO SC as set out below.

3.7 The proposed 'broad listing' restriction wording' is based on the recommended listing in the July 2025 nivolumab and ipilimumab PSD with September 2025 addendum for the 'broad listing'.

3.8 An outline of the proposed NIVO SC restrictions with the Secretariat suggested changes in *italics* and amendments in ~~strikethrough~~ from the restrictions above:

MEDICINAL PRODUCT Form		PBS item code	Max. Amount	№. of Rpts
NIVOLUMAB subcutaneous injection		NEW (CT) NEW (GE)	1200mg	13
Available brands				
nivolumab 600 mg/5 mL solution for subcutaneous injection				
Restriction Summary [new1] / Treatment of Concept: [new1A]				
	Category / Program: Section 100 – Chemotherapy Related Benefits (CT) and General Schedule (GE)			
	Prescriber type: ☒Medical Practitioners			
	Restriction type: ☒Authority Required (STREAMLINED) [NEW]			
	Indication: Immunotherapy sensitive advanced or metastatic cancer			
	Clinical criteria:			
	Patient must not have developed disease progression while receiving PBS-subsidised treatment with this drug for the condition which treatment was commenced for.			
	Prescribing instruction Patients must only receive 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen.			
	Administrative Advice: No increase in the maximum number of repeats may be authorised.			
	Administrative advice: Special Pricing Arrangements apply.			

3.9 The submission also requested that any new PBS listings for NIVO dosed at 2- or 4-weekly intervals include both the intravenous (maximum 480 mg) and subcutaneous (maximum 2 vials = 1200 mg) methods of administration.

3.10 The Secretariat noted that, while the submission requested that NIVO SC be listed for indications where ipilimumab is not used in combination with nivolumab and for flat dosing regimens, this limitation could not be enforced should NIVO SC be included in the advanced and metastatic cancers (broad) listing. As a result, there would be potential for its use both in weight-based dosing regimens and in combination with ipilimumab under the proposed listing. The pre-PBAC Response proposed prescribing instructions specifying that patients must only receive 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen to restrict to use as part of a flat dosing regimen given on a 2- or 4-weekly basis and prevent use in combination with ipilimumab.

4 Comparator

4.1 The submission proposes a new form and strength of nivolumab (solution for subcutaneous injection 600 mg in 5 mL) and compares this to the currently listed 100 mg/10 mL injection, 10 mL vial of nivolumab.

4.2 Given the proposed intervention of NIVO SC at a flat dose of 600 mg Q2W or 1200 mg Q4W, flat dose NIVO IV administered 2- or 4- weekly (240 mg or 480 mg respectively) is the appropriate comparator.

4.3 The submission noted that selection of NIVO IV as the main comparator is supported by precedent from previous PBAC decisions for SC formulations of existing IV medicines, including atezolizumab SC (March 2024 PBAC meeting), daratumumab (July 2021 PBAC meeting), trastuzumab SC (July 2015 PBAC meeting) and rituximab (November 2014 PBAC meeting).

4.4 IV flat dosing was approved by the TGA in December 2018 as an alternative dosing schedule to IV weight-based dosing. Flat dosing at 2- or 4-weekly intervals was subsequently recommended by the PBAC at the March 2019 meeting as an alternative to the existing 3 mg/kg Q2W weight-based dosing regimen for all existing and future PBS indications were nivolumab monotherapy is used (paragraph 5.1, nivolumab PSD, March 2019). The PBAC concluded that "…based on overall evidence…the efficacy and safety of the flat and weight-based dosing regimens would likely be comparable" (paragraph 5.2, nivolumab PSD, March 2019).

5 Consideration of the evidence

Sponsor hearing

There was no hearing for this item.

Consumer input

5.1 The PBAC noted and welcomed the input from individuals (4), health care professionals (2) and organisations (11) via the Office of Health Technology Assessment Consultation Hub. The inputs described a range of benefits of treatment with NIVO SC including the reduction in treatment time, less invasive mode of administration, no additional system burden and the avoidance of infusion chair utilisation. Some inputs also expressed that NIVO SC should only be listed under the Section 100 (EFC – Public/Private Hospital) Schedule noting the higher patient co-payments associated with General Schedule and Section 100 (EFC – Related Benefits) listings and that compounding-related activities involved in the safe preparation, handling, dispensing, and distribution of hazardous cancer medicines are not remunerated under General Schedule and Section 100 (EFC – Related Benefits) listings.

Clinical trials

5.2 The submission was based on the head-to-head clinical trial, CM67T of NIVO SC versus NIVO IV in pretreated patients with clear cell renal cell carcinoma (ccRCC). The primary aim was to demonstrate the pharmacokinetic (PK) non-inferiority of the 2 methods of administration. Secondary endpoints investigating treatment efficacy and safety between the 2 methods of administration were also investigated. A claim of non-inferiority is made on the available PK and clinical data outlined in Section 2.5.1 of the submission. Supplementary PK and safety information is provided from study CA8KX.

5.3 The submission conducted a bridging analysis to establish similar clinical pharmacological profile for weight-based dosing (3 mg/kg) used in treatment experienced ccRCC in CM67T to the different NIVO SC flat dosed regimens (1200 mg Q4W and 600 mg Q2W) and to establish the non-inferiority of PK of each regimen to the analogous approved indications for NIVO IV. The submission stated that the Clinical Evaluation Report analysis was sufficient to bridge from nivolumab SC in 2L RCC being evaluated in the Phase 3 study CA20967T to the proposed therapeutic indications for this submission (all currently approved adult solid tumour indications for nivolumab IV, where nivolumab SC is to be used as monotherapy or in combination with certain chemotherapies or cabozantinib, but not in combination with ipilimumab.

5.4 The CheckMate 67T (CM67T) is a multicentre, randomised, open-label study evaluating PK and efficacy of VIVO SC vs NIVO IV and safety and tolerability of NIVO SC in subjects with advanced or metastatic ccRCC who have evidence of progression after having received no more than 2 prior systemic treatment regimens.

5.5 The CheckMate 8KX (CA8KX) is a multicentre, randomised, open-label, Phase ½ study evaluating the PK, safety and tolerability of NIVO SC administered with and without recombinant human hyaluronidase (rHuuPH20) subcutaneously in subjects with 1 of the following tumour types: metastatic non-small cell cancer (NSCLC), advanced or metastatic renal cell carcinoma (RCC), unresectable or metastatic melanoma, hepatocellular carcinoma (HCC), or metastatic colorectal cancer (CRC). In addition to the above tumours, Part E included subjects with metastatic urothelial carcinoma (mUC).

Table 1: CheckMate 67T, CheckMate 8KX and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
CheckMate 67T CA209-67T NCT04810078	CheckMate 67T Albiges L, Bourlon MT, Chacon M et al. Subcutaneous versus intravenous nivolumab for renal cell carcinoma. Author(s). Title.	19 December 2023 *Annals of Oncol 2024: in press.* *Journal* Year; Vol(No.): pages
CheckMate 8KX CA209-8KX NCT03656718	CheckMate 8KX Lonardi S, Kugowska I, O'Donnell A et al. Pharmacokinetics and safety of subcutaneous nivolumab: Results from the phase I/II CheckMate 8KX study Author(s). Title.	August 7 2023 *J ImmunoTher Canc 2025, 13 (10)* *Journal* Year; Vol(No.): pages

Source: Table 15, p54 of the submission

Comparative effectiveness

CM67T

5.6 The co-primary PK endpoints for the study were average serum concentration over 28 days (Cavgd28) and trough serum concentration at a steady state (Cminss). The primary analysis was performed with stratification factors as recorded in the CRF (i.e., weight category [< 80 kg or ≥ 80 kg] and IMDC risk group [favourable, intermediate, or poor]) and treatment (NIVO SC or NIVO IV) as fixed effects.

5.7 The key secondary efficacy endpoint for CM67T was objective response rate (ORR). ORR was defined as the sum of those patients achieving a best overall response (BOR)

of complete response (CR) or partial response (PR) and was assessed once a minimum follow-up time of 6 months was reached.

5.8 NIVO SC demonstrated non-inferiority to NIVO IV across both key PK measures (Cavgd28 and Cminss). In the primary analysis, noninferiority of NIVO SC to NIVO IV was concluded for a Cavgd28 geometric mean ratio (GMR) (90% CI) of 2.098 (2.001, 2.200) and a Cminss GMR (90% CI) of 1.774 (1.633, 1.927) as the lower bounds of the 2-sided 90% CIs for both endpoints were above 0.8.

5.9 NIVO SC demonstrated non-inferiority to NIVO IV for the secondary efficacy endpoint of ORR per blinded independent central review (BICR). Within a minimum of 15 months follow-up, the ORR for patients who received NIVO SC was 26.6% (n=66/248, 95%CI 21.2, 32.6) compared with 20.6% (n=51/247, 95%CI 15.8, 26.2) for patients who received NIVO IV. To declare non-inferiority, the lower boundary of the 95%CI of the relative risk of ORR had to be 0.60 or greater: the relative risk ratio for ORR between the two groups was 1.28 (95%CI 0.93, 1.77). NIVO SC therefore met its key powered secondary endpoint and demonstrated non-inferiority of ORR by BICR versus NIVO IV.

5.10 The secondary efficacy endpoints of PFS, DCR and TTR were consistent and similar between the NIVO SC and NIVO IV arms. These outcomes, with a minimum follow-up of 15 months show that NIVO SC shows efficacy consistent with its IV formulation.

Comparative harms

CM67T

5.11 Overall, NIVO SC demonstrated a manageable safety profile, consistent with the well-documented safety profile of nivolumab IV, with no new safety signals or concerns identified across trials. The safety profile was manageable based on the already established management guidelines.

CA8KX

5.12 Most treatment related adverse events (TRAEs) were low grade and manageable: there were no injection site treatment related adverse events ≥ grade 3, there were no treatment related deaths were reported.

Clinical claim

5.13 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of NIVO SC 600 mg Q2W or 1200 mg Q4W compared with NIVO IV Q2W or 480 mg Q4W, respectively.

5.14 NIVO SC demonstrated non-inferiority to NIVO IV across key PK measures (Cavgd28 and Cminss) and secondary efficacy endpoint, ORR by BICR in study CM67T.

5.15 NIVO SC demonstrated manageable and comparable safety profile across both trials. No new safety signals or concerns were identified for NIVO SC compared to NIVO IV.

5.16 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable.

Economic analysis

5.17 As a Category 4 submission, the economic analysis has not been independently evaluated.

5.18 The submission presented a cost-minimisation approach of NIVO SC compared with NIVO IV, assuming a 1:1 substitution as a 2- or 4-weekly weekly infusion. The submission assumed that the introduction of NIVO SC will not result in any change in the utilisation of nivolumab.

5.19 The proposed equi-effective doses are 1200 mg NIVO SC = 480 mg NIVO IV.

5.20 The submission's calculation of the cost-minimising factor is presented in Table 2. As shown below, the cost-minimising AEMP of a NIVO SC 600 mg vial is equivalent to 2.4 times that of a NIVO IV 100 mg vial.

Table 2: Calculation of cost-minimising factor

Row		IV	SC	Source
A	Equi-effective dose (mg, Q4W)	480	1200	study CM67T
B	AEMP cost parity per dose	$[redacted]	$[redacted]	Example
C	Cost per mg	$[redacted]	$[redacted]	= B / A
D	Presentation per vial (mg)	100	600	Product Information
E	AEMP per vial	$[redacted]	$[redacted]	= C * D
F	Conversion factor	2.4		= $[redacted] / $[redacted]

Abbreviations: AEMP = Approved ex-manufacturer price, mg = milligram.
Source: p150 of the submission; NIVO SC_CMA, CMA tab (N5:P13).

5.21 As shown in Table 3, the submission applied the conversion factor to the NIVO IV 100 mg AEMP price per indication to calculate the corresponding cost-minimised price per NIVO SC 600 mg vial per indication. The Secretariat noted that in the submission, the AEMP for NIVO IV 100 mg and NIVO SC 600 mg in first- and second-line treatment of RCC were interchanged. This has been amended below.

Table 3: Cost-minimised price for NIVO SC 600 mg vial per indication

Disease Area	PBS indication	NIVO IV AEMP 100 mg	NIVO SC AEMP 600 mg
Melanoma	Resected Stage IIIB, IIIC, IIID or Stage IV malignant melanoma	$[redacted]	$[redacted]
	Unresectable Stage III or Stage IV malignant melanoma		
NSCLC	Locally advanced or metastatic non-small cell lung cancer	$[redacted]	$[redacted]
RCC	Stage IV clear cell variant renal cell carcinoma – 1L	$[redacted]	$[redacted]
	Stage IV clear cell variant renal cell carcinoma – 2L	$[redacted]	$[redacted]
SCCHN	Recurrent or metastatic squamous cell carcinoma of the oral cavity, pharynx or larynx	$[redacted]	$[redacted]
UC	Urothelial carcinoma	$[redacted]	$[redacted]
	Unresectable or metastatic urothelial carcinoma	$[redacted]	$[redacted]
OSCC	Advanced or metastatic gastro-oesophageal cancers	$[redacted]	$[redacted]
GC/GOJC/OAC			
OC/GOJC	Adjuvant treatment of stage II or III oesophageal cancer or gastro-oesophageal junction cancer	$[redacted]	$[redacted]

Abbreviations: AEMP = Approved ex-manufacturer price, mg = milligram.
Source: p150 of the submission; NIVO SC_CMA, CMA tab (N5:P13).

5.22 The submission provided cost-minimised prices consistent with the PBAC recommended indication 'immunotherapy sensitive advanced or metastatic cancer'. These were calculated using the conversion factor from Table 2.

Table 4: Cost-minimising price for NIVO SC 600mg vial per indication (broad listing)

Disease Area	PBS indication	NIVO IV AEMP 100mg	NIVO SC AEMP 600mg
Melanoma	Stage IIIB, IIIC, IIID or Stage IV malignant melanoma	$[redacted]	$[redacted]
UC	Urothelial carcinoma	$[redacted]	$[redacted]
OC/GOJC	Adjuvant treatment of stage II or III oesophageal cancer or gastro-oesophageal junction cancer	$[redacted]	$[redacted]
All	Immunotherapy sensitive advanced or metastatic cancer	$[redacted]	$[redacted]

Abbreviations: AEMP = Approved ex-manufacturer price, mg = milligram.
Source: p19 of Appendix 1, Table 5

Estimated PBS usage and financial implications

5.23 The submission used a market-share approach to estimate the financial impact to the PBS/RPBS of the requested listings. The submission stated that the proposed listing was not expected to impact the overall market size.

5.24 As a result of the broad listing, the submission estimated that 70,000 to < 80,000 NIVO SC infusions would be supplied over the first six years of listing (5,000 to < 10,000 in Year 1 to 10,000 to < 20,000 in Year 6).

5.25 The submission stated that the estimated cost savings is due to the lower fees associated with the requested listings compared with the existing Section 100 (Efficient Funding of Chemotherapy) listings for NIVO IV.

5.26 As a result of broad listing, the submission estimated a net cost save to the PBS of $0 to < $10 million in Year 6 of listing, with a total net cost save to the PBS of $0 to < $10 million over the first six years of listing.

Table 5: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of SC scripts substituting IV scrips	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of NIVO SC						
Cost to PBS/RPBS less co-payment	$[redacted][3]	$[redacted][4]	$[redacted][4]	$[redacted][4]	$[redacted][5]	$[redacted][5]
Estimated financial implications of NIVO IV						
Cost to PBS/RPBS less co-payment	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]
Net financial implications						
Net cost to PBS/RPBS	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]

Abbreviations: IV = intravenous, NIVO = nivolumab, SC = subcutaneous

Source: Worksheets 2e. Scripts market, 3a. Scripts – proposed & 5. Impact- net

1. NIVO SC_BIM_melanoma (adjuvant)
2. NIVO SC_BIM_UC adjuvant
3. NIVO SC_BIM_OC GOJC adjuvant
4. NIVO SC_BIM_IO sensitive adv met

The redacted values correspond to the following ranges:

[1] *5,000 to < 10,000*

[2] *10,000 to < 20,000*

[3] *$10 million to < $20 million*

[4] *$20 million to < $30 million*

[5] *$30 million to < $40 million*

[6] *net cost saving*

5.27 The PBAC noted the modest cost savings in both scenarios that were estimated due to the listing of NIVO SC. The PBAC considered the financial impact to be reasonable.

Quality use of medicines

5.28 The submission stated that the sponsor will commit to continuing education/quality use of medicine initiatives. The submission included an outline of the QUM approach to ensuring that the immunotherapeutic profile of NIVO is well understood and that through experienced prescribers, the oncology treating community collectively uses NIVO in the most effective way.

Risk-sharing arrangements

5.29 The submission considered that NIVO SC would be subject to the existing risk-sharing arrangement for NIVO IV.

6 PBAC Outcome

6.1 The PBAC recommended the dual Section 85 General Schedule and Section 100 (Efficient Funding of Chemotherapy [EFC] – Related Benefits) Authority Required listings of nivolumab solution for subcutaneous injection 600 mg in 5 mL (NIVO SC) for all existing indications of nivolumab 100 mg/10 mL injection, 10 mL vial (NIVO IV), except where nivolumab is administered 3-weekly or where nivolumab is used in combination with ipilimumab. The PBAC's recommendation for listing was based on, among other matters, its assessment that NIVO SC would be cost-effective if it were cost-minimised to NIVO IV.

6.2 The PBAC considered the claim of non-inferior comparative effectiveness and safety to NIVO IV was reasonable.

6.3 The PBAC advised the equi-effective doses to be 1200 mg NIVO SC = 480 mg NIVO IV.

6.4 The PBAC considered that dual Section 85 General Schedule and Section 100 (Efficient Funding of Chemotherapy – Related Benefits) listings would be appropriate noting it previously recommended dual listing for subcutaneous forms of I.V. infusions for the treatment of cancer including atezolizumab, trastuzumab, rituximab and daratumumab. The PBAC noted consumer inputs, which included input from organisations, which expressed a preference for Section 100 (EFC – Public/Private Hospital) listings on the basis that certain compounding-related activities are not remunerated under General Schedule and Section 100 (EFC – Related Benefits) listings. However, the PBAC noted that NIVO SC is only intended for flat dosing regime and would not require the same level of chemotherapy compounding in comparison to other Section 100 (EFC – Public/Private) items.

6.5 The PBAC noted that the dual Section 100 EFC (Related Benefits) and General Schedule listings would likely result in a modest cost saving to the PBS/RPBS due to differences in mark-ups between the requested listings and the existing Section 100 (EFC – Public/Private Hospital) listings for NIVO IV.

6.6 The PBAC considered that the prescribing instructions proposed by the sponsor in the pre-PBAC Response specifying that patients must only receive 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen would be appropriate to differentiate the use of NIVO SC to use as part of a flat dosing regimen and not in combination with ipilimumab.

6.7 The PBAC considered that it would be reasonable for NIVO SC to join the existing risk-sharing arrangements in place for NIVO IV without any changes to caps.

6.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because NIVO SC is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over NIVO IV or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

6.9 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:

Stage IIIB, IIIC, IIID or Stage IV malignant melanoma (based on current item codes 11906P & 11900H)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
NIVOLUMAB					
nivolumab 600 mg/5 mL injection, 5 mL vial	NEW (CT)	2	2	5	Opdivo SC
nivolumab 600 mg/5 mL injection, 5mL vial	NEW (GE)	2	2	5	Opdivo SC

Concept ID (for **internal** Dept. use)	Category / Program: ☒ GENERAL – General Schedule (Code GE) ☒ Section 100 – Efficient Funding of Chemotherapy – Related Benefits (Code CT)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (Telephone/Online)
	Indication: Stage IIIB, IIIC, IIID or Stage IV malignant melanoma
	Treatment Phase: Initial treatment
	Clinical criteria:
	The treatment must be in addition to complete surgical resection,
	AND
	Patient must have a WHO performance status of 1 or less,
	AND
	Patient must not have received prior PBS-subsidised treatment for this condition,
	AND
	The treatment must commence within 12 weeks of complete resection,
	AND
	Patient must not receive more than 12 months of combined PBS-subsidised and non-PBS-subsidised adjuvant therapy.
	Prescribing instructions: Patients must only receive 600mg every 2 weeks or 1200mg every 4 weeks under a flat dosing regimen.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Stage IIIB, IIIC, IIID or Stage IV malignant melanoma
	Treatment Phase: Continuing treatment
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition

	AND
	Patient must have undergone surgical resection
	AND
	Patient must not have experienced disease recurrence,
	AND
	The treatment must be the sole PBS-subsidised therapy for this condition,
	AND
	Patient must not receive more than 12 months of combined PBS-subsidised and non-PBS-subsidised adjuvant therapy.
	Prescribing instructions: Patients must only receive 600mg every 2 weeks or 1200mg every 4 weeks for a maximum of 12 months of adjuvant treatment.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.

Urothelial carcinoma (based on current item codes 14231B & 14260M)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
NIVOLUMAB					
nivolumab 600 mg/5 mL injection, 5mL vial	NEW (CT)	2	2	5	Opdivo SC
Nivolumab 600 mg/5 mL injection, 5mL vial	NEW (GE)	2	2	5	Opdivo SC

Concept ID (for internal Dept. use)	Category / Program: ☒ GENERAL – General Schedule (Code GE) ☒ Section 100 – Efficient Funding of Chemotherapy – Related Benefits (Code CT)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (STREAMLINED)
	Indication: Urothelial carcinoma
	Treatment Phase: [Blank]
	Clinical criteria:
	The treatment must be for each of: (i) adjuvant therapy that is/was initiated within 6 months days of radical surgical resection, (ii) muscle invasive type disease, (iii) disease considered to be at high risk of recurrence based on pathologic staging of radical surgery tissue (ypT2-ypT4a or ypN+), but yet to recur, (iv) use as the sole PBS-subsidised anti-cancer treatment for this condition,
	AND
	Patient must have received prior platinum containing neoadjuvant chemotherapy,
	AND
	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/have had at the time of initiating treatment with this drug, a WHO performance status no higher than 1.
	Treatment criteria:
	Patient must be undergoing treatment with a dosing regimen as set out in the drug's Therapeutic Goods Administration (TGA) approved Product Information,
	AND
	Patient must be undergoing treatment that does not occur beyond the following, whichever comes first: (i) the first instance of disease progression/recurrence, (ii) 12 months in total for this condition from the first administered dose; mark any remaining repeat prescriptions with the words 'cancelled' where (i)/(ii) has occurred.
	Prescribing instructions: Patients must only receive 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.

Adjuvant treatment of stage II or III oesophageal cancer or gastro-oesophageal junction cancer (based on current item codes 13240W and 13246E)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
NIVOLUMAB					
nivolumab 600 mg/5 mL injection, 5 mL vial	NEW (CT)	2	2	5	Opdivo SC
nivolumab 600 mg/5 mL injection, 5 mL vial	NEW (GE)	2	2	5	Opdivo SC

Concept ID (for internal Dept. use)	Category / Program: ☒ GENERAL – General Schedule (Code GE) ☒ Section 100 – Efficient Funding of Chemotherapy – Related Benefits (Code CT)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (Telephone/Online)
	Indication: Adjuvant treatment of stage II or III oesophageal cancer or gastro-oesophageal junction cancer
	Clinical criteria:
	The condition must have histological evidence confirming a diagnosis of a least one of: (i) adenocarcinoma, (ii) squamous cell cancer; document this evidence in the patient's medical records,
	AND
	The condition must have been treated with neoadjuvant platinum-based chemoradiotherapy,
	AND
	The treatment must be for the purposes of adjuvant use following complete surgical resection that occurred within 16 weeks prior to initiating this drug,
	AND
	The condition must have evidence, through resected specimen, that residual disease meets the Tumour Nodes Metastases (TNM) staging system (as published by the Union for International Cancer Control) of either: (i) at least ypT1, (ii) at least ypN1; document this evidence in the patient's medical records,
	AND
	Patient must have/have had at the time of initiating treatment with this drug, a WHO performance status no higher than 1,
	AND
	The treatment must be the sole PBS-subsidised therapy for this condition.
	Treatment criteria:
	Patient must be undergoing treatment with a dosing regimen as set out in the drug's approved Australian Product Information,
	AND
	Patient must not be undergoing PBS-subsidised treatment with this drug where this prescription extends treatment beyond whichever comes first: (i) 12 months from treatment initiation, irrespective of whether initial treatment was PBS-subsidised/non-PBS-subsidised, (ii) disease recurrence despite treatment with this drug; annotate any remaining repeat prescriptions with the word 'cancelled' where this occurs.
	Prescribing instructions: Patients must only receive 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.

Immunotherapy sensitive advanced or metastatic cancer (based on item codes 15238B and 15224G)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
NIVOLUMAB					
nivolumab 600 mg/5 mL injection, 5 mL vial	NEW (CT)	2	2	13	Opdivo SC
nivolumab 600 mg/5 mL injection, 5 mL vial	NEW (GE)	2	2	13	Opdivo SC

	Category / Program: ☒ Section 100 – Chemotherapy Related Benefits (CT) ☒General Schedule (GE)
	Prescriber type: ☒Medical Practitioners
	Restriction type: ☒Authority Required (STREAMLINED) [NEW]
	Indication: Immunotherapy sensitive advanced or metastatic cancer
	Clinical criteria:
	Patient must not have developed disease progression while receiving PBS-subsidised treatment with this drug for the condition which treatment was commenced for.
	Prescribing instructions: Patients must only receive 600 mg every two weeks or 1200 mg every four weeks under a flat dosing regimen.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative advice: Special Pricing Arrangements apply.

These restrictions 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.