# 6.14 NIVOLUMAB, Injection concentrate for I.V. infusion 40 mg in 4 mL, Injection concentrate for I.V. Infusion 100 mg in 10 mL, Opdivo®, IPILIMUMAB Injection concentrate for I.V. infusion 50 mg in 10 mL, Injection concentrate for I.V. infusion 200 mg in 40 mL, Yervoy® BRISTOL-MYERS SQUIBB AUSTRALIA PTY LTD.

## 1 Purpose of Submission

1.1 To consider a submission from Bristol-Myers Squibb Australia for a multi-indication (broad) listing for nivolumab ± ipilimumab in unresectable advanced or metastatic cancers.

## 2 Background

### *Previous PBAC considerations*

2.1 The PBAC's most recent consideration of a multi-indication listing for PD-(L)1 inhibitors was at the September 2024 meeting.

2.2 The PBAC was supportive of implementing simplified listings for PD-(L)1 inhibitors if this would facilitate appropriate and timely access for patients and reaffirmed its previous advice, that in the context of the extensive experience with applications for PD-(L)1 inhibitors, it would be appropriate and desirable to have a simplified process for listing future indications.

2.3 The PBAC remained concerned about the lack of subsidised patient access to PD-(L)1 inhibitors for rare tissue types and the resulting unmet clinical need. The PBAC noted that some rare tissue types were not dMMR/MSI-H nor TMB-H and consequently did not have (and were unlikely to obtain) a registered TGA indication.

2.4 The PBAC noted that the financial estimates for any multi-indication listing would inherently be subject to uncertainty. Any proposal for a multi-indication listing should include a risk-sharing arrangement that shared the risk associated with this uncertainty between the Sponsor and the Commonwealth.

2.5 The PBAC also advised that access to indications where PD-(L)1 inhibitors are used in combination with other high-cost agents should not be affected. A PBS listing which provided access to one of the components of a combination regimen ahead of the other(s) would be problematic.

# 3 Outline of July 2025 Proposal

3.1 The submission proposed a single weighted, effective approved ex-manufacturer price (AEMP) ('weighted price' hereafter) for each of nivolumab and ipilimumab based on existing PBS listed indications. The proposed weighted prices are set out in Table 1 as a price per vial and price per 4-week treatment at standard doses (q4w) for nivolumab.

**Table 1: Current and previous proposed weighted prices per vial and per four-weeks of treatment for nivolumab and ipilimumab**

| Medicine | December 2024 Proposed price per vial | Current proposed price per vial | December 2024 Proposed price per q4w | Current proposed price per q4w |
|---|---|---|---|---|
| Nivolumab 100 mg | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| Ipilimumab 50 mg | $[redacted] | $[redacted] | N/A | N/A |

3.2 The December 2023 and September 2024 proposals requested a price-volume agreement (PVA) with fixed price reductions over future years to offset increased utilisation due to additional indications. These fixed reductions were based on forecast utilisation across a five-year period. The RSA proposal in the current submission is different in that it proposes

- [redacted] subsidisation caps [redacted]
- [redacted].
- [redacted] proposed a [redacted] rebate for expenditure [redacted].
- [redacted].

3.3 In its December 2023 submission, the sponsor provided an RSA proposal that included a [redacted]% rebate for expenditure of tier 2 of that proposal. The PBAC considered at the time "…that a cap on overall expenditure was appropriate, however given the significant financial impact of such a listing, and the numerous uncertainties and risks outlined above, it would be reasonable to have greater certainty of the total budget impact with 100% rebate applying above the level of the financial estimates". The current submission does not propose any hard cap, and the Commonwealth assumes the majority of risk ([redacted]%) of use beyond the utilisation estimates.

# 4 Scope of the proposed listing

4.1 The proposed multi-indication listing (with a single item-code duplicated for the Public and Private hospital settings and single weighted price for nivolumab; and a single item-code duplicated for the Public and Private hospital schedules and single weighted price for ipilimumab) was "Unresectable advanced or metastatic cancer".

4.2 The proposed listing would not include early-stage cancers such as use in the peri-operative, neoadjuvant or adjuvant setting.

4.3 The HCC and dMMR-CRC indications were considered as separate submissions at the July 2025 PBAC meeting and the first-line urothelial indication was recommended at the November 2024 meeting. These indications are included in the new/additional indications modelled in the submission.

4.4 The submission presented the following table with current and future indications for nivolumab and ipilimumab (as Table 2):

**Table 2: Current and future nivolumab and ipilimumab indications**

| Drug/s | Indication | Pivotal trial code |
|---|---|---|
| NIVO+IPI | 1L RCC | CM214 |
| NIVO | 2L RCC | CM025 |
| NIVO±IPI | Metastatic melanoma | CM204 |
| NIVO+IPI | 1L NSCLC | CM9LA |
| NIVO | 2L NSCLC | CM057/CM017 |
| NIVO | 2L SCCHN | CM141 |
| NIVO+IPI | Mesothelioma | CM743 |
| NIVO | UGI | CM648/CM649/ATT-3 |
| NIVO | 1L mUC | CM901 (Arm C) |
| NIVO+IPI | 1L CRC | CM8HW |
| NIVO+IPI | 1L HCC | CM9DW |
| NIVO+AVD | Newly diagnosed stage III-IV cHL (1L) | CM8UT |
| NIVO | 3L cHL | CM205 |
| NIVO | 2L HCC | CM040 |
| NIVO | 2L urothelial | CM275 |
| NIVO+IPI | 1L NSCLC (9LA NSQ) | CM9LA |
| (NIVO)+IPI | 1L OSCC | CM649 |

**Abbreviations:** AVD = doxorubicin, vinblastine, dacarbazine; cHL = classical Hodgkin's lymphoma; CRC = colorectal cancer; HCC = hepatocellular carcinoma; NSCLC = non-small cell lung cancer; NSQ = non-squamous; OSCC = oesophageal squamous cell carcinoma; RCC = renal cell carcinoma; SCCHN = squamous cell carcinoma of the head and neck; UGI = upper gastro-intestinal.
**Source:** Table 3, p17 from the submission

| Legend |
|---|
| PBS listed |
| Submitted to PBAC |
| TGA registered (no PBS) |
| Future PBS indications |

4.5 Currently subsidised indications (proposed Subsidy Cap 1 (SC1))

- melanoma (± ipilimumab induction)
- first-line squamous non-small cell lung cancer (+ ipilimumab induction) (also a previous second-line listing in squamous and non-squamous)
- renal cell carcinoma (intermediate/poor risk) (+ ipilimumab induction) (also a previous second-line listing)
- mesothelioma (± ipilimumab induction)
- upper GI
    - First-line (1L) adenocarcinoma HER2-neg
    - OSCC
- Second-line (2L) SCCHN

4.6 There is a listing for the combination drug nivolumab with relatlimab for unresectable advanced/metastatic melanoma that is not considered as part of this proposal.

4.7 Proposed new/additional indications calculated as utilisation above SC1:

- HCC (+ ipilimumab induction) and dMMR/MSI-H CRC (+ ipilimumab induction)
  - *The sponsor has made individual submissions to the PBAC for these indications which were considered at the July 2025 meeting.*
- 1L UC (recommended by PBAC at the November 2024 meeting)
- first-line non-squamous NSCLC (+ ipilimumab induction)
  - *first-line squamous NSCLC was listed in 2021 (as above)*
- newly-diagnosed cHL
- retreatment
- rare tissue types (± ipilimumab)
- minor: SCCO nivolumab (± ipilimumab)
  - nivolumab is currently subsidised for this indication and included in SC1, ipilimumab is not currently subsidised and included in SC2 numbers.

4.8 The submission noted that current listings for early-stage melanoma, early-stage NSCLC, early-stage gastro-oesophageal and MIUC are not included in the scope of this submission.

# 5 Requested Listing

5.1 The requested listing is presented below and is intended to replace all existing advanced and metastatic listings for nivolumab and ipilimumab.

5.2 Secretariat has provided updates to the requested restriction with proposed deletions in strikethrough and additions in italics.

<table>
<tr><td colspan="6">Category/Program: Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals</td></tr>
<tr><td colspan="2">MEDICINAL PRODUCT</td><td>PBS item code</td><td>Max. Amount</td><td>№.of Rpts</td><td>Manufacturer</td></tr>
<tr><td colspan="2">NIVOLUMAB<br>Injection</td><td>NEW (Public)<br>NEW (Private)<br>MP</td><td>480mg</td><td>13</td><td>Bristol-Myers Squibb Australia Pty Ltd</td></tr>
<tr><td colspan="6">Available brands</td></tr>
<tr><td colspan="6">Opdivo (nivolumab 40 mg/4 mL injection, 4 mL vial)<br>Opdivo (nivolumab 100 mg/10 mL injection, 4 mL vial)</td></tr>
<tr><td colspan="6">Restriction Summary [number – For. Dept. use] / Treatment of Concept: [number – For. Dept. use]: Authority Required (STREAMLINED)</td></tr>
<tr><td>This column – for Dept. use</td><td colspan="5">Indication: Unresectable advanced or metastatic cancer</td></tr>
<tr><td></td><td colspan="5"></td></tr>
<tr><td></td><td colspan="5"><s>Treatment criteria:</s></td></tr>
</table>

| | |
|---|---|
| | ~~Treatment with this drug must cease as a PBS benefit if they have experienced disease progression for that indication.~~ |
| | ***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.* |
| | ~~**Note:**~~ |
| | ~~In the first few months after starting immunotherapy, a transient tumour flare may occur that may be mistaken as disease progression despite an overall positive response to treatment.~~<br>~~The stated maximum amount in this listing is based on 480mg administered every 4 weeks. Alternative dosing schedules can be utilised. The drug may be prescribed in a quantity up to this amount but need not be this amount for every cancer type.~~<br>~~Special Pricing Arrangements apply.~~<br>~~No increase in the maximum number of repeats may be authorised.~~ |
| | *Prescribing instruction: 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.* |
| | *Administrative advice: No increase in the maximum number of repeats may be authorised.* |
| | *Administrative advice: Special Pricing Arrangements apply.* |

**Category/Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals

| **MEDICINAL PRODUCT** | **PBS item code** | **Max. Amount** | **№.of Rpts** | **Manufacturer** |
|---|---|---|---|---|
| IPILIMUMAB<br>Injection | NEW (Public)<br>NEW (Private)<br>MP | 360mg | 4 | Bristol-Myers Squibb Australia Pty Ltd |

**Available brands**

Yervoy (ipilimumab 50 mg/10 mL injection, 10 mL vial)
Yervoy (ipilimumab 200 mg/40 mL injection, 40 mL vial)

**Restriction Summary** [number – For. Dept. use] **/ Treatment of Concept:** [number – For. Dept. use]: **Authority Required (STREAMLINED)**

| | |
|---|---|
| This column – for Dept. use | **Indication:** Unresectable advanced or metastatic cancer |
| | |
| | ~~**Treatment**~~ ***Clinical*** **criteria:** |
| | ~~Treatment with this drug must cease as a PBS benefit if they have experienced disease progression for that indication.~~<br>*Patient must not have developed disease progression while receiving PBS-subsidised treatment with this drug for the condition which treatment was commenced for* |
| | |
| | **Note:** |
| | ~~In the first few months after starting immunotherapy, a transient tumour flare may occur that may be mistaken as disease progression despite an overall positive response to treatment.~~<br>~~The stated maximum amount in this listing is based on 360mg. Alternative dosing schedules can be utilised. The drug may be prescribed in a quantity up to this amount but need not be this amount for every cancer type.~~<br>~~Special Pricing Arrangements apply.~~ |

| | |
|---|---|
| | ~~No increase in the max number of repeats may be authorised.~~ |
| | *Prescribing instruction: The stated maximum amount in this listing is based on 360mg. Alternative dosing schedules can be utilised. The drug may be prescribed in a quantity up to this amount but need not be this amount for every cancer type.* |
| | *Administrative advice: No increase in the maximum number of repeats may be authorised.* |
| | *Administrative advice: Special Pricing Arrangements apply.* |

5.3 The submission states "To ensure that patients do not receive treatment beyond progression where they are no longer deriving benefit…", the sponsor has proposed the following treatment criteria be applied to listings for both drugs:

> Treatment with this drug must cease as a PBS benefit if they have experienced disease progression for that indication.

The Secretariat proposed that this could be replaced with the following clinical criteria for consistency with restrictions in other PBS listings:

> Patient must not have developed disease progression while receiving PBS-subsidised treatment with this drug for the condition which treatment was commenced for.

5.4 The sponsor claimed a maximum amount of 480 mg and 13 repeats would be appropriate for nivolumab on the basis this would provide for patients receiving flat 240 mg, 360 mg and 480 mg dosing, as well as weight-based dosing. 13 repeats would allow for 12 months of therapy at monthly dosing or 6 months at two-weekly dosing. The PBAC noted nivolumab is currently listed for a range of maximum quantities and repeats for individual indications. While the majority are for maximum quantities or maximum repeats less than the proposed amount, listings for 480 mg with 13 repeats exist for NSCLC and advanced or metastatic gastro-oesophageal cancers. These indications would be included under the broad listing.

5.5 The sponsor has proposed a maximum amount of 360 mg and four repeats be applied to the broad ipilimumab listing. This is on the basis ipilimumab is dosed either in induction or ongoing therapy and at 1 mg/kg or 3 mg/kg, making 360 mg the dose required for a 120 kg patient. This is consistent with existing listings for Unresectable Stage III or Stage IV malignant melanoma.

5.6 The sponsor has also requested that no increases in maximum repeats be permitted under the broad listings.

5.7 The sponsor requested an administrative advice be included on ipilimumab of:

> In the first few months after starting immunotherapy, a transient tumour flare may occur that may be mistaken as disease progression despite an overall positive response to treatment.

5.8 The Secretariat noted some listings for ipilimumab where it is intended to be used in combination with nivolumab also contain the following administrative advice:

> Combination treatment with ipilimumab and nivolumab is associated with an increased incidence and severity of immune-related adverse reactions

compared with monotherapy with these agents. Monitoring at least prior to each dose is recommended.

5.9 In the pre-PBAC response, the sponsor indicated it considered the proposed amendments to the restriction wording would be acceptable if recommended by the PBAC.

# 6 Proposed Pricing

6.1 The submission proposed that a lower price for the broader additional indications is achieved through a PVA enacted via Risk Share Arrangement (RSA).

6.2 The submission stated this was important to ensure the cost-effective price for nivolumab and ipilimumab for the existing listings is retained under the broad listing and did not consider an up-front price reduction would be appropriate as the PBAC had already considered cost-effectiveness for these indications.

6.3 The submission proposed to maintain the current effective prices through implementing a single, weighted, effective price (AEMP) for a 100 mg vial of nivolumab of $[redacted] ($[redacted] for 480 mg (q4w)). The weighted price considered by PBAC in December 2023 and September 2024 was $[redacted] per 100 mg ($[redacted] for 480 mg (q4w)).

6.4 A weighted price is required to consolidate the listings as the proposed PBS restriction would require a single muti-indication PBS item, covering existing and new/additional unresectable advanced or metastatic indications.

6.5 The proposed weightings were based on the PBS Benefits (reported on the Medicare Statistic website) for each advanced/metastatic indication currently PBS listed over a recent 12-month period (April 2024 – March 2025).

6.6 The proposed weightings per indication and resultant effective prices for nivolumab are provided in Table 3.

**Table 3: Proposed indication and price weighting to achieve proposed effective price for nivolumab**

| Indication | % PBS Benefits Apr-24 to Mar-25 | ex-man price 100 mg | cost per q4w 480 mg |
|---|---|---|---|
| 1L NSCLC | 2.2% | $[redacted] | $[redacted] |
| 1L RCC | 8.7% | $[redacted] | $[redacted] |
| 2L NSCLC | 6.7% | $[redacted] | $[redacted] |
| 2L RCC | 9.6% | $[redacted] | $[redacted] |
| Mesothelioma | 10.3% | $[redacted] | $[redacted] |
| 2L SCCHN | 4.8% | $[redacted] | $[redacted] |
| UGI | 23.0% | $[redacted] | $[redacted] |
| Metastatic melanoma | 34.7% | $[redacted] | $[redacted] |
| Total | 100.0% | $[redacted] | $[redacted] |

Source: Table 27 of submission, p 50

6.7 The submission outlined that the overall proposal was intended to achieve a [redacted]% price reduction for the additional modelled population. This would result in an AEMP of $[redacted] per 100 mg vial (or $[redacted] for 480 mg Q4W) in the extended population.

6.8 The proposed weighted ipilimumab price is $[redacted] per 50 mg vial. The proposed weighted price considered by PBAC in December 2023 and September 2024 was $[redacted] per 50 mg vial.

6.9 The proposed weightings per indication and resultant effective prices for ipilimumab are provided in Table 4.

**Table 4: Proposed weighting and utilisation of existing indications of ipilimumab to calculate proposed effective price**

| Indication | % PBS Benefits Apr-24 to Mar-25 | ex-man price 50 mg | dosing in TGA PI |
|---|---|---|---|
| 1L NSCLC, sq | 4.4% | $[redacted] | 1 mg/kg q6w until progression or unacceptable toxicity |
| Melanoma | 67.1% | $[redacted] | 3 mg/kg q3w for 4 doses |
| Mesothelioma | 18.2% | $[redacted] | 1 mg/kg q6w until progression or unacceptable toxicity |
| RCC | 10.2% | $[redacted] | 1 mg/kg q3w for 4 doses |
| Total | 100.0% | $[redacted] | |

# 7 Risk-sharing arrangement

7.1 The submission states that the foundation of the proposal is an RSA which it intends to function as a PVA s., with the following components:

- [redacted] subsidisation cap [redacted].
- Rebates applicable to nivolumab and ipilimumab for utilisation that exceeds the caps [redacted].
- Governance framework for the PVA with regular review, which the Sponsor likens to a managed access program (MAP) based on script volumes.

7.2 The submission did not propose any overall (i.e. [redacted]%) cap on total expenditure.

7.3 *Nivolumab and ipilimumab are currently subject to RSAs for all listed indications. Most include a [redacted]% reimbursement for expenditure above caps (gastro-oesophageal cancer has [redacted] and mesothelioma has a rebate of [redacted]% over caps). [redacted].*

7.4 In its pre-PBAC response, the sponsor claimed that while most of the existing indications were subject to RSAs with a [redacted]% cap, two indications (gastro-oesophageal and mesothelioma) had a rebate [redacted]. The sponsor argued that this submission [redacted] risk sharing would involve a rebate [redacted].

7.5 The submission estimates that in 2025 approximately 5,000 to < 10,000 patients will be treated with nivolumab ± ipilimumab across currently PBS listed indications. The sponsor estimated Government expenditure on nivolumab and ipilimumab would be

approximately $200 million to < $300 million (approximately nivolumab: $100 million to < $200million and ipilimumab: $40 million to < $50 million).

7.6 The sponsor estimates utilisation under the proposed broad listing would include an additional 500 to < 5,000 patients being treated per year with a subsequent increase in Government expenditure of $100 million to < $200 million, totalling $300 million to < $400 million per year.

7.7 The sponsor proposed rebates for the spend above the caps that would amount to approximately $40 million to < $50 million in its estimation. This would reduce the increased cost of the broad listing to $80 million to < $90 million and total expenditure to $300 million to < $400 million per year.

7.8 The submission states that the RSA would provide a net price reduction for nivolumab and ipilimumab of [redacted]% for patients who would be newly eligible under a broad listing (i.e., from $[redacted] q4w to $[redacted] q4w) based on its estimates of utilisation.

**Table 5: Estimated total drug cost to government (effective PBS/RPBS, with PVA structure)**

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 |
|---|---|---|---|---|---|---|
| **Estimated cost to PBS/RPBS** | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][1] |
| **Proposed cap** | | | | | | |
| Subsidisation Cap 1 | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| Subsidisation Cap 2 | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| **Estimated RSA rebate** | | | | | | |
| Subsidisation Cap 1 rebate | $[redacted][3] | $[redacted][3] | $[redacted][3] | $[redacted][3] | $[redacted][3] | $[redacted][3] |
| Subsidisation Cap 2 rebate | $[redacted][4] | $[redacted][4] | $[redacted][4] | $[redacted][4] | $[redacted][5] | $[redacted][5] |
| **Total RSA rebate** | **$**[redacted][5] | **$**[redacted][5] | **$**[redacted][5] | **$**[redacted][6] | **$**[redacted][6] | **$**[redacted][6] |
| **Estimated cost to PBS/RPBS after RSA rebates** | **$**[redacted][1] | **$**[redacted][1] | **$**[redacted][1] | **$**[redacted][1] | **$**[redacted][1] | **$**[redacted][1] |

Source: Table 31 of the submission

*The redacted values correspond to the following ranges:*

[1] *$300 million to < $400 million*

[2] *$200 million to < $300 million*

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

[4] *$30 million to < $40 million*

[5] *$40 million to < $50 million*

[6] *$50 million to < $60 million*

7.9 The financial estimates for both current listings and new/additional listing are projected by the Sponsor to be stable over the six years of the forward estimates.

7.10 The Pre-PBAC Response stated the sponsor may consider a simplified RSA structure that consolidated the discount into a single rebate applied after SC1.

## *Governance framework for the RSA*

7.11 To manage the risk to both parties of using an RSA to achieve an acceptably cost-effective price, the submission proposes that any potential agreement should

incorporate an annual review. The sponsor indicated it could work in a similar way to a Managed Access Program specific to this proposal.

7.12 The submission proposed that the annual review include:

- Updates from the Sponsor re: data disclosure dates for future indications.
- Review of PBS sales data for previous year.
- Discussion on potential impact of the update from the sponsor on data disclosure for future indications and the review of PBS sales data for the previous year on financial estimates for NIVO±IPI for current and future indications.
- Discussion on a formalised process for PBAC consideration of information/ outcomes from the annual meeting (akin to a Managed Access Program).

7.13 The PBAC noted that in creating a new cap arrangement for a broad listing, nivolumab and ipilimumab would need to be removed from some existing shared RSAs (melanoma combined resected/unresectable; NSCLC; RCC; SCCHN; gastro-oesophageal combined with adjuvant).

7.14 The pre-PBAC response proposed a 2-year review initiated by sponsor submission of utilisation since PBS listing. The measures would focus on whether utilisation was in line with the agreed estimates and to consider whether early-stage listings had impacted that utilisation. The sponsor noted reliance on the framework would be minimised to the degree the RSA and estimates were set in a manner that ensured proposed expenditure was reasonable and did not result in the caps being exceeded. The sponsor acknowledged the final details of any framework would need to be negotiated with the Department in the post-PBAC process.

# 8 Additional indications/usage

8.1 The Sponsor acknowledged the difficulty in accurately predicting the following inputs in the financial forecasts

- future patient numbers
  - uptake is assumed constant across the 6 years
  - for some settings it is difficult to accurately predict patient numbers (e.g., retreatment, rare cancers)
  - the utilisation in 1L UC will be impacted if a listing for enfortumab-vedotin with pembrolizumab is implemented
  - There is a lack of data to support the rate of substitution for alternative PD-(L)1 inhibitors in some indications (e.g., HCC, dMMR CRC, NSq NSCLC).

8.2 The PBAC noted under the broad listing as proposed it would not be possible to track utilisation in specific indications based on the administrative data from the PBS alone. PBAC commented that while linkage of the PBS data to other health data could be considered to identify the indication of use, it was uncertain whether this would be feasible to do in a timely way.

**Time-on-treatment (i.e., number of doses and resultant script volumes)**

8.3 For nivolumab, many of the new/additional indications forecast 10 - 11 (mean) doses at 480 mg q4w, including for retreatment.

8.4 Some indications have alternative forecast (mean) dosing, such as cHL (6 doses at 240 mg q2w doses) and rare cancers (5 doses at 480 mg q4w).

8.5 The Sponsor states that 10 to 11 months on treatment is the mean nivolumab time-on-treatment for advanced/metastatic indications.

8.6 For ipilimumab, the submission uses the dosing from the pivotal registration RCTs for marketing approval. One exception is rare cancers, which assumes dosing similar to that used in the Phase-2 single-arm CheckMate-538 trial.

8.7 To help understand the proposed RSA, it might be useful to consider the forecast relative PBS script volumes for the additional indications/usage provided in Table 6 and Table 7.

**Table 6: Modelled mean number of doses and relative percent spend for additional nivolumab indications**

| Indication | modelled dose | modelled number of doses/scripts | total forecast PBS expenditure across 6 years (effective) ($M) | relative percentage of all additional PBS expenditure |
|---|---|---|---|---|
| 1L UC | 360 mg q3w | 11.3 | [redacted][1] | 20% |
| 1L CRC | 480 mg q4w | 13.0 | [redacted][1] | 26% |
| 1L HCC | 480 mg q4w | 13.0 | [redacted][2] | 4% |
| 1L stage III-IV cHL | 240 mg q2w | 6.0 | [redacted][3] | 5% |
| 3L cHL | 480 mg q4w | 14.0 | [redacted][4] | <1% |
| 2L HCC | 480 mg q4w | 6.7 | [redacted][4] | 1% |
| 2L UC | 480 mg q4w | 8.0 | [redacted][4] | 1% |
| 1L NSQ NSCLC | 360 mg q3w | 13.7 | [redacted][3] | 6% |
| IO retreatment | 452 mg q4w | 10.8 | [redacted][5] | 17% |
| Rare cancers | 480 mg q4w | 5.0 | [redacted][6] | 18% |
| | | Total | [redacted][7] | 100% |

*The redacted values correspond to the following ranges:*
*[1] $100 million to < $200 million*
*[2] $20 million to < $30 million*
*[3] $30 million to < $40 million*
*[4] $0 to < $10 million*
*[5] $90 million to < $100 million*
*[6] $100 million to < $200 million*
*[7] $500 million to < $600 million*

**Table 7: Modelled mean number of doses and relative percent spend for additional ipilimumab indications**

| Indication | modelled dose | modelled number of doses/scripts | total forecast PBS expenditure across 6 years (effective) ($M) | relative percentage of all additional PBS expenditure |
|---|---|---|---|---|
| 1L OSS | 80 mg | 4.3 | [redacted][1] | 1% |
| 1L CRC | 80 mg | 4.0 | [redacted][2] | 15% |
| 1L HCC | 240 mg | 3.0 | [redacted][3] | 31% |
| 1L NSq NSCLC | 80 mg | 7.0 | [redacted][4] | 11% |
| rare | 80 mg | 4.0 | [redacted][5] | 42% |
| | | Total | [redacted][6] | 100% |

*The redacted values correspond to the following ranges:*
*[1] $100 million to < $200 million*
*[2] $20 million to < $30 million*
*[3] $30 million to < $40 million*
*[4] $0 to < $10 million*
*[5] $90 million to < $100 million*
*[6] $100 million to < $200 million*
*[7] $500 million to < $600 million*

8.8 For nivolumab

- 26% of the forecast spend is for 1L dMMR CRC, which depends on nivolumab + ipilimumab taking [redacted]% of the market share from pembrolizumab
- 20% of the forecast spend is for 1L UC, which assumes that enfortumab-vedotin + pembrolizumab (recommended by PBAC, Nov-24) will not be listed
- 18% of the forecast spend is for rare cancers (see Table 8, below for assumptions).
- 17% of the forecast spend is for retreatment (see Table 8, below for assumptions).

8.9 For ipilimumab

- 42% of the forecast spend is for rare cancers, which is reliant on the assumption that all patients would be offered ipilimumab (in addition to nivolumab) and that dosing would be 80 mg x 4 as per CheckMate-538

**Table 8: Forecast number of patient and assumptions for new/additional indications**

| | |
|---|---|
| 1L UC | ~ [redacted][1] to [redacted][1] patients/year<br>• recommended Nov-24 not listed as 1 June 2025<br>• utilisation will be much lower if EV+P listed |
| 1L dMMR CRC | ~ [redacted][2] to [redacted][1] patients/year<br>• assumes [redacted]% uptake of current pembrolizumab PBS scripts |
| 1L HCC | ~ [redacted][2] to [redacted][2] patients/year<br>• assumes [redacted]% substitution for atezolizumab + bevacizumab<br>• assumes growth of the overall market around 10% |
| 1L cHL | ~ [redacted][2] to [redacted][2] patients/year<br>• *assumption of high uptake (>[redacted]%) seems reasonable due to lower toxicity compared to SoC.* |
| 3L cHL | ~ [redacted][2] patients/year |
| 2L HCC | ~ [redacted][2] to [redacted][2] patients/year<br>• seems high given availability of 1L atezolizumab + bevacizumab<br>• metastatic-to-metastatic retreatment excluded form the Sponsor's retreatment forecasts |
| 2L UC | ~ [redacted][2] patients/year<br>• seems high given pending listing of 1L PD-1i's & availability of 2L pembrolizumab<br>• assumes nivolumab:pembrolizumab [redacted]%:[redacted]%; [redacted]% might be an over-estimate |
| 1L NSq NSCLC | ~ [redacted][2] -[redacted][2]patients/year<br>• assumes [redacted]% market share<br>• difficult to assess the accuracy of this prediction |
| retreatment | ~ [redacted][2] patients/year; stable across the 6 years<br>• only considers early-to-metastatic retreatment<br>metastatic-to-metastatic retreatment is excluded<br>• mean(ToT) assumed to be the same as for PD-(L)1i-naïve patients<br>~ 10 to 11 q4w doses, this may over estimate script numbers<br>• minor: assumes ~ 12 extra retreated melanoma patients, although retreatment in melanoma has PBS listing (6 month treatment-free interval will no longer apply) |
| rare cancers | ~ [redacted][1] to [redacted][1] patients/year<br>• uptake is assumed to be immediate and then constant across the 6 years which may over-estimate prescription numbers<br>• mean time-on-treatment for nivolumab (5 months) is uncertain<br>• the extent to which ipilimumab will be used is uncertain based on available data |
| 1L OSCC ipilimumab only | ~ [redacted][2] patients/year<br>• assumes [redacted]% of patients unsuitable for chemotherapy |

*The redacted values correspond to the following ranges:*
*[1] 500 to < 5,000*
*[2] < 500*

8.10 The PBAC considered the estimated uptake for 1L HCC ([redacted]% substitution for atezolizumab and bevacizumab, which represents 31% of estimated spend for additional ipilimumab indications) was substantially overestimated, given that NIVO +IPI is not a preferred regimen in international guidelines (NCCN/ESMO).

# 9 Additional considerations

**Retreatment**

9.1 The submission proposes PD-(L)1i retreatment. Indications approved by Regulatory Agencies (e.g., FDA, EMA, TGA, MHRA, Health Canada, etc) are agnostic to retreatment and as such are taken to allow retreatment.

9.2 The submission includes retreatment from year 1 for tissue types where an early-stage listing does not currently exist (but is anticipated) including RCC, CRC, SCCHN and HCC.

**Classical Hodgkin's Lymphoma (cHL)**

9.3 A phase 3 RCT sponsored by the National Cancer Institute (NCI) (NCT03907488) (S1826) compared nivolumab with doxorubicin, vinblastine and dacarbazine (N+AVD) to brentuximab vedotin with AVD (BV+AVD) [Herrera AF et al. Nivolumab+AVD in Advanced-Stage Classic Hodgkin's Lymphoma. N Engl J Med. 2024 Oct 17;391(15):1379-1389. doi: 10.1056/NEJMoa2405888. PMID: 39413375; PMCID: PMC11488644].

9.4 Patients were randomly assigned to receive N+AVD intravenously (nivolumab at a dose of 240 mg in adults and 3 mg per kilogram of body weight in children 12 to <18 years of age [capped at 240 mg], doxorubicin at a dose of 25 mg per square meter of body-surface area, vinblastine at a dose of 6 mg per square meter, and dacarbazine at a dose of 375 mg per square meter) or BV+AVD (brentuximab vedotin at a dose of 1.2 mg per kilogram [capped at 100 kg], and AVD at the doses listed above) on days 1 and 15 of each 28-day cycle for six cycles.

9.5 The intention-to-treat group comprised 970 patients (487 vs 483).

9.6 After a median follow-up of 2.1 years (range: 0 to 4.2 years), the 2-year PFS was 92% vs 83%; HR(PFS) = 0.45 95% CI (0.30, 0.65). Deaths at 2 years were 7 vs 14 with OS 99% vs 98%.

9.7 UpToDate lists N+AVD as the preferred option for initial treatment of Stage III/IV disease.

**Marketing approvals for rare tissue types**

9.8 Nivolumab (± ipilimumab) does not have marketing approval for rare tissue types. Some (but not all) of these rare tissue types are dMMR/MSI-H or TMB-H.

In Australia, pembrolizumab has pan-tissue (i.e., tissue agnostic) regulatory marketing approval for dMMR/MSI-H and TMB-H tumours. In the United States, dostarlimab has FDA pan-tissue accelerated approval for dMMR/MSI-H.

- Toripalimab was recommended at the March 2025 PBAC meeting for NPC.

**Genomic testing for MSI-H and TMB**

9.9 dMMR can be reasonably accurately detected via immune histochemistry (IHC) testing and there is an MBS item for IHC that covers all tissue types. IHC is sufficient in most cases; in a few cases (e.g., staining doesn't work) genomic MSI testing is needed.

9.10 TMB is different: genomic testing is needed, for which there is currently no MBS item. Patients would have to access TMB testing via referral to the CaSP program operated by Omico, case by case public hospital funding, or private funding.

9.11 The Sponsor assumed that 90% of eligible patients would have IHC testing for dMMR. For TMB-H, the assumption was that 40% of patients would be tested, either via Omico, public-hospital funding, or self-funding.

## *Sponsor hearing*

9.12 There was no hearing for this item.

## *Consumer comments*

9.13 The PBAC noted and welcomed the input from health care professionals (8) and clinical organisations (3) and consumer representatives organisations (2). The PBAC noted input from medical oncologists and the clinical groups were broadly supportive for expanded listing of nivolumab and ipilimumab, particularly where there is evidence of benefit in the advanced/metastatic setting. Consumer organisations noted the significant financial burden associated with treatment and the perceived inequity of access across the existing PBS listed indications. Input highlighted the benefits of broader access for individuals with rare, advanced cancers, with examples of efficacy provided across a range of rare cancer types. Some input noted the importance of ensuring that utilisation occurred only in conditions for which there was evidence of efficacy. However, others highlighted that ongoing treatment was unlikely to occur where there was no demonstrated patient response.

**Quality Use of medicines**

9.14 In the pre-PBAC response, the sponsor noted the following:

"Key to the careful and successful implementation of the proposed broad PBS listing will be education and QUM initiatives. If recommended, the Sponsor would seek to partner with key stakeholders (e.g. MOGA, oncology health care organisations, the PBAC & Department) to develop and roll-out a range of educational and QUM activities that will aid Australian medical oncologists to optimally identify and manage patients with unresectable advanced/metastatic cancer. This could include, but is not limited to:

1. Educational sessions for medical oncologists run by clinical bodies (e.g. MOGA) prior to and immediately post PBS restriction change
2. Educational sessions for oncology Health Care Organisations (HCOs) run by Rare Cancers Australia (RCA) prior to and immediately post PBS restriction change
3. Ongoing peer-to-peer Health Care Professionals (HCPs) education sessions – detailing learnings and experiences post PBS restriction change

4. BMS Medical Information resourcing to support HCPs off-label enquires, including sourcing of available evidence in the BMS database (data on file; BMS congress data and/or publications) and evidence from literature searches
5. BMS Medical Affairs support for any off-label HCP enquires, including scientific exchange to enable evidence-based discussions on the efficacy and safety of NIVO and IPI, including where there is no activity in tumours

These initiatives would occur in addition to the current QUM activities that the Sponsor undertakes to support the use of NIVO and IPI.

Furthermore, modifications to the PBS restriction wording may complement this QUM work. For example, the addition of a clinical criterion that specifies "*Prescribing with this drug should be informed by available clinical evidence and an assessment of the risk/benefit profile of treatment specific to each individual patient*" would act as a prompt to drive evidence-based prescribing of NIVO and IPI for unresectable advanced/metastatic cancer."

# 10 Forecast PBS usage and financial implications

10.1 The utilisation and financial estimates presented in the submission were examined by the Drug Utilisation Section.

10.2 The submission used a mixed model approach to estimate the financial implications associated with the proposed listings, including (1) current listings, (2) new proposed listings, (3) retreatment and (4) rare cancers.

**Current listings**

10.3 The financial estimates include eight currently listed PBS indications for either nivolumab monotherapy, nivolumab in combination with ipilimumab, nivolumab in combination with chemotherapy, or ipilimumab monotherapy. The submission presents projections of the current expenditure based on the PBS data provided by the Drug Utilisation Section to the sponsor. Among the listings, the submission assumes a 15% annual reduction for 2L NSCLC and 2L SCCHN. Other indications were projected based on linear growth.

**New proposed listings**

10.4 There are nine future indications in the proposal and of these, seven new epidemiological models are presented in this submission. The two remaining indications including first-line metastatic urothelial cancer and first-line oesophageal squamous cell carcinoma, use previously agreed financial estimates based on the November 2024 and March 2023 PBAC recommendations, respectively. The Drug Utilisation Section examined the structure of the epidemiological models and offered feedback to the sponsor at the pre-submission stage. Overall, the structure of the epidemiological models was considered reasonable and relevant suggested changes were addressed by the sponsor.

Eligible patients for each indication are predominantly derived based on the product of the incidence data for the populations sourced from the Australian Institute of Health and Welfare (AIHW) populations, assumptions for the eligibility criteria for each listing, treatment uptake assumptions and market share assumptions. The derivation of these cohorts are arithmetically appropriate.

10.5 It was noted that some indications require multiple dose regimens. The sponsor has presented a simplified single dose approach. The sponsor states that the dosing regimens were calculated by using the mean duration of treatment from the pivotal trials divided by a pre-specified dose. It is unclear how the pre-specified doses were determined and whether varying the dosing assumptions would have a significant impact on the overall cost on the PBS/RPBS and on the administration costs for the MBS.

10.6 It is understood that many of the current comparators for the proposed new listings are watchful waiting or chemotherapy. In the December 2023 submission, the sponsor proposed that other immunotherapy or targeted therapy may also be replaced by the proposed listings.

**Retreatment**

10.7 The submission estimates the impact of additional services for retreatment for eight indications (melanoma, NSCLC, RCC, gastro-oesophageal cancers, urothelial carcinoma, CRC, SCCHN and HCC).

10.8 The Drug Utilisation Section examined the structure of the retreatment model and provided feedback to the sponsor at the pre-submission stage which was considered in preparing the financial estimates for the submission (refer to Table 14 of the submission). The eligible patients for retreatment were primarily derived from either the most recent PBS service data or the first year estimates from various clinical trials. The submission projected a consistent retreatment population across the six years of the forward estimates.

10.9 The Secretariat noted that the submission included clinical trial data for RCC, CRC, SCCHN and HCC to derive the retreatment cohort. However, the associated indications are not PBS-listed. Including these indications in the estimates contributes approximately 50% of the treatable retreatment cohort.

10.10 The Drug Utilisation Section noted that nivolumab was only listed for NSCLC and urothelial carcinoma in August 2024. The submission estimated the service volumes for these indications using service volumes for August 2024 – March 2025, then divided by eight multiplied by 12 to give a full year and then multiplied by [redacted]% to reflect the estimated services once implemented into clinical practice. The submission considered that as the utilisation had not reached a steady peak, it was necessary for the prescription volumes to be artificially inflated to reach estimated peak values. The Drug Utilisation Section compared the submission's forecast to the financial estimates agreed with the Department of Finance, noting that the submission's estimates are within the previously agreed estimates (see Table 9).

**Table 9: Number of nivolumab prescriptions for NSCLC and urothelial cancer estimated for 2026 based on the previously agreed financial estimates model versus the submission forecast**

| Indication | Submission estimated | Department estimated at listing (2026) |
|---|---|---|
| NSCLC | [redacted]*[1] | [redacted][1] |
| Urothelial carcinoma | [redacted][1] | [redacted][1] |

*The sponsor also included an atezolizumab component for the retreatment
*The redacted values correspond to the following ranges:*
*1 500 to < 5,000*

### Rare cancers

10.11 To estimate the uptake of nivolumab for rare cancers under a broad listing, the sponsor engaged Omico, an organisation involved in the delivery of genomic cancer medicine clinical trials.

10.12 Omico created a refined rare cancer list, incorporating Australian Institute of Health (AIHW) classifications, RARECAREV2 classifications, and consideration of cases of Carcinoma of Unknown Primary (CUP). The submission considered that this data was more robust than the AIHW data which includes 49 indications ('Cancer Data in Australia 2024', Table S1a.1).

10.13 The pre-PBAC response confirmed that CUP was not included in the estimates. The sponsor noted it was difficult to accurately quantify this population and that it may be preferable to exclude and consider this as a source of uncertainty instead. The sponsor highlighted that this may result in an underestimate of the treatable population and the risk form this would be borne by the sponsor under the proposed RSA.

10.14 The Omico analysis excluded all cases deemed to have existing PBS-eligibility and identified suitability for IO based on:

- The presence of biomarkers that have a pan-tumour application (including TMB, MSI-H and dMMR).
- Assessment of specific histotypes with sufficient data indicating effectiveness in rare cancer populations.

10.15 The number of estimated patients with rare cancers eligible for treatment with nivolumab +/- ipilimumab in the advanced or metastatic setting are shown in Table 10.

**Table 10: Estimated patients with rare cancers treated with NIVO±IPI in the advanced or metastatic setting**

| Parameter | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 |
|---|---|---|---|---|---|---|
| Number of cases of rare cancers[1] | [redacted][1] | [redacted][1] | [redacted][1] | [redacted][1] | [redacted][1] | [redacted][1] |
| Proportion regional or metastatic[2] | 47.20% | 47.20% | 47.20% | 47.20% | 47.20% | 47.20% |
| Cancer subtype considered candidate for IO[3] | 51.64% | 51.64% | 51.64% | 51.64% | 51.64% | 51.64% |
| Treatment eligibility[4] | 18.52% | 18.52% | 18.52% | 18.52% | 18.52% | 18.52% |
| **Treated rare cancer patients** | [redacted][2] | [redacted][2] | [redacted][2] | [redacted][2] | [redacted][2] | [redacted][2] |

Sources:
[1] Forecast based on AIHW Cancer in Australia Data 2024, Table S1a.1. Accessed at: https://www.aihw.gov.au/getmedia/2bea39d6-4cb9-4fa7-815d-3bb56a795bb5/CDiA-2024-Book-1a-Cancer-incidence-age-standardised-rates-5-year-age-groups.xlsx
[2] De Heus et al. (2022).
[3] Rare cancer subtypes being considered a candidate for treatment with IO. Excludes indications where a PD-(L)1 treatment is available on the PBS and those not suitable for immunotherapy.
[4] Uptake rate based on the Omico clinico-genomic analysis.
*The redacted values correspond to the following ranges:*
*[1] 20,000 to < 30,000*
*[2] 500 to < 5,000*

10.16 At year 6, the submission estimated number of patients was 20,000 to < 30,000 and the net cost to the PBS and RPBS would be $> 1 billion (excluding RSA rebates).

# 11 PBAC Outcome

11.1 The PBAC deferred making a recommendation for an expanded listing of nivolumab and ipilimumab for unresectable advanced and metastatic cancer. The PBAC considered the proposal had addressed most of its expectations for a broad listing proposal but that a deferral would be appropriate to allow the sponsor to consider revisions to the RSA structure requested by the committee and give time for the sponsor to provide an updated proposal that aligns with these parameters.

11.2 The PBAC reaffirmed its December 2023 advice that a broad listing for nivolumab and ipilimumab would be appropriate with a Risk Sharing Arrangement (RSA) that provided confidence regarding total cost to Government and cost-effectiveness of a broad listing, and that a substantial price reduction versus the current PBS prices would likely be required and a cap on total expenditure.

**Proposed restriction and scope**

11.3 The PBAC supported the Secretariat's proposed amendments to the proposed restriction, including the inclusion of the 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.

11.4 The PBAC noted the sponsor requested an administrative advice be included on ipilimumab of:

> In the first few months after starting immunotherapy, a transient tumour flare may occur that may be mistaken as disease progression despite an overall positive response to treatment.

The PBAC noted recent listings for nivolumab and ipilimumab have not contained this note. It recalled the note was introduced when PD-(L)1 inhibitors were relatively new to the Australian market. Given there is now considerable experience in the use of these drugs in the Australian context, the note may no longer be required. The PBAC considered it would be appropriate to remove this advice in the proposed restriction for the broad listing and for the relevant existing listings for any other PD-(L)1 inhibitors.

11.5 The Secretariat noted some listings for ipilimumab where it is intended to be used in combination with nivolumab also contain the following administrative advice:

> Combination treatment with ipilimumab and nivolumab is associated with an increased incidence and severity of immune-related adverse reactions compared with monotherapy with these agents. Monitoring at least prior to each dose is recommended.

The PBAC did not consider this administrative advice would be required for the proposed listing.

11.6 The PBAC considered the proposed maximum amounts and repeats for the listing were appropriate.

11.7 The PBAC noted the word 'unresectable' was used in different contexts clinically and is not consistently defined in clinical literature. It considered the inclusion of 'unresectable' in the proposed indication may result in confusion as to the intent of the listing and unintentionally inhibit some patients' access to the medicines. The PBAC considered it may be appropriate to remove the word 'unresectable'. The PBAC also considered it appropriate to add the words 'immunotherapy sensitive'', given the expectation of use restricted to evidence-based indications. The PBAC asked the sponsor to consider this alternate wording, or wording to the same effect, in any updated proposals.

**Pricing**

11.8 The PBAC noted a single weighted price based on the PBS Benefits was proposed for the existing advanced/metastatic indications currently PBS listed over a recent 12-month period. The PBAC considered that while use of a weighted price was an acceptable approach, it may be relevant to consider the modelled utilisation over the forward years and an appropriate approach be negotiated with the Department should a positive recommendation be made.

11.9 The PBAC noted this weighted price would be applied to utilisation under the first tier of the proposed RSA and the cap for utilisation would be set based on extrapolated utilisation of the exiting listings. This was intended to effectively maintain the existing prices for current listings.

11.10 The PBAC reaffirmed its view that a cap on overall expenditure would be appropriate given the level of uncertainty in uptake and potential for leakage outside the intended populations.

11.11 The PBAC noted the proposal was to provide a [redacted]% discount overall through a two-tier rebate arrangement. The PBAC considered that nivolumab and ipilimumab were likely to be acceptably cost-effective in the identified additional populations eligible under a broad advanced and metastatic cancer listing, with a [redacted]% reduction in the current advanced/metastatic weighted prices.

**Financial and utilisation estimates**

11.12 The PBAC considered the time on treatment and estimated dosing for rare cancers in the financial estimates was likely over-estimated.

11.13 The PBAC noted there remained uncertainty in the financial estimates and agreed a risk sharing arrangement would be appropriate.

**Risk Sharing Arrangement**

11.14 The PBAC proposed that the RSA structure should be guided by the following:

- A two-tier subsidisation cap (SC) arrangement, where the rebate above SC1 delivers a price reduction for the additional population, while SC2 is intended to manage overall expenditure and mitigate use beyond the identified population.
- the utilisation and financial estimates provided for the currently listed indications as the basis for SC1.
- the discount ([redacted]%) for utilisation in the new extended population to be consolidated and provided as a single rebate above SC1. This would provide greater certainty in achieving the proposed cost-effective price for the broader population.
- an upper tier (SC2) that is based on total utilisation estimated in the submission (i.e. including the currently listed indications, future indications, IO retreatment and rare cancers as presented).
- a rebate of [redacted]% above SC2 to provide a cap on overall expenditure. It was noted the scope of the listing introduced several uncertainties regarding how prescriber behaviour may be affected by the availability of the broad listing for both the affected drugs and other PD-L1 inhibitors. Given the impact on utilisation remains unclear, the PBAC considered that a high level of rebate above the estimates would be required. As noted in paragraph 11.12, the estimates informing SC2 were likely over-estimated and represented assumptions at the upper threshold favourable to the sponsor.

11.15 The PBAC noted the pre-PBAC response argued against a [redacted]% reimbursement above subsidisation caps. The PBAC considered that where the sponsor is not in a position to put forward an offer of a rebate of [redacted]% above SC2, it could alternatively propose a structure as outlined below that would ensure the same net budget impact:

- Same approach to weighted price and utilisation for existing indications to derive SC1
- A [redacted]% rebate applied above SC1
- A new tier of rebate applied at an SC2 based on more conservative assumptions regarding treatment duration (e.g. up to a 50% reduction in these values)
- a lower than [redacted]% rebate (e.g. [redacted]%) above this threshold (SC2)
- a SC3 based on the submission's proposed estimates with a minor (less than [redacted]%) uplift to utilisation.
- a rebate approaching [redacted]% above SC3.

11.16 The PBAC considered that it would be appropriate for the Committee to review the RSA following a listing, to monitor the performance and any issues associated with the novel approach, including opportunity to review available clinical evidence to monitor comparative effectiveness and ensuring TGA approvals continue to be sought for new indications with available evidence within expected timeframes.

11.17 The PBAC considered that a review at two or three years post-listing would be appropriate. Where any matters arise that require more urgent review, these could be managed on an ad-hoc basis.

11.18 The PBAC acknowledged the sponsor's willingness to continue to engage on the RSA through its proposed RSA governance framework. The PBAC considered this framework may not be necessary if the RSA is structured in a way that acceptably controls the risk to Government, particularly where utilisation is greater than estimated.

**Impact on other listings and RSAs**

11.19 The PBAC noted that in creating a new RSA for a broad listing, nivolumab and ipilimumab would need to be removed from some existing shared RSAs (melanoma combined resected/unresectable; NSCLC; RCC; SCCHN; gastro-oesophageal combined with adjuvant). This matter would be negotiated with the Department in a post-PBAC process should a positive recommendation be made in the future.

**Quality use of medicines**

11.20 The PBAC considered there were potential QUM issues with a broad listing and considered that, if a recommendation was made to provide clinicians with discretion to use medicines in an evidence-based manner such as this proposal, it would be incumbent upon the sponsor and clinical community to ensure use remained appropriate and consistent with this intent.

11.21 The PBAC reiterated its expectation that prescribers would utilise any potential broad listing only in indications for which there is a reasonable expectation of a positive risk/benefit outcome for the patient, and that this was necessary to support the ongoing viability of the listing.

11.22 The PBAC welcomed the sponsor's proposed approach to educational and training resources and considered these would be crucial to support the ongoing functioning of the listing. The PBAC supported the proposed approach of maintaining resources on the evolving evidence supporting the efficacy and safety of nivolumab and ipilimumab in different indications, as well as to provide evidence on indications where there is insufficient evidence to demonstrating efficacy. The PBAC considered this would support clinicians in decision making in both whether to prescribe the medicines and in whether the use of the medicine should be subsidised by the Commonwealth or funded privately.

**Outcome:**
Deferred

# 12 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.

# 13 Sponsor's Comment

While disappointed that the PBAC has deferred a decision with regards to this submission to broaden the PBS listing for OPDIVO (nivolumab) and YERVOY (ipilimumab) at the July PBAC meeting, Bristol Myers Squibb Australia (BMSA) remains committed to working with the PBAC to navigate a prompt pathway to approval.

## Addendum to the July 2025 PBAC PSD:

# 4.02 NIVOLUMAB, Injection concentrate for I.V. infusion 40 mg in 4 mL, Injection concentrate for I.V. Infusion 100 mg in 10 mL, Opdivo®, IPILIMUMAB, Injection concentrate for I.V. infusion 50 mg in 10 mL, Injection concentrate for I.V. infusion 200 mg in 40 mL, Yervoy®, BRISTOL-MYERS SQUIBB AUSTRALIA PTY LTD.

## 14 Purpose of Submission

14.1 To consider a revised proposal from Bristol-Myers Squibb Australia (BMSA) for a multi-indication (broad) listing for nivolumab ± ipilimumab in advanced or metastatic cancers, addressing the issues raised by the PBAC in its July 2025 consideration.

## 15 Restriction

15.1 In July 2025, the PBAC considered the term 'unresectable' could be removed from the proposed restriction wording and replaced with the term 'immunotherapy sensitive' (paragraph 11.7).

15.2 In this revised proposal the sponsor accepted this change and provided updated proposed restrictions incorporating other recommended changes to the restrictions from the July 2025 PBAC outcome (paragraphs 11.3 - 11.7).

### *Nivolumab – proposed restriction*

| **Category/Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals | | | | |
|---|---|---|---|---|
| **MEDICINAL PRODUCT** | **PBS item code** | **Max. Amount** | **№.of Rpts** | **Manufacturer** |
| NIVOLUMAB<br>Injection | NEW (Public)<br>NEW (Private)<br>MP | 480 mg | 13 | Bristol-Myers Squibb Australia Pty Ltd |
| **Available brands** | | | | |
| Opdivo (nivolumab 40 mg/4 mL injection, 4 mL vial) | | | | |

| | |
|---|---|
| Opdivo (nivolumab 100 mg/10 mL injection, 4 mL vial) | |
| **Restriction Summary** [number – For. Dept. use] **/ Treatment of Concept:** [number – For. Dept. use]: **Authority Required (STREAMLINED)** | |
| This column – for Dept. use | **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 a maximum of 240 mg every two weeks or 480 mg every four weeks under a weight based or flat dosing regimen.* |
| | ***Administrative advice:*** *No increase in the maximum number of repeats may be authorised.* |
| | ***Administrative advice:*** *Special Pricing Arrangements apply.* |

### *Ipilimumab – proposed restriction*

| **Category/Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals | | | | |
|---|---|---|---|---|
| **MEDICINAL PRODUCT** | **PBS item code** | **Max. Amount** | **№.of Rpts** | **Manufacturer** |
| IPILIMUMAB Injection | NEW (Public) NEW (Private) MP | 360 mg | 4 | Bristol-Myers Squibb Australia Pty Ltd |
| **Available brands** | | | | |
| Yervoy (ipilimumab 50 mg/10 mL injection, 10 mL vial) Yervoy (ipilimumab 200 mg/40 mL injection, 40 mL vial) | | | | |
| **Restriction Summary** [number – For. Dept. use] **/ Treatment of Concept:** [number – For. Dept. use]: **Authority Required (STREAMLINED)** | | | | |
| This column – for Dept. use | **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:*** *The stated maximum amount in this listing is 360mg however alternative dosing schedules may be prescribed in a quantity up to this amount, but need not be this amount for every cancer type.* | | | |
| | ***Administrative advice:*** *No increase in the maximum number of repeats may be authorised.* | | | |
| | ***Administrative advice:*** *Special Pricing Arrangements apply.* | | | |

## 16 Sources of uncertainty in utilisation estimates

16.1 In the proposal, the sponsor argued there remained sources of uncertainty in the utilisation estimates that may result in under-estimation of utilisation. The PBAC previously considered there was likely to be an over-estimate of patient and script numbers, primarily owing to the time-on-treatment and dosing in rare cancers

calculations (paragraph 11.12). The revised proposal did not directly address these areas of potential over-estimation.

## *Changes to the treatment paradigm due to a broad listing*

16.2 The proposal stated it anticipated scenarios where clinician decision making could be impacted if nivolumab and ipilimumab were listed under the proposal. It identified two key examples, provided in Table 11.

**Table 11: Examples of potential prescribing practice changes under a broad listing**

| Indication | Relevant drug | Current funding status | Implications |
|---|---|---|---|
| Malignant melanoma | Opdualag (nivolumab + relatlimab) | PBS listed for Stage III or Stage IV malignant melanoma. Patient must not have received prior treatment with ipilimumab or a PD-1 (programmed cell death-1) inhibitor. | Under a broad listing, patients with malignant melanoma will be able to access NIVO+IPI in the 2L setting, which was not previously possible.<br><br>As the Opdualag listing is unchanged, utilisation would likely increase in the 1L setting as this represents the only point in the treatment pathway where Opdualag is funded. |
| RCC | Lenvima (lenvatinib) | PBS listed for previously untreated intermediate-poor risk Stage IV clear cell variant RCC in combination with Keytruda (pembrolizumab). | Currently, patients are eligible to receive either PD-1+VEGF TKI or PD-1+CTLA-4 (NIVO+IPI) combination therapy in the 1L setting only, due to PBS restrictions.<br><br>Under a broad listing, access to PD-1+CTLA-4 (NIVO+IPI) would not be restricted by line of therapy – this may influence treatment choice towards PD-1+VEGF TKI combination therapy in the 1L setting, as this would not be available for patients in the 2L+ setting. |

Source: Table 4, pp11-12 of the proposal main body
CTLA-4 = cytotoxic T-lymphocyte-associated antigen 4; NIVO+IPI = nivolumab + ipilimumab; PBS = Pharmaceutical Benefits Scheme; PD-1 = programmed cell death-1; RCC = renal cell carcinoma; TKI = tyrosine kinase inhibitor; VEGF = vascular endothelial growth factor; 1L = first line; 2L = second line.

16.3 The proposal also noted there were positive PBAC recommendations that had not yet been implemented that may have flow on impacts to the utilisation of other PD-(L)1 inhibitors.

16.4 It highlighted the positive recommendation for pembrolizumab + enfortumab vedotin for 1L urothelial carcinoma and the deferral of zolbetuximab for 1L upper gastro-intestinal cancers.

## *Changes to restriction wording*

16.5 The sponsor noted the replacement of the word ‘unresectable’ with ‘immunotherapy sensitive’ may affect prescribing behaviour and create a risk of utilisation outside the intended population.

16.6 The sponsor noted the definition of ‘advanced’ in the context of advanced or metastatic cancer is subject to a degree of clinical interpretation.

16.7 The sponsor noted two examples where utilisation may occur outside the populations modelled in the proposal:

- Patients with advanced non-small cell lung cancer may be eligible for treatment using the CheckMate77T protocol (that is, neoadjuvant treatment with NIVO+chemo followed by adjuvant NIVO).
- Patients with locally advanced mismatch repair–deficient colon cancer (dMMR CRC) may be treated under the NICHE2 protocol (neoadjuvant NIVO+IPI).

16.8 The sponsor therefore considered this wording change may result in the financial estimates being under-estimated. However, the sponsor advised it was willing to accept this financial risk and did not seek changes to the financial estimates on this account.

16.9 The sponsor provided examples of indications in which nivolumab and/or ipilimumab could be prescribed under the proposed listing that were not accounted for in the model. The sponsor noted these were not accounted for largely owing to the difficulty in creating a robust approach to extrapolating current expenditure to cover possible expanded usage. The examples provided were:

- Non-clear cell renal cell carcinoma (nccRCC).
- No specification of performance status in the proposed PBS restrictions – applicable to all cancer types.
- Treatment must not exceed a maximum total of 24 months in a lifetime for this condition – deviation from existing mesothelioma (NIVO+IPI), NSCLC (NIVO only), and UGI listings (NIVO only).
- No limitation on maximum doses for IPI across cancer types.
- Ability for patients to receive treatment with NIVO±IPI twice in the advanced/metastatic setting – applicable to all cancer types.

16.10 The sponsor argued these points further supported its claim that utilisation would be under-estimated but that it was willing to accept this financial risk and proceed with the estimates as provided.

### *Other PD-(L)1 Inhibitors*

16.11 The sponsor noted there were some advanced and metastatic cancer indications for which other PD-(L)1 inhibitors are registered with the TGA and for which nivolumab and ipilimumab are not registered.

16.12 The sponsor indicated there was potential for leakage in use for these indications if nivolumab and ipilimumab were the only drugs available under a broad listing.

16.13 The sponsor noted usage in these additional indications (shaded orange in Table 12) was not modelled in the financial estimates. The sponsor noted this as a potential

source of under-estimation in the estimates but advised it was willing to accept this financial risk and did not seek changes to the financial estimates on this account.

**Table 12: Current PBS listings for PD-(L)1 inhibitors**

| | NIVO±IPI | PEMBRO | ATEZO | DURVA | TISLE | CEMI | DOSTAR | AVE |
|---|---|---|---|---|---|---|---|---|
| 1L RCC | ✓ | ✓[1] | | | | | | |
| 2L RCC | ✓ | | | | | | | |
| Metastatic melanoma | ✓ | ✓ | | | | | | |
| 1L NSCLC | ✓ | ✓ | ✓[2] | | | ✓ | | |
| 2L NSCLC | ✓ | | ✓ | | | | | |
| 2L SCCHN | ✓ | | | | | | | |
| Mesothelioma | ✓ | | | | | | | |
| UGI | ✓ | | | | ✓ | | | |
| 1L mUC | ✓ | | | | | | | |
| 1L CRC dMMR | | ✓ | | | | | | |
| 1L HCC | | | ✓[2] | | | | | |
| 3L cHL | | ✓ | | | | | | |
| 2L urothelial | | ✓ | | | | | | |
| Maintenance mUC | | | | | | | | ✓ |
| 1L SCCHN | | ✓ | | | | | | |
| TNBC | | ✓ | | | | | | |
| Cervical | | ✓ | | | | | | |
| Endometrial | | ✓[1] | | ✓ | | | ✓ | |
| Biliary tract | | | | ✓ | | | | |
| Merkel cell | | | | | | | | ✓ |
| Cutaneous SCC | | | | | | ✓ | | |
| Stage III NSCLC | | | | ✓ | | | | |
| SCLC | | | ✓ | ✓ | | | | |
| PMBCL | | ✓ | | | | | | |

Source: Table 3, p10 of the proposal main body

[1] Treatment in combination with lenvatinib.

[2] Treatment in combination with bevacizumab.

ATEZO = atezolizumab; AVE = avelumab; CEMI = cemiplimab; cHL = classical Hodgkin's lymphoma; CRC = colorectal cancer; dMMR = mismatch repair–deficient; DOSTAR = dostarlimab; DURVA = durvalumab; HCC = hepatocellular carcinoma; IPI = ipilimumab; mUC = metastatic urothelial carcinoma; NIVO = nivolumab; NSCLC = non-small cell lung cancer; PEMBRO = pembrolizumab; PMBCL = primary mediastinal B-cell lymphoma; RCC = renal cell carcinoma; SCC = squamous cell carcinoma; SCCHN = squamous cell carcinoma of the head and neck; SCLC = small cell lung cancer; TISLE = tislelizumab; TNBC = triple negative breast cancer; UGI = upper gastro-intestinal; 1L = first line; 2L = second line; 3L = third line.

Notes: Only advanced/metastatic indications included. Some regimens may be used in combination with chemotherapy. As of August 2025.

# 17 Revised Pricing and RSA structure

## *Weighted Price*

17.1 The proposal used the same approach to generating a weighted price for its existing PBS listed indications with minor updates since the July submission.

17.2 In the revised financial model, the proposal updated the weighted price calculations using the most recent data available (PBS Benefits, July 2024 to June 2025).

17.3 The sponsor noted the indication of nivolumab (in combination with chemotherapy) for metastatic urothelial carcinoma was listed on the PBS on 1 August 2025. As there

was not utilisation data available at the time of resubmission, this indication was retained in the utilisation above SC1 and not incorporated into the weighted price.

17.4 The updated weighted prices calculated in the resubmission were nivolumab 100 mg price per vial of $[redacted] and ipilimumab 50 mg price per vial of $[redacted].

### *Revised Risk Sharing Arrangement*

17.5 The proposal used the same approach to estimating utilisation for existing advanced and metastatic PBS-listed indications [redacted].

17.6 The proposal applied the PBAC's recommended rebate of 40% from the weighted price for utilisation above [redacted].

17.7 The sponsor did not accept the PBAC's proposed 100% rebate for utilisation above the total forecast utilisation estimates.

17.8 Instead, the sponsor proposed setting [redacted]

17.9 The sponsor acknowledged the PBAC's request for a higher level of rebate beyond the forecast utilisation and that the PBAC had considered a 100% rebate appropriate. However, the sponsor proposed that setting [redacted] would more equitably shared the financial risk and support viability of the listing.

17.10 The sponsor argued that, as it had identified a number of potential instances of under-estimation [redacted] the financial risk would remain appropriately contained by the RSA with a rebate lower than a 100% rebate for utilisation above SC2.

17.11 The sponsor also considered it would retain [redacted]

17.12 A comparison of the effective pricing offers from the July 2025 proposal and this revised proposal are provided in Table 13.

**Table 13: Comparison of (effective) AEMP for July 2025 and September 2025 proposals**

| July 2025 Proposal | | | | | September 2025 Revised Proposal | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Nivolumab (Opdivo)** | **Price per 100 mg vial** | **Price q4w** | **Ipilimumab (Yervoy)** | **Price per 50 mg vial** | **Nivolumab (Opdivo)** | **Price per 100 mg vial** | **Price q4w** | **Ipilimumab (Yervoy)** | **Price per 50 mg vial** |
| **Weighted Price** | $[redacted] | $[redacted] | **Weighted Price** | $[redacted] | **Weighted Price** | $[redacted] | $[redacted] | **Weighted Price** | $[redacted] |
| **Between SC1 and SC2 (rebate [redacted]%)** | $[redacted] | $[redacted] | **Between SC1 and SC2 (rebate [redacted]%)** | $[redacted] | **Between SC1 and SC2 (rebate [redacted]%)** | $[redacted] | $[redacted] | **Between SC1 and SC2 (rebate [redacted]%)** | $[redacted] |
| **Above SC2 (rebate [redacted]%)** | $[redacted] | $[redacted] | **Above SC2 (rebate [redacted]%)** | $[redacted] | **Above SC2 (rebate [redacted]%)** | $[redacted] | $[redacted] | **Above SC2 (rebate [redacted]%)** | $[redacted] |

Source: July 2025 and September 2025 submission documents
SC1 = subsidisation cap 1; SC2 = subsidisation cap 2; q4w = every 4 weeks

### *Financial Impact*

17.13 The overall financial impact of the proposal was > $1 billion ($[redacted]) over the forward estimates (see Table 14), compared to > $1 billion (> $1 billion[redacted] of the July 2025 proposal (see Table 5).

17.14 As the total financial impact includes expenditure for existing PBS-listed indications that would otherwise have been incurred, the cost of use in the extended indications and treatment settings is captured by use beyond SC1. The total financial impact for use above SC1 across the forward estimates, after the proposed rebates, was $100 million to < $200 million.

**Table 14: Estimated total drug cost for nivolumab and ipilimumab to PBS/RPBS (effective PBS/RPBS, with RSA structure)**

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 | Total |
|---|---|---|---|---|---|---|---|
| Estimated cost to PBS/RPBS* (less copayments) | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][1] | $[redacted][11] |
| **Proposed subsidisation caps** | | | | | | | |
| SC1 | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| SC2 | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| **Estimated RSA rebate** | | | | | | | |
| SC1 rebate | $[redacted][2] | $[redacted][2] | $[redacted][2] | $[redacted][2] | $[redacted][2] | $[redacted][2] | $[redacted][3] |
| SC2 rebate | $[redacted][4] | $[redacted][5] | $[redacted][5] | $[redacted][5] | $[redacted][3] | $[redacted][3] | $[redacted][6] |
| Total RSA rebate | $[redacted][3] | $[redacted][3] | $[redacted][7] | $[redacted][7] | $[redacted][7] | $[redacted][7] | $[redacted][8] |
| Estimated cost after RSA rebates | $[redacted][9] | $[redacted][9] | $[redacted][9] | $[redacted][9] | $[redacted][9] | $[redacted][9] | $[redacted][1] |
| Cost attributed to use beyond SC1** | $[redacted][10] | $[redacted][10] | $[redacted][10] | $[redacted][10] | $[redacted][10] | $[redacted][10] | $[redacted][7] |

Source: "Summary & inputs" tab, Attachment 1 - BMSA-NIVO+IPI Broad Listing Workbook September 2025.
PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; RSA = Risk Sharing Arrangement; SC1 = subsidisation cap 1; SC2 = subsidisation cap 2.
*Cost prior to any rebates
**After rebates
*The redacted values correspond to the following ranges:*
[1] *$300 million to < $400 million*
[2] *$10 million to < $20 million*
[3] *$90 million to < $100 million*
[4] *$70 million to < $80 million*
[5] *$80 million to < $90 million*
[6] *$500 million to < $600 million*
[7] *$100 million to < $200 million*
[8] *$600 million to < $700 million*
[9] *$200 million to < $300 million*
[10] *$30 million to < $40 million*
[11] *> $1 billion*

## 18 Review and Governance Framework

18.1 The sponsor acknowledged the PBAC's view that a governance framework may not be necessary if the RSA is structured in a way that acceptably controls the risk to Government, particularly where utilisation is greater than estimated.

18.2 However, the sponsor considered a 3-year review period would be appropriate to support the listing. It noted the additional rebates offered in the revised proposal which it considered extensively minimised the financial risk to Government under the proposed listing.

18.3 The sponsor sought that this 3-yearly review would allow both the sponsor and the Department to review, discuss and negotiate any potential changes to the Deed conditions (including subsidisation cap amounts). However, the sponsor did not propose any specific thresholds or actions associated with the caps that should be included in such an arrangement.

18.4 The sponsor noted its expectation for flow-on implications for some existing shared RSAs that apply to nivolumab and ipilimumab (as referenced in paragraph 7.13 of the PBAC minutes July 2025). It also noted that new cap arrangements for this broad listing would be required. The PBAC noted that the implementation arrangements for RSAs would be administered by the Department per its usual practices.

# 19 Other matters

## *Interim Patient Access Program*

19.1 The sponsor noted, should this proposal be recommended, it would implement a patient access program (PAP) in the intervening period between the positive recommendation and implementation of the listing. This program would provide access for patients with first line CRC MSI-H and access to the program would be more restricted than the proposed PBS restriction wording.

19.2 The sponsor anticipated that there will be approximately [redacted] patients per month enrolled in the PAP. The sponsor requested that these patients are accurately captured in financial estimates used to set SC2 (i.e. to result in an increase to where SC2 is applied in the first year of listing) and be grandfathered to PBS-subsidised therapy at time of PBS listing. The PBAC noted the proposed restriction wording would not disadvantage patients who had received prior therapy under a patient access program provided they otherwise met the restriction criteria.

## *Quality Use of Medicines*

19.3 The sponsor reiterated its commitment to working with healthcare professionals and professional bodies to support appropriate use of the broad listing, if implemented.

19.4 The sponsor noted it would undertake quality use of medicine activities and education with representative bodies, particularly in the early period of a potential PBS listing. The sponsor considered it would be helpful for the PBAC to provide a statement on the intent of the listing to support this work.

# 20 PBAC Outcome

20.1 The PBAC recommended, under section 101(3) of the Act, a change to the circumstances under which nivolumab and ipilimumab are made available as pharmaceutical benefits under Part VII of the Act to enable their use for advanced and metastatic cancers. The PBAC is satisfied that the listings will provide, for some patients, a significant improvement in efficacy over alternate therapies (or watchful

waiting). The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, the listing would be cost-effective within the context of an RSA.

20.2 The PBAC considered the proposed restriction criteria were appropriate. The PBAC noted the listing was restricted to advanced and metastatic cancers and therefore did not include early-stage cancers. It noted the listing would provide clinicians with appropriate discretion to treat patients with these cancers based on the best available evidence.

20.3 The PBAC considered the proposed approach was acceptable for calculating the weighted price using the most recent PBS expenditure data for advanced/metastatic indications. The PBAC noted under the proposed Risk Sharing Arrangement, the weighted price would be applied to utilisation under the first tier of the proposed RSA and the cap for utilisation would be set based on extrapolated utilisation of the existing listings. This was intended to effectively maintain the existing prices for current listings. The PBAC consider this was appropriate.

20.4 The PBAC noted the sponsor proposed a [redacted]% rebate for utilisation between the first tier and second tiers of the RSA, which would represent utilisation in the extended indications and treatment scenarios. The PBAC considered this was appropriate.

20.5 The PBAC recalled it had considered a total cap on expenditure would be appropriate for utilisation beyond the total estimated utilisation and that it had acknowledged there was uncertainty in the estimates. While the PBAC had identified areas of potential over-estimation in the estimates in its July 2025 consideration, it also noted the sponsor had identified areas of potential under-estimation in the current proposal.

20.6 On balance, the PBAC supported the sponsor's proposal to apply a [redacted]% rebate for utilisation beyond SC2, which was set once expenditure above SC1 reached $[redacted]. The PBAC noted SC2 was below the total estimated utilisation. The PBAC considered there would be a reduction in expenditure within the total estimated utilisation through this approach that would offset the application of a 90% rebate beyond the estimated utilisation.

20.7 The PBAC considered the medicines would be cost-effective across the extended circumstances with these rebates applied and that the financial risk to Government was sufficiently contained by the structure of the RSA. Given this, the PBAC did not consider that the RSA would require a governance framework.

20.8 The PBAC considered it would be appropriate for the Department to prepare a review of the utilisation of the listing three years after implementation. The purpose of this review would be to assess whether the medicines were being used consistent with the intention of the listing and that utilisation was for indications where there was a reasonable expectation of clinical benefit. The PBAC noted that if there were significant utilisation above the estimates or indicators of high levels of inappropriate

prescribing under the listing at that time, it may be necessary to make amendments to the restriction wording or authority level to address this.

20.9 The PBAC noted the sponsor's request to include up to [redacted] patients per month in the population between SC1 and SC2 to accommodate grandfathering patients who access nivolumab and ipilimumab under a proposed patient access program for CRC MSI-H. The PBAC noted the revised proposal had modelled the CRC population using the same market share approach that it considered in a separate submission for this indication in July 2025. The PBAC recalled it had considered these to be over-estimated and so it was likely these additional patients would be captured under the proposed estimates. The PBAC noted that the 2026 incident population had been included in the model and so it would not be appropriate to grandfather patients in the patient access program beyond 2025. On these bases, the PBAC did not support a further increase to the patient numbers modelled in the financial estimates.

20.10 The PBAC reiterated its support for the sponsor's proposed quality use of medicines educational activities and the importance of engagement from prescribers in ensuring the medicines were used under the listing as intended. It considered this would be crucial in supporting the listing and ensuring the medicines were utilised only where there was a reasonable expectation of benefit for the patient.

20.11 The PBAC noted as this had received a positive recommendation it was not eligible for an independent review.

**Outcome:**
Recommended

# 21 Recommended listing

21.1 Add the following new listing and restriction to replace all current listings for nivolumab across all PBS indications in the metastatic or advanced settings:

| **MEDICINAL PRODUCT Form** | **PBS item code** | **Max. Amount** | **№.of Rpts** |
|---|---|---|---|
| NIVOLUMAB Injection | NEW (HS)<br>NEW (HB) | 480mg | 13 |
| **Available brands** | | | |
| Opdivo<br>(nivolumab 40 mg/4 mL injection, 4 mL vial) | | | |
| Opdivo<br>(nivolumab 100 mg/10 mL injection, 10 mL vial) | | | |
| | | | |
| **Restriction Summary [new1] / Treatment of Concept: [new1A]** | | | |
| **Concept ID** (for internal Dept. use) | **Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals | | |
| | **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**<br>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. |
| | **Administrative Advice:** No increase in the maximum number of repeats may be authorised. |
| | **Administrative advice:** Special Pricing Arrangements apply. |

21.2 Add the following new listing and restriction to replace all current listings for ipilimumab across all PBS indications in the metastatic or advanced settings:

| **MEDICINAL PRODUCT**<br>**Form** | **PBS item code** | **Max. Amount** | **№.of Rpts** |
|---|---|---|---|
| IPILIMUMAB Injection | NEW (HS)<br>NEW (HB) | 360mg | 4 |
| **Available brands** | | | |
| Yervoy<br>(ipilimumab 50 mg/10 mL injection, 10 mL vial) | | | |
| Yervoy<br>(ipilimumab 200 mg/10 mL injection, 40 mL vial) | | | |
| | | | |
| **Restriction Summary [new2] / Treatment of Concept: [new2A]** | | | |
| **Concept ID**<br>(for internal Dept. use) | **Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals | | |
| | **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:** The stated maximum amount in this listing is 360mg however alternative dosing schedules may be prescribed in a quantity up to this amount, but need not be this amount for every cancer type. | | |
| | **Administrative Advice:** No increase in the maximum number of repeats may be authorised. | | |
| | **Administrative advice:** Special Pricing Arrangements apply. | | |

# 22 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.

# 23 Sponsor's Comment

Bristol Myers Squibb Australia (BMSA) is pleased that our submission to broaden the Pharmaceutical Benefits Scheme (PBS) listing for Opdivo® (nivolumab) and Yervoy® (ipilimumab) has been recommended by the PBAC. We look forward to working with the Department of Health, Disability and Ageing and the Minister of Health to expand access and improve equity to immunotherapy treatment for Australian patients.