

**5.25 PEMBROLIZUMAB
concentrated injection, 100 mg
Keytruda[®],
Merck Sharp and Dohme Australia Pty Ltd.**

***Corrigendum** Replace the November 2016 Public Summary Document for 5.25 pembrolizumab with the following revised minutes (7.1 recommended listing is revised for correct repeats).*

1 Purpose of Application

- 1.1 The minor submission requested the listing of a new 100 mg strength of pembrolizumab as a concentrated injection, with the same indications and dosing regimen as for the current PBS listing of the 50 mg powder for injection.

2 Requested listing

- 2.1 The submission requested the same restriction as for the currently listed pembrolizumab 50 mg powder for injection.

| Name, Restriction, Manner of administration and form | Max. Amt | No.of Rpts | Dispensed Price for Max. Qty | Proprietary Manufacturer | Name and |
|---|-------------|---------------|---|-----------------------------|---|
| PEMBROLIZUMAB Concentrated injection, 100 mg | 240 mg | 7 | Public: \$11,233.22 Private: \$11,427.40 | Keytruda [®] | Merck, Sharp & Dohme Australia Pty. Ltd. |

3 Background

- 3.1 The 100 mg concentrated injection presentation of pembrolizumab was registered in the ARTG on 8 March 2016 as monotherapy for the treatment of unresectable or metastatic melanoma in adults. This is consistent with the PBS restriction for the currently listed 50 mg powder for injection.

4 Clinical place for the proposed therapy

- 4.1 The submission indicated that the 100 mg concentrated injection would be used as an alternative to the currently listed 50 mg powder in order to make up the current dosing regimen for the treatment of unresectable or metastatic melanoma, which is 2 mg/kg every three weeks.

5 Consideration of the evidence

Sponsor hearing

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

Consumer comments

5.2 The PBAC noted that no comments relating to this item were received via the Consumer Comments facility on the PBS website. The PBAC also noted the input from the Assistant Director of Pharmacy-Cancer Services, Princess Alexandra Hospital that outlined the potential efficiencies that could be gained through the use of pembrolizumab 100 mg concentrated injection.

Clinical trials

5.3 As a minor submission, no clinical trials were presented in the submission.

Economic analysis

5.4 As a minor submission, there was no economic comparison presented.

Estimated PBS usage & financial implications

5.5 The minor submission estimated there to be no financial implications to the PBS as the 100 mg concentrated injection will substitute for the currently listed 50 mg powder for injection. The PBAC considered that this was reasonable and noted that Risk Share Arrangement is currently in place for pembrolizumab for the treatment of unresectable or metastatic melanoma, and if recommended, the 100 mg formulation will be included in this arrangement.

5.6 Recent trials of pembrolizumab have adopted a fixed dose of 200 mg every three weeks rather than 2 mg/kg every three weeks, which is likely to translate gradually into clinical practice across cancer indications. The PBAC noted the pre-PBAC response (pg 3) confirmed that the dosing regimen would be unchanged, and that any change to the dosing regimen would be the subject of a separate submission.

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

6 PBAC Outcome

6.1 The PBAC recommended the listing of pembrolizumab 100 mg concentrated injection as a new form, and under the same conditions, as the currently PBS-listed pembrolizumab 50 mg powder for infusion for the treatment of metastatic melanoma.

6.2 The PBAC noted that pembrolizumab 100 mg concentrated injection would be included in the current Risk Sharing Arrangement for pembrolizumab for the treatment of metastatic melanoma, and that the cost per patient would not increase as a result of this listing.

6.3 The PBAC considered that there would be no financial impact to the PBS as a result

of this listing as pembrolizumab 100 mg concentrated injection would be listed at the same price per mg as the currently listed form of pembrolizumab, and the cost per patient is capped under the Deed of Agreement.

- 6.4 The PBAC noted that this submission is not eligible for an Independent Review as it is a form of a currently listed drug.

Outcome:

Recommended

7 Recommended listing

- 7.1 Add new item:

Initial treatment 1

| Name, Restriction, Manner of administration and form | Max. Amt. | No. of Rpts | Proprietary Name and Manufacturer |
|--|-----------|-------------|--|
| PEMBROLIZUMAB Concentrated injection, 100 mg | 240 mg | 5 | Keytruda® Merck, Sharp & Dohme Australia Pty. Ltd. |

| | |
|------------------------------------|--|
| Category / Program | Section 100 – Efficient Funding of Chemotherapy |
| Prescriber type: | <input checked="" type="checkbox"/> Medical Practitioners |
| PBS Indication: | Unresectable Stage III or Stage IV malignant melanoma |
| Treatment phase: | Initial treatment 1 |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - Streamlined |
| Clinical criteria: | <p>The condition must be positive for a BRAF V600 mutation, AND The condition must have progressed following treatment with a BRAF inhibitor (with or without a MEK inhibitor) unless contraindicated or not tolerated according to the TGA approved Product Information, AND Patient must not have received prior treatment with ipilimumab or a PD-1 (programmed cell death-1) inhibitor for this condition, AND The treatment must be the sole PBS-subsidised therapy for this condition, AND The treatment must not exceed a total of 6 doses at a maximum dose of 2 mg per kg every 3 weeks.</p> <p>The patient's body weight must be documented in the patient's medical records at the time treatment is initiated.</p> |
| Prescriber Instruction | <p>Note In the first few months after start of immunotherapy, some patients can have a transient tumour flare with subsequent disease response. When progression is suspected, this should be confirmed through a confirmatory scan, taken at least 4 weeks later</p> |

Initial treatment 2

| Name, Restriction, Manner of administration and form | Max. Amt. | No. of Rpts | Proprietary Name and Manufacturer |
|---|--------------|----------------|--|
| PEMBROLIZUMAB Concentrated injection, 100 mg | 240 mg | 5 | Keytruda® Merck, Sharp & Dohme Australia Pty. Ltd. |

| | |
|------------------------------------|---|
| Category / Program | Section 100 – Efficient Funding of Chemotherapy |
| Prescriber type: | <input checked="" type="checkbox"/> Medical Practitioners |
| PBS Indication: | Unresectable Stage III or Stage IV malignant melanoma |
| Treatment phase: | Initial treatment 2 |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - Streamlined |
| Clinical criteria: | The condition must be negative for a BRAF V600 mutation, AND Patient must not have received prior treatment with ipilimumab or a PD-1 (programmed cell death-1) inhibitor for this condition, AND The treatment must be the sole PBS-subsidised therapy for this condition, AND The treatment must not exceed a total of 6 doses at a maximum dose of 2 mg per kg every 3 weeks. The patient's body weight must be documented in the patient's medical records at the time treatment is initiated. |
| Prescriber Instruction | Note In the first few months after start of immunotherapy, some patients can have a transient tumour flare with subsequent disease response. When progression is suspected, this should be confirmed through a confirmatory scan, taken at least 4 weeks later |

Grandfathering treatment 1

| Name, Restriction, Manner of administration and form | Max. Amt. | No. of Rpts | Proprietary Name and Manufacturer |
|--|-----------|-------------|--|
| PEMBROLIZUMAB Concentrated injection, 100 mg | 240 mg | 5 | Keytruda® Merck, Sharp & Dohme Australia Pty. Ltd. |

| | |
|------------------------------------|--|
| Category / Program | Section 100 – Efficient Funding of Chemotherapy |
| Prescriber type: | <input checked="" type="checkbox"/> Medical Practitioners |
| PBS Indication: | Unresectable Stage III or Stage IV malignant melanoma |
| Treatment phase: | Grandfathering treatment 1 |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - Streamlined |
| Clinical criteria: | The condition must be positive for a BRAF V600 mutation, AND The condition must have progressed following treatment with a BRAF inhibitor (with or without a MEK inhibitor) unless contraindicated or not tolerated according to the TGA approved Product Information, AND Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to 1 September 2015, AND Patient must not have received prior treatment with ipilimumab or any other PD-1 (programmed cell death-1) inhibitor for this condition, AND Patient must have stable or responding disease, AND The treatment must be the sole PBS-subsidised therapy for this condition, AND The treatment must not exceed a maximum dose of 2 mg per kg every 3 weeks. |

Grandfathering treatment 2

| Name, Restriction, Manner of administration and form | Max. Amt. | No. of Rpts | Proprietary Name and Manufacturer |
|--|-----------|-------------|--|
| PEMBROLIZUMAB Concentrated injection, 100 mg | 240 mg | 5 | Keytruda® Merck, Sharp & Dohme Australia Pty. Ltd. |

| | |
|------------------------------------|---|
| Category / Program | Section 100 – Efficient Funding of Chemotherapy |
| Prescriber type: | <input checked="" type="checkbox"/> Medical Practitioners |
| PBS Indication: | Unresectable Stage III or Stage IV malignant melanoma |
| Treatment phase: | Grandfathering treatment 2 |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - Streamlined |
| Clinical criteria: | The condition must be negative for a BRAF V600 mutation, AND Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to 1 September 2015, AND Patient must not have received prior treatment with ipilimumab or any other PD-1 (programmed cell death-1) inhibitor for this condition, |

| | |
|--|---|
| | AND Patient must have stable or responding disease, AND The treatment must be the sole PBS-subsidised therapy for this condition, AND The treatment must not exceed a maximum dose of 2 mg per kg every 3 weeks. |
|--|---|

Continuing treatment

| Name, Restriction, Manner of administration and form | Max. Amt. | No. of Rpts | Proprietary Name and Manufacturer |
|--|-----------|-------------|--|
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| | |
|------------------------------------|--|
| Category / Program | Section 100 – Efficient Funding of Chemotherapy |
| Prescriber type: | <input checked="" type="checkbox"/> Medical Practitioners |
| PBS Indication: | Unresectable Stage III or Stage IV malignant melanoma |
| Treatment phase: | Continuing treatment |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - Streamlined |
| 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, AND The treatment must not exceed a maximum dose of 2 mg per kg every 3 weeks. |

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

The sponsor had no comment.