

**4.03 VORINOSTAT
capsule, 100 mg,
Zolinza[®], Merck Sharp & Dohme (Australia) Pty Ltd**

1 Purpose of Application

- 1.1 The minor resubmission provided an updated proposed restriction, patient numbers and financial estimates, and a risk sharing arrangement proposal in response to the PBAC November 2016 deferral of an application to list vorinostat for cutaneous T-cell lymphoma (CTCL).

2 Requested listing

- 2.1 The submission proposed that the restriction be consistent with the secretariat proposed wording from the November 2016 PBAC meeting. However the submission did not include additional amendments recommended by the PBAC (vorinostat Public Summary Document (PSD), November 2016, paragraphs 2.7 and 7.10); these have been indicated below in italics for additions and strikethrough for deletions. An abridged version of the proposed listing, which omits the Administrative Advice, including the notes that no increase to the maximum quantity or repeats will be authorised, is presented.

Public Summary Document – March 2017 PBAC Meeting

Name, Restriction, Manner of administration and form	Max. Qty. (units)	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
VORINOSTAT vorinostat 100 mg capsule, 120	120	Initial therapy: 2 Continuing therapy: 1	\$ [REDACTED]	Zolinza® Merck Sharp & Dohme (Australia) Pty Ltd

Category / Program	General Schedule
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Cutaneous T-cell lymphoma
PBS Indication:	Cutaneous T-cell lymphoma
Treatment phase:	Initial treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Clinical criteria:	The treatment must be for curative intent, AND Patient must have received systemic treatment with chemotherapy curative intent chemotherapy, AND Patient must demonstrate relapsed or chemotherapy-refractory disease, AND Patient must be ineligible for a stem cell transplantation, AND The treatment must be the sole PBS-subsidised therapy treatment for this condition.
Prescriber Instructions	Applications for authorisation of initial treatment must be in writing and must include: (a) a completed authority prescription form; and (b) a completed <i>cutaneous T-cell lymphoma</i> (CTCL) vorinostat PBS Authority Application - Supporting Information Form [to be determined] which includes the following: (i) A copy of the histology report; with the histological diagnosis of relapsed or chemotherapy refractory cutaneous T-cell lymphoma; (ii) a declaration of whether the patient's disease is relapsed or refractory, and the date and means by which the patient's disease was assessed as being relapsed or refractory; (iii) details of prior <i>chemotherapy</i> treatment including name(s) of drug(s) and date of most recent treatment cycle; and (iv) a declaration of the patient's ineligibility for stem cell transplant, and (v) a signed patient acknowledgement.

Treatment phase:	Continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must not have progressive disease while receiving PBS-subsidised treatment with this drug for this condition, AND The treatment must be a <i>the</i> sole PBS-subsidised treatment with this drug for this condition.

For more detail on PBAC's view, see section 5 "PBAC outcome".

3 Background

- 3.1 At the November 2016 meeting, the PBAC deferred its decision on whether to recommend the General Schedule Authority Required listing of vorinostat for the treatment of CTCL. The PBAC considered that the uncertainty of the cost-effectiveness analysis presented in the original March 2011 submission was diminished in the context of the substantial price reduction offered in the November 2016 resubmission. The PBAC considered that given the high and unmet clinical need in a small group of patients, the reasonable evidence of some clinical benefit, and the modest overall financial impact, it would be appropriate to seek further clarification from the sponsor regarding the financial impact of listing on the PBS, specifically, the patient numbers and a proposed risk sharing arrangement.

For more detail on PBAC's view, see section 5 "PBAC outcome".

4 Current Submission

Sponsor hearing

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

Consumer comments

- 4.2 The PBAC noted that no consumer comments were received for this item.

Clinical claim

- 4.3 Unchanged from the November 2016 submission.

Price

- 4.4 Merck Sharp & Dohme (MSD) confirmed an ex-manufacturer price for vorinostat 100 mg x 120 of \$ [REDACTED]. This corresponds to a Dispensed Price for Maximum Quantity (DPMQ) of \$ [REDACTED], which was the same as the DPMQ proposed in the November 2016 submission.
- 4.5 At the price proposed in the 2011 submission for vorinostat and with a responder rate of 49% based on $\geq 25\%$ decrease in the modified Severity-Weighted Assessment Tool (mSWAT), the cost per responder was \$ [REDACTED].
- 4.6 When the price in the November 2016 submission (DPMQ of \$ [REDACTED]) was used in the 2011 economic model, the cost per responder decreased to \$ [REDACTED].

Estimated PBS Usage & Financial Implications

- 4.7 The minor submission estimated a net cost to the PBS of less than \$10 million in Year 5 of listing, with a total net cost to the PBS of less than \$10 million over the first 5 years of listing. This is summarised in Table 1 below, along with the expected patient/prescription numbers.

- 4.8 The November 2016 submission indicated that there were less than 10,000 active patients with CTCL receiving vorinostat treatment through the MSD Expanded Access Program (EAP). However, the sponsor proposed that only less than 10,000 patients would be eligible for PBS subsidy if the proposed PBS restriction was applied. In the pre-PBAC response the sponsor confirmed that the additional amendments to the restriction (outlined above) would not affect this number.
- 4.9 The PBAC noted the number of patients as outlined in the submission appeared to be a reasonable estimation of the expected numbers and noted that a grandfathering arrangement was not required for this indication.
- 4.10 The PBAC considered that there remained a risk of use beyond progression and in patients with other indications where cost effectiveness had not been established.

Table 1. Proposed patient numbers and financial impact of listing vorinostat

Item	2017	2018	2019	2020	2021
New PBS eligible CTCL patients ^a	■	■	■	■	■
MSD EAP patients ^b	■	■	■	■	■
TOTAL patient numbers	■	■	■	■	■
Vorinostat uptake ^c	100%	100%	100%	100%	100%
Vorinostat patients ^d	■	■	■	■	■
Financial Impact to PBS (net of co-payments)^e	\$ ■■■■■	\$ ■■■■■	\$ ■■■■■	\$ ■■■■■	\$ ■■■■■

Source: adapted from submission

Assumptions:

^a CTCL rate of ■■■■■ population, ■■■% successfully treated with curative intent. Eligible patients (■■■%) × New CTCL Patients. Assumption that all eligible patients will be treated with vorinostat at some stage during the course of their disease.

^b MSD EAP database accessed 12 January 2017. Patients included in EAP eligible for ZOLINZA as per proposed PBS restriction who commenced ZOLINZA therapy within the last 12 months.

^c MSD assumption

^d Assumption on patient utilisation of vorinostat at any point of CTCL treatment

^e Vorinostat PBS pack price here is equal to DPMQ - Average Co-payment (\$21.10 determined by data analysis for Brentuximab between 2015 and 2016. PBS online, 2016. (www.pbsonline.gov.au) presented in Section E, ZOLINZA PBAC Submission 7.11)

The redacted table shows that at year 5, the estimated number of patients was less than 10,000 and the net cost to the PBS would be less than \$10 million.

Risk Sharing Arrangements

The sponsor proposed a risk sharing arrangement with a patient number cap of less than 10,000 in the first year of listing, increasing by less than 10,000 patient per year for the first five years of listing. This was less than 10,000 patients per year higher than the estimated utilisation. The sponsor proposed a rebate of 50% for any patients exceeding these caps. The submission claimed that this was similar to other RSAs that the company has with the Department and that a rebate of this amount would allow it to cover costs.

- 4.11 The PBAC considered that a patient cap based on the eligible CTCL patients and grandfathering the MSD EAP patients (less than 10,000 in Year 1) of less than 10,000 was reasonable. The PBAC noted that the sponsor had included an increasing number of grandfathered patients beyond Year 1. The PBAC recommended that the grandfathered patients should only be included in Year 1. This results in less than 10,000 patients in Year 1 and less than 10,000 patients in year 5. In addition, the PBAC considered that there remained a concern of use beyond progression or in other indications where cost-effectiveness was not established and therefore a rebate in the order of 70% for expenditure above the cap was required.

For more detail on PBAC's view, see section 5 "PBAC outcome".

5 PBAC Outcome

- 5.1 The PBAC recommended the Authority Required listing of vorinostat for the treatment of cutaneous T-cell lymphoma (CTCL) in the General Schedule.
- 5.2 The PBAC recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of vorinostat would be acceptable at the price proposed in the submission.
- 5.3 The PBAC considered that a patient cap based on the eligible CTCL patients and grandfathering the MSD EAP patients (less than 10,000 in Year 1) of less than 10,000 was reasonable. The PBAC noted that the sponsor had included an increasing number of grandfathered patients beyond Year 1. The PBAC recommended that the grandfathered patients should only be included in Year 1. This resulted in patient caps of less than 10,000 patients in Year 1 and less than 10,000 patients in year 5. In addition, the PBAC considered that there remained a concern of use beyond progression or in other indications where cost-effectiveness was not established and therefore a rebate in the order of 70% for expenditure above the cap was required.
- 5.4 The PBAC previously considered that the restriction criterion "Patient must be ineligible for a stem cell transplantation" might not be appropriate, as vorinostat may be used as a bridging therapy to transplantation (vorinostat PSD, November 2016, paragraphs 7.10). Therefore, the PBAC recommended that the patient must be ineligible for stem cell transplantation at the time of initiation.
- 5.5 The PBAC recommended that the restriction for initiation of treatment be an Authority Required in writing benefit and the continuing treatment restriction an Authority Required telephone benefit. The PBAC considered that a grandfathering restriction was not required for this indication.
- 5.6 The PBAC recommended that Early Supply Rule should apply to the listing of vorinostat. It has a standard dosing regimen, and the proposed maximum quantity is sufficient for one month's treatment.
- 5.7 The PBAC advised that under subsection 101(3BA) of the *National Health Act, 1953* that vorinostat should not be treated as interchangeable on an individual patient basis with any other drugs.

5.8 The PBAC advised that vorinostat for CTCL is not suitable for prescribing by nurse practitioners.

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

Outcome:

Recommended

6 Recommended listing

6.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty.	No. of Rpts	Proprietary Name and Manufacturer	
VORINOSTAT vorinostat 100 mg capsule, 120	1	Initial therapy: 2 Continuing therapy: 1	Zolinza®	Merck Sharp & Dohme (Australia) Pty Ltd

Category / Program	Section 85 – General Schedule
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Cutaneous T-cell lymphoma
PBS Indication:	cutaneous T-cell lymphoma
Treatment phase:	Initial treatment
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Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required – Telephone
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must not have progressive disease while receiving PBS-subsidised treatment with this drug for this condition, AND The treatment must be the sole PBS-subsidised treatment for this condition.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.

7 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.

8 Sponsor's Comment

MSD welcomed this opportunity to work with Rare Cancers Australia and the PBAC to find different ways to ensure that patients with rare and less common cancers gain the benefits from new therapies. MSD is pleased that the PBAC have made the decision to recommend vorinostat for patients with cutaneous T-cell lymphoma (CTCL). This is a very positive outcome for patients living with a rare cancer and their carer's and families.

Rare Cancers Australia (RCA) is delighted with the decision to recommend vorinostat. We are delighted that it will give patients with CTCL additional treatment options with the security of a PBS funded medicine. RCA believes that this decision will bring hope to all patients with a rare cancer and we look forward to utilising the experience gained from this submission in the future.