

**7.17 IDELALISIB**  
**Oral tablet, 100mg, 150mg**  
**Zydelig®, Gilead Sciences Pty Ltd**

**1 Purpose of Application**

The minor resubmission requested a Section 85, Authority Required listing of idelalisib for the treatment of relapsed/refractory follicular lymphoma (FL) that has progressed despite prior treatment with rituximab and an alkylating agent.

**2 Requested listing**

2.1 The resubmission does not request any changes to the wording of the listing as described in November 2015 PBAC PSD.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
IDELALISIB Tablet, 150mg, 60 Tablet, 100mg, 60	1	5	\$ [REDACTED] (published) \$ [REDACTED] (effective)	Zydelig® Gilead

Category / Program	GENERAL – General Schedule (Code GE)
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
Episodicity:	Refractory
Severity:	
Condition:	follicular B-cell non-Hodgkin's lymphoma
PBS Indication:	Refractory follicular B-cell non-Hodgkin's lymphoma
Treatment phase:	
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - Telephone
Treatment criteria:	
Clinical criteria:	The condition must be refractory to rituximab  AND  The condition must be refractory to an alkylating agent  AND  The treatment must be as monotherapy

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<b>Prescriber Instructions</b>	<p>A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug.</p> <p>The condition is considered refractory to both rituximab and an alkylating agent if the agents were administered together or in successive treatment regimens.</p> <p>The condition is considered refractory if the patient experiences less than a partial response or progression of disease within 6 months after completion of a prior therapy.</p>
<b>Administrative Advice</b>	<p>No increase in the maximum quantity or number of units may be authorised.</p> <p>No increase in the maximum number of repeats may be authorised.</p> <p>Special Pricing Arrangements apply.</p>

2.2 At the November 2015 meeting, the PBAC accepted the restriction as proposed by the Secretariat, but considered that a telephone authority would be more appropriate than a streamlined authority. The PBAC considered that leakage into Waldenstrom's Macroglobulinemia was likely. In this minor resubmission, the sponsor did not object to the implementation of a telephone authority and the restriction was updated accordingly.

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

**3 Background**

3.1 Idelalisib was TGA registered on 9 February 2015 as monotherapy for the treatment of patients with refractory follicular lymphoma, who have received at least two prior systemic therapies.

3.2 This item was previously considered at the March 2015 and November 2015 PBAC meeting.

3.3 The November 2015 PBAC deferred its decision for listing idelalisib as it was considered to not be cost-effective at the price proposed.

**Table 1: Summary of previous submission and current resubmission:**

	<b>Idelalisib, November 2015, recommendations</b>	<b>Idelalisib, March 2016, response</b>
Requested Listing	The PBAC accepted the restriction as proposed by the Secretariat, but considered that a telephone authority would be more appropriate than a streamlined authority. The PBAC considered that leakage into Waldenstrom's Macroglobulinemia was likely.	The sponsor does not object to the implementation of a telephone authority. No comment was made regarding leakage into Waldenstrom's Macroglobulinemia.
Requested Price	The PBAC deferred its decision for listing idelalisib it was considered to be not cost-effective at the price proposed.	In the resubmission, the sponsor proposed an effective price of \$██████, requesting a ███% reduction of the proposed published price (\$██████). The pre-PBAC response proposed a new effective DPMQ of \$██████. The listing of the 100 mg strength, at the same price as the 150 mg strength, is

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	Idelalisib, November 2015, recommendations	Idelalisib, March 2016, response								
	<p>Previous requested price:</p> <table border="1"> <thead> <tr> <th></th> <th>Effective DPMQ</th> </tr> </thead> <tbody> <tr> <td>Oral tablet 150mg/100 mg</td> <td>\$ [REDACTED]</td> </tr> </tbody> </table>		Effective DPMQ	Oral tablet 150mg/100 mg	\$ [REDACTED]	<p>requested only for facilitation of dose reduction for adverse even management. Current requested price:</p> <table border="1"> <thead> <tr> <th></th> <th>Effective DPMQ (proposed in the pre-PBAC response)</th> </tr> </thead> <tbody> <tr> <td>Oral tablet 150mg /100 mg</td> <td>\$ [REDACTED]</td> </tr> </tbody> </table>		Effective DPMQ (proposed in the pre-PBAC response)	Oral tablet 150mg /100 mg	\$ [REDACTED]
	Effective DPMQ									
Oral tablet 150mg/100 mg	\$ [REDACTED]									
	Effective DPMQ (proposed in the pre-PBAC response)									
Oral tablet 150mg /100 mg	\$ [REDACTED]									
Economic evaluation	<p>The PBAC considered that the multivariate sensitivity analysis performed during the evaluation that resulted in an ICER of \$105,000/QALY - \$200,000/QALY whilst requiring acceptance of an uncertain extrapolation of overall survival, provided the most realistic estimate of cost effectiveness and should be used as the base-case. The Committee considered that this ICER was unacceptably high, and that a significant price reduction would be required in order to reduce the ICER to less than \$45,000/QALY - \$75,000/QALY. [7.8, Nov 2015 Public Summary Document]</p> <p>The PBAC agreed with the ESC that a five-year time horizon in the economic model was appropriate and more realistic for this condition. [7.7, Nov 2015 PSD]</p>	<p>When the base case of the economic model is re-specified in accordance with PBAC PSD, ICER is \$45,000/QALY - \$75,000/QALY. The ICER has been independently verified.</p> <p>Modifications to the base case were health state resource costs as per previous March 2015 submission; and the weighted cost of anti-cancer therapy in BSC limited to one course (3 or 4 months, rather than monthly ongoing cost).</p> <p>The re-specified base case continues to use a 5 year time horizon.</p> <p>In the pre-PBAC response, applying the requested price to the PBAC-specified base case economic model brought the ICER for idelalisib in the treatment of FL to 45,000/QALY - \$75,000/QALY.</p>								
Number of patients and Risk share	<p>The PBAC considered that the total patient population is uncertain and as such, a risk sharing arrangement with a cap based on the patient numbers as presented in the resubmission should be adopted once financial estimates are updated in line with the Committee's requested changes. The PBAC considered that due to the uncertainty in patient numbers, utilisation should be reviewed following listing. [7.9, Nov 2015 PSD]</p>	<p>The submission presents the upper end of patient estimates provided in the Pre-Sub-Committee-Response (PSCR), updated with the revised pricing (see table 2). The PSCR (p5, November 2015) provided a sensitivity analysis of the financial estimates, which was based on a [REDACTED]% increase in the number of patients with treated refractory disease. [6.42, Nov 2015 PSD]</p>								
Main Comparator	Unchanged from November PBAC submission									
Clinical evidence										
Key effectiveness data										

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	Idelalisib, November 2015, recommendations	Idelalisib, March 2016, response
Key safety data		
Clinical claim		

**4 Consideration of the evidence**

***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.

***Drug cost/patient/course: \$ [REDACTED]***

4.3 This was based on a mean duration of treatment of 11.4 months (mean progression free survival duration estimated in the economic model, November 2015 resubmission), 92.7% dose intensity, and cost of \$ [REDACTED] per pack (60 tablets, as proposed in the pre-PBAC response).

***Estimated PBS usage & financial implications***

4.4 Applying the requested price from the pre-PBAC response, the net cost of idelalisib (FL) to government is estimated to be less than \$10 million over the first five years of listing. The previous November 2015 PBAC submission was \$10 - \$20 million. In year 5, the cost to the PBS/RPBS was estimated to be less than \$10, with less than 10,000 patients estimated to be treated.

Table 2: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Estimated extent of use</b>					
Number treated – March 2015	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Number treated – November 2015	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Number treated- this resubmission (as in November 2015 PSCR)	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Uptake rate – March 2015	35%	55%	65%	70%	80%
Uptake rate – November 2015	35%	55%	65%	70%	80%
Uptake rate- this resubmission (as in November 2015 PSCR)	42%	66%	78%	84%	96%
<b>Estimated net cost to PBS/RPBS/MBS</b>					
Net cost to PBS/RPBS – March 2015	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to PBS/RPBS – November 2015	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to PBS/RPBS – this resubmission	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to PBS/RPBS- this resubmission updated with pre-PBAC price proposal	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

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	Year 1	Year 2	Year 3	Year 4	Year 5
Net cost to MBS – March 2015	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net cost to MBS – November 2015	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net cost to MBS- this submission	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net cost to hospitals – March 2015	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to hospitals – November 2015	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to hospitals-this submission	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

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

*For more detail on PBAC’s view, see section 5 “PBAC outcome”*

## **5 PBAC Outcome**

- 5.1 The PBAC recalled that the Committee at its November 2015 meeting deferred its decision for the Authority Required listing of idelalisib for the treatment of follicular lymphoma as idelalisib was not considered to be cost-effective at the price proposed. The PBAC therefore considered that the deferral would enable the Department to negotiate a reduced price, adopting a pragmatic approach that would reduce the base-case ICER as presented in the multivariate sensitivity analysis to a more appropriate range.
- 5.2 The PBAC noted the modifications to the economic model and the price proposed in the pre-PBAC response of this resubmission which resulted in an ICER of \$45,000/QALY - \$75,000/QALY. The PBAC considered that such an ICER was high but acceptable in the context of a tight restriction.
- 5.3 The PBAC noted the modification in patient utilisation, based on PSCR from the November 2015 meeting, which presented the upper end of patient estimates. The PBAC considered this estimate to be more reasonable, but remained concerned that the total patient population is uncertain. The PBAC reiterated a risk sharing arrangement with a cap based on the patient numbers as presented in the resubmission should be adopted. The PBAC reiterated that due to the uncertainty in patient numbers, utilisation should be reviewed 3 years following listing.
- 5.4 The PBAC recalled that during the November 2015 meeting, the Committee:
- reiterated that there is a high unmet clinical need for an effective treatment for patients with double-refractory follicular lymphoma. The PBAC also noted with caution the significant toxicities that can be experienced by patients using this drug, and considered that the incidence of these in Australian practice should be closely monitored.

- noted that harms, particularly relating to severe diarrhoea and colitis, are likely to be significant for many patients.
- 5.5 The PBAC noted recent global concerns about an increased rate of serious adverse events, including deaths, mostly due to infections in current on-going clinical trials studying idelalisib in combination with other medicines. The PBAC noted that, while these on-going trials are being carried out in different diseases or in different patient populations compared to the patient population for which listing is being sought, these serious adverse events represent harms in addition to those raised in clinical data provided in the submission. The PBAC was also mindful that these additional harms associated with idelalisib may have an impact on the evaluation of cost-effectiveness.
- 5.6 The PBAC deferred the listing of idelalisib for the treatment of follicular lymphoma that is refractory to both rituximab and an alkylating agent to seek additional information regarding safety given the recent concerns raised by regulators. The PBAC requested the sponsor to update the PBAC on adverse events in the clinical areas in which listing is being sought, and if, or how, the recent emergence of additional serious adverse events in the current trials may impact patients if idelalisib becomes available in the broader PBS population.
- 5.7 Further, the PBAC noted that sponsor agreed with an Authority required (Telephone) listing. If idelalisib for this condition was listed, the PBAC were of a mind to recommend that:
- The Early Supply Rule should apply to idelalisib as the requested maximum quantity is sufficient supply for 30 days of treatment.
  - Idelalisib is not suitable for prescribing by nurse practitioners as antineoplastic agents are currently considered to be out of scope for prescribing by nurse practitioners.
  - Under Section 101 (3BA) of the National Health Act, idelalisib would not be treated as interchangeable with any other drug(s) or medicinal preparation(s) on an individual patient basis.

**Outcome:**  
Deferred

## **6 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.

## **7 Sponsor's Comment**

The sponsor had no comment.