

4.05 LENVATINIB capsule, 4 mg and 10 mg, Lenvima®, Eisai Australia

1 Purpose of Item

- 1.1 To inform the PBAC of a new price offered by the sponsor for lenvatinib for the treatment of radioactive iodine refractory differentiated thyroid cancer (RAI-R DTC).

2 Background

- 2.1 Lenvatinib is TGA registered for the treatment of patients with progressive, locally advanced or metastatic, radioactive iodine refractory differentiated thyroid cancer.
- 2.2 Lenvatinib has previously been considered for the treatment of RAI-R DTC by the PBAC in November 2015 and March 2016.
- 2.3 At the November 2015 meeting, the PBAC deferred the submission for lenvatinib for the treatment of RAI-R DTC pending further discussion with the sponsor regarding the eligible patient population, price, and finalisation of the TGA registration process. The PBAC considered that lenvatinib was not cost-effective at the price presented in the submission.
- 2.4 At its March 2016 meeting, the PBAC considered that the resubmission's base case ICER (\$45,000 – \$75,000/QALY) remained high and reiterated that lenvatinib would likely be cost-effective at a reduced price generating an ICER in the range of \$45,000- \$75,000/QALY.

3 PBAC Discussion

- 3.1 The PBAC noted the offer of a [REDACTED] % price reduction to the original (November 2015) submission price which results in an ICER of around \$45,000 – \$75,000/QALY.
- 3.2 The sponsor did not change the estimated patient numbers in their proposal from the March 2016 minor resubmission and claimed that the patient numbers proposed are reflective of the current Australian situation, based on:
- estimates of the number of eligible patients in the Australian participating centres for the SELECT trial (19 patients recruited);
 - number of patients enrolled in the sponsor's named patient program and product familiarisation program (49 patients on treatment as of 24 April 2016); and
 - the sponsor's knowledge of a number of Australian centres which have radioactive iodine refractory patients but have not yet participated in the clinical trials or access programs.

Table 1: Estimated use and financial implications

	Year 1 (2016)	Year 2 (2017)	Year 3 (2018)	Year 4 (2019)	Year 5 (2020)
Estimated number treated with a TKI	█	█	█	█	█
Estimated number treated with lenvatinib	█	█	█	█	█
Estimated number treated with sorafenib	█	█	█	█	█
Basecase: assuming all patients are treated with lenvatinib					
Estimated number treated with lenvatinib	█	█	█	█	█
Total cost to the PBS	\$ █	\$ █	\$ █	\$ █	\$ █
Total Co-payment	\$ █	\$ █	\$ █	\$ █	\$ █
Total net cost to the PBS	\$ █	\$ █	\$ █	\$ █	\$ █
Total net cost to the PBS (March 2016)	\$ █	\$ █	\$ █	\$ █	\$ █

Source: Section E excel spreadsheet of the sponsor's proposal

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

Risk Sharing Arrangements

3.3 The sponsor has proposed a Risk Sharing Arrangement (RSA) in the form of a financial cap consistent with the estimated use presented in Table 1, with a █% rebate paid to the Commonwealth for utilisation above the cap.

4 Requested listing

4.1 The sponsor has requested the PBAC to reconsider the criterion in the continuing restriction that states that patients must have stable or responding disease according to RECIST, as the sponsor states that this is not normal clinical practice, and would require additional expertise and resources. However, the sponsor is willing to accept inclusion of this criterion if the PBAC consider it necessary.

4.2 The PBAC noted the sponsor's request that patients on their compassionate access programs be grandfathered on to the PBS. As per the sponsor's proposal, there are 49 patients on treatment through the programs as of 24 April 2016.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of lenvatinib for the treatment of radioactive iodine refractory differentiated thyroid carcinoma (RAI-R DTC) on the basis of acceptable cost effectiveness over best supportive care (BSC).
- 5.2 The PBAC considered the new price offer resulted in an ICER that is acceptably cost-effective for the eligible patient population.
- 5.3 The PBAC considered that the restriction, as previously recommended, should be consistent with what the PBAC had previously advised in its consideration of sorafenib for RAI-R DTC (refer to Sorafenib, Public Summary Document, March 2015), including restricting to patients who have symptomatic progressive disease prior to treatment, or progressive disease at critical sites with a high risk of morbidity or mortality if progression continues and where local control cannot be achieved by other measures, and using the RECIST criteria to assess response for continuing therapy.
- 5.4 The PBAC considered that the patient estimates were reflective of current Australian situation and a reasonable basis for Risk Sharing Arrangement.
- 5.5 The PBAC accepted the proposed Risk Sharing Arrangement in the form of a financial cap with a ■■■% rebate paid to the Commonwealth for utilisation above the cap.
- 5.6 The PBAC recommended that patients from the sponsor's compassionate access programs be allowed to be grandfathered to the PBS.
- 5.7 The PBAC advised that lenvatinib is not suitable for prescribing by nurse practitioners.
- 5.8 The PBAC recommended that the Early Supply Rule should not apply.
- 5.9 The PBAC noted that this submission is not eligible for an Independent Review as 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 Manufacturer	Name and
LENVATINIB lenvatinib 4 mg capsule, 30	1	2	Lenvima®	Eisai Australia
lenvatinib 10 mg capsule, 30	2	2		

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:	-
Severity:	<i>Locally advanced or metastatic Stage III or IV (including high risk patients aged less than 45 years)</i>
Condition:	Differentiated thyroid cancer
PBS Indication:	Locally advanced or metastatic differentiated thyroid cancer
Treatment phase:	Initial treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined

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Clinical criteria:	<p>Patient must have radiologically determined symptomatic progressive disease prior to treatment; OR <i>Patient must have progressive disease at critical sites with a high risk or morbidity or mortality where local control cannot be achieved by other measures</i></p> <p>AND</p> <p>Patient must have TSH adequately repressed [TSH ≤0.50 µIU/mL]</p> <p>AND</p> <p>Patient must have a WHO performance status of 2 or less</p> <p>AND</p> <p>Patient must be one in whom surgery is inappropriate</p> <p>AND</p> <p>Patient must not be a candidate for radiotherapy with curative intent</p> <p>AND</p> <p>The condition must be refractory to radioactive iodine.</p> <p>AND</p> <p>The treatment must be the sole PBS-subsidised therapy for this condition.</p>
Prescriber Instructions	<p>Radioactive iodine refractory is defined as:</p> <ul style="list-style-type: none"> - A lesion without iodine uptake on a radioactive iodine (RAI) scan, or - Receiving cumulative RAI ≥ 600 mCi, or - Experiencing a progression after a RAI treatment within 12 months of enrolment, or - After two RAI treatments within 12 months of each other
Administrative Advice	<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>A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug.</p>

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:	-
Severity:	<i>Locally advanced or metastatic Stage III or IV (including high risk patients aged less than 45 years)</i>
Condition:	Differentiated thyroid cancer
PBS Indication:	Locally advanced or metastatic differentiated thyroid cancer
Treatment phase:	Continuing treatment

Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>Patient must have previously been issued with an authority prescription for this drug for this condition</p> <p>AND</p> <p>Patient must have stable or responding disease according to the Response Evaluation Criteria in Solid Tumours (RECIST)</p> <p>AND</p> <p>The treatment must be the sole PBS-subsidised therapy for this condition.</p>
Administrative Advice	<p><i>Response Evaluation Criteria In Solid Tumours (RECIST) is defined as follows:</i></p> <p><i>Complete response (CR) is disappearance of all target lesions.</i></p> <p><i>Partial response (PR) is a 30% decrease in the sum of the longest diameter of target lesions.</i></p> <p><i>Progressive disease (PD) is a 20% increase in the sum of the longest diameter of target lesions.</i></p> <p><i>Stable disease (SD) is small changes that do not meet above criteria.</i></p> <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>A patient who has progressive disease when treated with this drug is no longer eligible for PBS-subsidised treatment with this drug.</p>

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

The sponsor had no comment.