

6.13 LENALIDOMIDE

Capsule 5 mg, 10 mg, 15 mg, 25 mg, Revlimid®, Celgene Pty Limited

1 Purpose of Application

- 1.1 The minor submission sought to amend the restriction level of the existing PBS listings for lenalidomide for multiple myeloma from Authority Required (Written) to Authority Required (STREAMLINED).
- 1.2 The request applied to the:
 - current PBS listings for the treatment of patients with:
 - newly diagnosed symptomatic multiple myeloma (ND MM) who are ineligible for stem cell transplant; and
 - relapsed or refractory multiple myeloma (RR MM).
 - proposed PBS listing for the maintenance treatment of patients who have undergone a stem cell transplant (considered as a major submission at the March 2019 PBAC submission – Item 7.07).

2 Background

Registration status

- 2.1 At the time of the PBAC meeting, lenalidomide was approved by the TGA for the following multiple myeloma indications:
 - Treatment of patients with newly diagnosed multiple myeloma who are ineligible for a primary stem cell transplantation.
 - In combination with dexamethasone, for treatment of multiple myeloma patients whose disease has progressed after one therapy.
 - Maintenance treatment of patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.
- 2.2 On the [REDACTED], a new application was submitted to the TGA seeking an [REDACTED].
- 2.3 That application has also asked the TGA to consider whether lenalidomide [REDACTED] of 'multiple myeloma'.

Previous PBAC considerations

- 2.4 At the November 2008 PBAC meeting, lenalidomide was recommended for listing for the treatment of RR MM on basis of cost-minimisation with bortezomib. The PBAC advised that the listing of lenalidomide should be administered by written authority applications in a similar way to bortezomib (Section 12, Lenalidomide Public Summary Document (PSD), November 2008).
- 2.5 In March 2016, the PBAC recommended the listing of lenalidomide for the treatment of patients with ND MM who were ineligible for stem cell transplant. The PBAC recommended that the restriction for lenalidomide, in combination with dexamethasone, should be aligned with that of bortezomib for first line therapy in the treatment of multiple myeloma in the transplant-ineligible population (paragraph 4.2, Lenalidomide PSD, March 2016).
- 2.6 At the July 2017 PBAC meeting, the PBAC recommended the listing of carfilzomib for the treatment of relapsed or refractory multiple myeloma. The PBAC advised that a telephone authority, rather than a written authority, was appropriate as patients will have already demonstrated that they have multiple myeloma when they received first-line therapy (paragraph 7.10, Carfilzomib PSD, July 2017). Carfilzomib is listed at the same line of therapy as lenalidomide.
- 2.7 At the March 2018 meeting, the PBAC supported a proposal from the Department to streamline the current written Authorities for bortezomib for all its multiple myeloma PBS restrictions (March 2018 PBAC Outcomes – Other matters).
- 2.8 At the 23 May 2018 Multiple Myeloma Stakeholder meeting, the key priorities identified included simplification of restrictions in the relapsed and refractory setting. It was noted that any requested changes would need to be considered in the context of the effective PBS prices.

For more detail on PBAC's view, see Section 4 PBAC outcome.

3 Current situation and proposal

Sponsor hearing

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

Consumer comments

- 3.2 The PBAC noted and welcomed the input from individuals (51), health care professionals (2) and organisations (3) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of streamlining the prescribing process of lenalidomide including improved and expedited access.
- 3.3 The PBAC noted the advice received from the Leukaemia Foundation, Myeloma Australia, and the Medical and Scientific Advisory Group (MSAG) of Myeloma Australia clarifying the likely improved access to lenalidomide in clinical practice. The PBAC specifically noted the advice that the streamlining of lenalidomide prescribing would reduce prescriber burden and stress and improve patient access.

Proposal

3.4 The table below provides a summary of the current authority requirements for bortezomib, carfilzomib and lenalidomide in the treatment of multiple myeloma.

Table 1: Current authority requirements for bortezomib, carfilzomib and lenalidomide

	Newly diagnosed MM		Relapsed or refractory MM	
	Initial	Continuing	Initial	Continuing
Bortezomib	Authority Required (STREAMLINED)	Authority Required (STREAMLINED)	Authority Required (STREAMLINED)	Authority Required (STREAMLINED)
Carfilzomib	-	-	Authority Required (Telephone)	Authority Required (Telephone)
Lenalidomide - current	Authority Required (Written)	Authority Required (Telephone)	Authority Required (Written)	Authority Required (Telephone)
Lenalidomide - proposed	Authority Required (STREAMLINED)	Authority Required (STREAMLINED)	Authority Required (STREAMLINED)	Authority Required (STREAMLINED)

MM = multiple myeloma

Source: Table 2, p10 of the submission

3.5 No changes to the treatment criteria were proposed. The minor submission solely requested that the authority levels of the PBS listings for lenalidomide for multiple myeloma be amended from written (for initial and continuing) or telephone (for continuing) to Authority Required (STREAMLINED).

3.6 The submission stated that the Authority Required (Written) process resulted in administrative burden and delays in treatment, creating a significant level of differentiation from bortezomib, an otherwise comparable treatment.

Estimated PBS usage & financial implications

3.7 The sponsor recognised that the proposed change to Authority Required (STREAMLINED) may result in some usage beyond the intended PBS population.

3.8 To mitigate the risk, the sponsor offered a ■% discount on the expected total expenditure of lenalidomide in ND MM patients who are ineligible for stem cell transplant. This equated to a ■% discount on the estimated total expenditure for lenalidomide in 2019, increasing to a ■% discount in 2022, because of the expected shift in market dynamics from relapsed to front-line utilisation.

3.9 When compared with the actual utilisation of lenalidomide in ND MM patients in 2017-2018 (see Table 4), the total expenditure estimates provided in the submission appear overestimated.

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Table 2: Estimated saving to the PBS/RPBS

	2019	2020	2021	2022
Volume (21 capsule packs)				
NDMM TNE				
RRMM				
Total				
Estimated total expenditure, without proposed discount - AEMP				
NDMM TNE				
RRMM				
Total				
Estimated total expenditure, with proposed % NDMM TNE discount – AEMP				
NDMM TNE				
RRMM				
Total				
Total saving				
Average total discount				

AEMP = approved ex-manufacturer price; NDMM TNE = newly diagnosed multiple myeloma, transplant not eligible; RRMM = relapsed or refractory multiple myeloma

Source: Table 3, p13 of the submission

3.10 The minor submission estimated that the % discount offered in ND MM patients who are ineligible for stem cell transplant will result in a less than \$10 million saving to the PBS/RPBS over the next four years. The submission did not provide assumptions for the projected estimates used to determine the less than \$10 million in savings.

3.11 To realise a % discount on expected total expenditure in ND MM patients, the submission determined that a % increase to the rebates provided to achieve the effective price under the current Risk Sharing Arrangement (RSA) for lenalidomide for ND MM in patients who are ineligible for stem cell transplant would be required. The submission did not propose a renegotiation of the current Deed of Agreement for lenalidomide in this population beyond adjustment of the rebate percentages. The % increase in the current rebate was calculated on uncertain estimates; it was uncertain whether the % rebate would achieve an actual % reduction in expenditure for ND MM.

Table 3: Current and proposed effective AEMP prices for lenalidomide

Lenalidomide strength	Current public DPMQ	Current rebate	Current effective AEMP	Proposed rebate (Current rebate + %)	Proposed effective AEMP
5 mg	\$5,122.76				
10 mg	\$5,361.16				
15 mg	\$6,252.53				
25 mg	\$6,587.49				

AEMP = approved ex-manufacturer price; DPMQ = dispensed price for maximum quantity

Source: Lenalidomide – Budget Impact Model – Excel

3.12 Utilisation of lenalidomide in the ND MM population has been below that estimated in the November 2015 and March 2016 PBAC submissions – see table below. Should there be an increase in use with the streamlining of the PBS indications; the use in ND MM is likely to remain under the current RSA caps.

Table 4: Proportion of lenalidomide NDMM TNE subsidisation cap reached^a

	Deed, Year 1 Feb 2017-Jan 2018	Deed, Year 2 Feb 2018-Jan 2019
Subsidisation cap	\$ [redacted] million	\$ [redacted] million
Commonwealth payment ^b	\$ [redacted] million	\$ [redacted] million ^c
Proportion of cap reached	[redacted] %	[redacted] % ^c

NDMM TNE = newly diagnosed multiple myeloma, transplant not eligible

Source: Table 4, p14 of the submission

^a PBS items 11029L, 11036W, 11063G, 11062F, 11042E, 11041D, 11055W

^b Expenditure figures based on the effective price

^c Figures from February 18 to October 18

Quality use of medicines

- 3.13 The submission claimed that the Authority Required (Written) process resulted in a significant impediment to providing patient care and unnecessarily delayed initiation of multiple myeloma treatment. The submission was concerned that the different level of authority between lenalidomide and bortezomib was unethical and unfairly discriminated patients for whom lenalidomide was deemed the more clinically appropriate treatment as they faced a delay in the commencement of treatment.

For more detail on PBAC's view, see Section 4 PBAC outcome.

4 PBAC Outcome

- 4.1 The PBAC decided not to recommend a change to the restriction level of the existing PBS listings for lenalidomide for multiple myeloma from Authority Required (Written) to Authority Required (STREAMLINED). Lenalidomide is currently PBS listed for the treatment of patients with newly diagnosed multiple myeloma (ND MM) who are ineligible for a stem cell transplant and relapsed or refractory multiple myeloma (RR MM).
- 4.2 The PBAC noted that the Sponsor requested a change to the listings of lenalidomide so that the authority process was aligned with that for bortezomib. The PBAC noted that the differing levels of authority could potentially delay treatment in those patients prescribed lenalidomide.
- 4.3 The PBAC recalled that at the May 2018 Multiple Myeloma Stakeholder meeting one of the key priorities included simplification of restrictions in the relapsed and refractory setting, noting that any changes would need to be considered in context of the effective PBS prices. The PBAC noted that the Sponsor offered a [redacted] % discount on the expected total expenditure of lenalidomide in ND MM patients who are ineligible for stem cell transplant to mitigate the risk that a change in authority level might result in some use beyond the intended PBS population. This equated to a [redacted] % increase to the rebates provided to achieve the effective price under the current Risk Sharing Arrangement (RSA). The PBAC noted that the [redacted] % discount was based on utilisation estimates which, when compared to actual expenditure, appeared to have been overestimated. The PBAC considered that it was unlikely that the [redacted] % rebate would achieve an actual [redacted] % reduction in expenditure.
- 4.4 The PBAC considered that the proposed increase to the rebate for ND MM did not

sufficiently address the risk of use outside the current PBS indications with a relaxing of the authority level for prescribing. The PBAC considered any future proposed price reduction should be based on actual expenditure and consider combined caps across indications.

- 4.5 The PBAC noted that this submission is not eligible for an Independent Review as it was a request to modify an existing listing.

Outcome:

Rejected

5 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.

6 Sponsor's Comment

Celgene is committed to working with the PBAC to secure equitable access to Multiple Myeloma treatments for patients and physicians.