

## 6.14 POMALIDOMIDE capsule, 3 mg, 4 mg Pomalyst®, Celgene Pty Ltd

### 1 Purpose of Application

- 1.1 The minor submission sought to amend wording in the current listing for pomalidomide and lenalidomide (see 'other matters' below).

### 2 Requested listing

- 2.1 The submission requested the following changes to the existing listing for pomalidomide:

The patient:

- has experienced treatment failure with lenalidomide, as confirmed by progressive disease ~~during treatment or within 6 months of discontinuing treatment with lenalidomide~~

and

- has experienced treatment failure with bortezomib, as confirmed by failing to achieve at least a partial response to treatment, or as progressive disease ~~during treatment or within 6 months of discontinuing treatment with bortezomib~~

or

- has experienced severe intolerance or toxicity to bortezomib, unresponsive to clinically appropriate dose adjustment

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

### 3 Background

- 3.1 Pomalidomide was TGA registered on 1 July 2014: "Pomalidomide, in combination with dexamethasone, is indicated for the treatment of patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy".
- 3.2 A major submission for pomalidomide for multiple myeloma was rejected at the July 2014 PBAC meeting. The PBAC considered that cost-effectiveness had not been demonstrated. Following consideration of a minor submission, pomalidomide was recommended for listing by PBAC in November 2014.
- 3.3 In July 2014, the PBAC stated the following in regards to the proposed restriction: that a definition of failure of treatment, in line with that of the entry criteria of the MM-003 trial, is included in the restriction. i.e. "Treatment failure is defined as confirmed progressive disease during treatment or within 6 months of discontinuing treatment".

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

## **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 via the consumer comments portal. The PBAC noted the correspondence of the Haematology Society of Australia and New Zealand (HSANZ) on this matter and considered this letter alongside the submission from the sponsor.

### ***Clinical evidence***

4.3 No new clinical trials were presented in the submission.

4.4 The minor submission claimed that the clinical evidence from the primary clinical trial on which the pomalidomide PBS listing was based, trial MM-003, demonstrates that neither the reason for discontinuation of prior therapy or the period in which progression occurs are likely to be treatment effect modifiers. The submission presents subgroup analysis of the trial MM-003 (source not provided), including the following three distinct patient groups:

- Group 1: refractory subjects who had progressed on or within 60 days of both lenalidomide and bortezomib based treatments, N=249 (82.5%).
- Group 2: relapsed and refractory subjects who achieved at least partial response and progressed within 6 months after stopping treatment with lenalidomide and/or bortezomib, N=8 (2.6%).
- Group 3: refractory/intolerant subjects who had developed intolerance/toxicity after a minimum of 2 cycles of bortezomib, N=45 (14.9%).

The submission claims that there no significant difference in terms of overall survival and progression free survival for these patient subgroups.

4.5 The submission notes that the current restrictions were based upon the inclusion criteria from the pivotal MM-003 study and states the study was designed with conservative inclusion criteria in order to isolate the critical question whether pomalidomide is active in a truly refractory and thus most difficult to treat patient population.

### ***Economic analysis***

4.6 There was no economic analysis in regard to the requested change in listing and proposed widening of the eligible patient population.

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

4.7 The minor submission provided information on examples of patients who were not able to access subsidised treatment for multiple myeloma, including 38 of 119 patients in the sponsor's compassionate access program who failed to meet the PBS eligibility criteria to qualify for PBS subsidised pomalidomide.

- 4.8 The minor submission provided no overall estimate of patients who could access treatment following implementation of the proposed changes to the restriction. The proposed widening of the eligible patient population would likely increase the cost to the PBS in forward estimates, which was not addressed in the submission. The sponsor is requested to comment on the potential financial cost associated with approval of the submission request.
- 4.9 The pre-PBAC response argued that the financial cost accepted previously (when pomalidomide) was recommended included the patients who would be affected by the change in restriction, so there should be no additional financial impact.

**Other matters**

- 4.10 The minor submission also requests a change to the lenalidomide restriction to enable re-treatment with lenalidomide after a “treatment holiday”. No new data or proposed restriction changes were included in the minor submission to support a change in the listing of lenalidomide.

*For more detail on PBAC’s view, see section 6 “PBAC outcome”*

**5 PBAC Outcome**

- 5.1 The PBAC rejected the application to change restriction for pomalidomide.
- 5.2 The PBAC considered that the issue was not whether pomalidomide works in the broader group requested (that is those who have previously received lenalidomide or bortezomib), but whether pomalidomide in this setting is cost-effective against the additional comparators that would apply in those circumstances (for example re-use of lenalidomide or bortezomib with adjusted scheduling). The PBAC recalled their consideration of pomalidomide at the November 2014 meeting. The PBAC considered that ICER was at the high end of what would be considered cost effective for pomalidomide in this indication. The PBAC considered that to enable use in a broader group, a price reduction, in the order of ■%, would be required to address the concern about cost-effectiveness. This in turn would enable implementation of restriction changes that would define treatment failure for both lenalidomide and bortezomib as failure to achieve at least a partial response after an adequate trial.
- 5.3 The PBAC noted that the minor submission included a request a change to the lenalidomide restriction to enable re-treatment with lenalidomide after a “treatment holiday”. The PBAC recalled views previously expressed by the Myeloma Foundation and HSA NZ in support of such a change, and considered it would be reasonable to make the following changes:
- That the listing allow for re-use of lenalidomide in patients who have not previously failed lenalidomide treatment, since there are situations where it may be clinically appropriate to allow patients to take a ‘drug holiday’ and then recommence treatment.
  - That the need to try thalidomide treatment prior to accessing lenalidomide, upon relapsing after bortezomib treatment be removed.

- 5.4 The PBAC considered that these changes to the lenalidomide will address some of the concerns for clinicians and patients being treated for multiple myeloma, where lenalidomide has been discontinued for reasons other than failure of the medicine.
- 5.5 The PBAC noted that this submission is not eligible for an Independent Review; Independent Review is not available in response to a request to modify or extend an existing listing.

**Outcome:**

Rejected

**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**

Celgene would like to thank the HSANZ and Myeloma Australia for their support in helping the PBAC understand some of the unintended consequences of the current wording of the Pomalidomide restriction. There is still a group of patients who will not be eligible for PBS funded Pomalidomide as a consequence of this decision. Celgene will endeavour to work with the Department and the PBAC to address the needs of these patients.