Multiple Myeloma Stakeholder Meeting

Outcome Statement

Friday 25 July 2025

Attendees

Members of the Pharmaceutical Benefits Advisory Committee (PBAC), clinicians with expertise in the management of Multiple Myeloma (MM), representatives from Myeloma Australia, and the Department of Health, Disability and Ageing were in attendance.

Non-departmental attendees undertook confidentiality declarations and provided conflict of interest statements.

Purpose of meeting

Following the March 2025 PBAC consideration of submissions for daratumumab and elranatamab for the treatment of multiple myeloma, the Chair of the PBAC considered that it would be appropriate for a stakeholder meeting to be convened to better understand the evolving treatment landscape.

The PBAC Chair outlined that the objective of the stakeholder meeting was to discuss Pharmaceutical Benefits Scheme (PBS) listed therapies for multiple myeloma (MM) and relapsed or refractory multiple myeloma (RRMM), including the non-alignment of current PBS medicine restrictions with clinical guidelines and a future optimal PBS treatment paradigm that would be cost-effective and financially sustainable.

The following points were identified as areas for discussion:

- How does the current treatment landscape for PBS-listed medicines MM and/or RRMM differ to:
  - Australian and international clinical guidelines?
  - Therapeutic Goods Administration (TGA)-approved indications?
- What does the optimal treatment landscape for PBS-listed medicines for MM look like with respect to:
  - optimising sequencing and treatment combinations (e.g., using three or four drugs);
  - determining treatment duration (fixed durations versus continuation until progression);
  - selecting first-line PBS treatments for patients (e.g., assessing transplant eligibility. frailty);
  - reducing overtreatment and unnecessary medicine use;
  - use of bispecific therapies versus CAR T-cell therapy; and,
  - reducing barriers to optimal treatment based on patient location.
  - How can an optimal treatment and financially viable landscape be achieved?
- Is there clinical and economic evidence to support any required changes to PBS restrictions for upfront MM and RRMM medicines?

- What is the impact of proposed changes on the cost-effectiveness of current and future therapies?
- How can clinical practice be adjusted to support cost-effective and financially sustainable treatment of MM?
- How is the management of high-risk smouldering multiple myeloma expected to evolve in light of recent data?
- What data sources or linked data sources can be accessed to undertake a utilisation analysis to better understand treatment pathways/duration of treatment for PBS listed MM therapies?

A representative from the Department of Health, Disability and Aged Care presented findings on the utilisation and costs of PBS-listed medicines for multiple myeloma, and a member of PBAC provided an overview of the current myeloma PBS treatment landscape, anticipated changes over the next 24 months and the future myeloma PBS treatment algorithm with a view to emerging treatments.

Meeting discussion

- Stakeholders noted that the clinical landscape of MM and RRMM treatment has evolved from cytotoxic chemotherapy to novel therapies, including immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs), anti-CD38 monoclonal antibodies, and B-cell maturation antigen (BCMA)-targeted agents. In 2024-25, PBS expenditure on multiple myeloma listings was $341 million, comprising 11% of the total $3.1 billion expenditure on antineoplastic listings, at published prices.
- Stakeholders also noted the success of government policy in containing overall expenditure through statutory price reductions and first new brand reductions for bortezomib, lenalidomide, pomalidomide and carfilzomib.

<u>Discordance between clinical guidelines and PBS-listed medicines for MM and RRMM</u>

- The PBS restrictions for medicines used to treat MM/RRMM reflect the submissions as considered by the PBAC. The PBS restrictions inform clinical practice with regards to subsidised medicine combinations and lines of therapy and effectively act as quasi clinical guidelines.
- Differences between PBS restrictions and clinical guidelines can be attributed to the evolving treatment paradigm as the treatment approach to myeloma shifts from an acute to chronic condition. Applications for PBS listing may not reflect the most efficacious treatment combinations and sponsors delay bringing forward innovative therapies for PBS listing as developed for commercial reasons. Consequently, by the time of PBS listing, the place of a therapy of a medicine may have shifted due to emerging clinical evidence or changes in standard of care.
- Clinicians emphasised that optimal care requires an individualised treatment approach, with consideration given to age, frailty, prior treatment related toxicities and comorbidities. The current PBS treatment algorithm does not accommodate flexibility or the need for an individualised treatment approach as it is reliant on defined eligibility criteria including prior treatment history and other clinical parameters. The categorisation

of medicines by line of therapy reduces clinical discretion and may delay access to the optimal regimen.

- Clinicians agreed that the current PBS restriction 1st/2nd/3rd line nomenclature was no longer appropriate and that treatment sequencing could be improved if determined by prior drug exposure rather than lines of therapy. To reduce the variation in prescribing from real world data evidence, clinicians suggested that PBS restrictions for myeloma medicines could limit prescribing to haematologists. Limiting prescriber type will become more important as more toxic immune therapies become available.
- Clinicians reported the PBS restriction requirement to classify newly diagnosed multiple myeloma (NDMM) patients as autologous stem cell transplant (ASCT) ineligible or eligible is a historic and arbitrary distinction and emphasised that transplantation remains the most cost-effective method of managing myeloma for eligible patients. Clinicians also report suboptimal transplantation uptake, with fewer than 40% of eligible patients currently receiving transplants.
- Clinicians described the potential benefits of expanded PBS access to anti-CD38 monoclonal antibodies for all myeloma patients, based on robust efficacy data demonstrated across multiple clinical studies. Clinicians highlighted the limited access to anti-CD38 therapies under current PBS arrangements, noting daratumumab is only available for second line treatment in combination with bortezomib and dexamethasone.
- The March 2025 PBAC recommended but not yet implemented first line listing for daratumumab in combination with lenalidomide and dexamethasone for transplant ineligible patients was also noted. Clinicians suggested that this listing may result in more patients choosing to access daratumumab first line rather than proceeding to transplant.
- Clinicians highlighted the treatment gap for patients with long remissions who relapse post second line therapy. Daratumumab cannot be accessed third line, and in practice, access to fourth-line daratumumab treatment through compassionate access often requires prior use of all PBS-listed medicines, which may not align with individual clinical circumstances e.g., patient frailty.
- Patients who have relapsed post the PBS availability of anti-CD38 therapy may also be excluded from clinical trials, as prior exposure to anti-CD38 therapy may be a prerequisite for participation.

<u>Optimal treatment landscape for PBS-Listed medicines for MM & RRMM</u>

- Clinicians agreed that the most effective treatments should be available on the PBS as first-line options for optimal clinical effectiveness and the sustained financial viability of the PBS. Use of the most efficacious but more costly treatment upfront may reduce overall treatment costs.
- Stakeholders noted the median age at diagnosis for multiple myeloma is between 65 and 70 years, the median survival is five years, and the Australian life expectancy is around 85 years and considered that in the future most patients may only require two to three lines of therapy before age-related comorbidities limit further treatment or death from another cause occurs. Medicines used during the first three treatment phases of MM/RRMM will significantly impact patient health outcomes and Commonwealth expenditure.

- Clinicians acknowledged that more robust evidence should emerge from clinical trials over the next four to five years and that they would value the ability to use all PBS myeloma therapies flexibly until trial results become available that will translate to significant changes in clinical practice and practice stabilises.
- Streamlining PBS access to generic medicines such as lenalidomide, pomalidomide, and bortezomib would enable prescribing of more flexible and effective combination regimens, supporting a personalised treatment approach.
- Clinicians noted the substantial number of lenalidomide PBS restrictions due to multiple strengths and treatment phases and suggested that the restrictions be revised for improved usability.
- Ideally, clinicians would like the option to prescribe daratumumab + bortezomib + lenalidomide + dexamethasone (Dara-VRd) first line for all patients irrespective of transplant eligibility status, and more flexibility in prescribing PBS medicines for RRMM, where choice should be driven by medicine toxicity and prior medicine exposure not by previous lines of therapy.
- Clinicians would value the ability to use PBS daratumumab in third line or triple class exposed patients.
- The strategic use of horizon scanning will proactively identify emerging therapies and evolving treatment paradigms. Clinicians would be prepared to support the PBAC with structured advice on the clinical relevance of submissions requesting PBS listing in the horizon scanning context. The most efficient and effective way of providing that advice would need to be determined.
- Stakeholders anticipate that over the next two years there may be multiple tri and bi specific antibody and immunotherapy submissions to PBAC for RRMM, with submissions for first line treatment to follow.
- Clinicians questioned whether cross sponsor collaboration was an option to bring submissions for effective medicine combinations forward for PBAC consideration, noting the practical difficulties of this approach for non-generic combinations.
- Regarding treatment duration, clinicians agreed that treatment beyond progression adds cost without benefit. Regimens of fixed doses or predetermined numbers of cycles rather than continuous therapy may address this issue, if not an impediment to good clinical practice.
- Stakeholders noted that in April 2024, the Food and Drug Administration's Oncologic Drugs Advisory Committee (ODAC) agreed evidence does support the use of minimal residual disease (MRD) as an accelerated approval endpoint in MM clinical trials and that the 12-month timepoint was acceptable for MRD assessment. Sustained MRD negativity may be helpful to assess durability. This approach could deliver substantial economic and clinical benefits by enabling treatment decisions that support therapy cessation, reduce unnecessary medication use and minimise toxicity. Equitable access to funded technology to measure MRD would be required.
- Clinicians reported the decision to treat smouldering multiple myeloma continues to present a challenge as current modelling methods cannot reliably identify patients likely to progress to active disease. There is no evidence to demonstrate cost-effectiveness of

treatment, and it is not acceptable to expose patients that may not progress to toxic therapies.

- Clinicians considered that active treatment should be continued whilst disease remains stable and acknowledged the challenges of PBS restrictions in defining when disease progression occurs and when treatment should cease. The challenges of auditing compliance with PBS restrictions were noted.
- Regarding B cell maturation antigen (BCMA) therapies such as bi-specific antibodies (e.g. elranatamab), and chimeric antigen receptor T (CAR T) -cell therapy**,** differences in accessibility may influence uptake. In the short term, clinicians considered that use of bispecific antibodies may dominate use of CAR T-cell therapies due to simpler application processes, and the cost of CAR T cell therapy will decrease as new CAR T-cell therapies come to market.
- To improve patient choice of treatment options, clinicians expressed a preference for funded CAR T cell therapies to be available as a fourth line therapy with bi-specific antibodies and not positioned fifth line as currently requested by the sponsor and approved by MSAC[1]. Clinicians stated prior exposure to BCMAs should not preclude access to CAR T-cell therapy, despite some evidence that BCMA exposure may impact on CAR T cell therapy efficacy.
- Stakeholders noted the importance of health technology assessment (HTA) committees e.g. PBAC, Medical Services Advisory Committee (MSAC) having an awareness of the whole treatment environment so decisions regarding patient access to medicines and highly specialised therapies are complementary and not made in isolation.

Further Research

- Stakeholders identified the EpiMap Myeloma Model Project as a resource for estimating the number of patients initiating treatment over the next five years and projecting associated costs, which may assist in evaluating future treatment uptake and cost implications for the PBS.

Conclusion

The PBAC Chair thanked participants for their time in attending the stakeholder meeting and the advice provided.

The PBAC Chair requested that meeting participants provide consensus advice to the PBAC on issues raised in the discussion. The Medical and Scientific Group (MSAG) of Myeloma Australia agreed to provide a consensus view on the appropriate PBS restriction criteria for multiple myeloma medicines to the PBAC. The Department undertook to support MSAG by downloading the PBS restrictions for myeloma medicines.

[1] At the time of the stakeholder meeting, the implementation of the CAR T cell, Ciltacabtagene autoleucel, to treat refractory or relapsed multiple myeloma in public hospitals was not finalised, following MSAC's support of public funding under the National Health Reform Agreement (Application 1690.1).

The participants agreed that it would be beneficial to work with the Department towards developing a multiple myeloma medicines utilisation model.