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No time left to wait.

Urgent action needed to resolve how Australia assesses the value of innovative combination treatments for multiple myeloma to ensure equitable and timely reimbursed access for Australians.

A discussion paper
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Table of Contents

Glossary

Add-on therapy	An additional or newer therapy that is used in combination with the existing backbone therapy to provide a combination treatment for a disease.
Backbone therapy	An existing therapy that forms part of a combination treatment for a disease.
Combination treatment	Treatments with drug regimens comprising two or more concurrently administered therapies.
Multiple myeloma	A malignancy of plasma cells in the body that most commonly leads to bone loss, renal failure, hypercalcaemia, immune suppression, and anaemia.
NDMM	Newly diagnosed multiple myeloma.
PBAC	Pharmaceutical Benefits Advisory Committee.
PBS	Pharmaceutical Benefits Scheme.
RRMM	Relapsed/refractory multiple myeloma.
TGA	Therapeutic Goods Administration.

Executive Summary

Nearly 1 in 4 medicines approved by the Therapeutic Goods Administration (TGA), the national regulator, for multiple myeloma have never been submitted to the Pharmaceutical Benefits Advisory Committee (PBAC), the independent expert body appointed by the Australian government to assess new treatments for public reimbursement.

Multiple myeloma is a type of blood cancer that has a lower survival rate than other cancers, despite improvements in survival being made in recent years. Its incidence is increasing in the Australian population.

A growing number of new therapies are emerging that help prolong life in people with multiple myeloma. Increasingly, two or more medicines are used in combination to increase their effectiveness in treating the disease, thereby improving patient outcomes. Unfortunately, Australians with multiple myeloma are being denied access to many innovative treatment options because these therapies are not reimbursed under Australia's Pharmaceutical Benefits Scheme (PBS). Why is this happening? While there are clear clinical benefits for patients from these new combination therapies, the way health technology assessment (HTA) is applied to evaluate the value of these therapies makes it inherently difficult for sponsors to demonstrate cost-effectiveness.

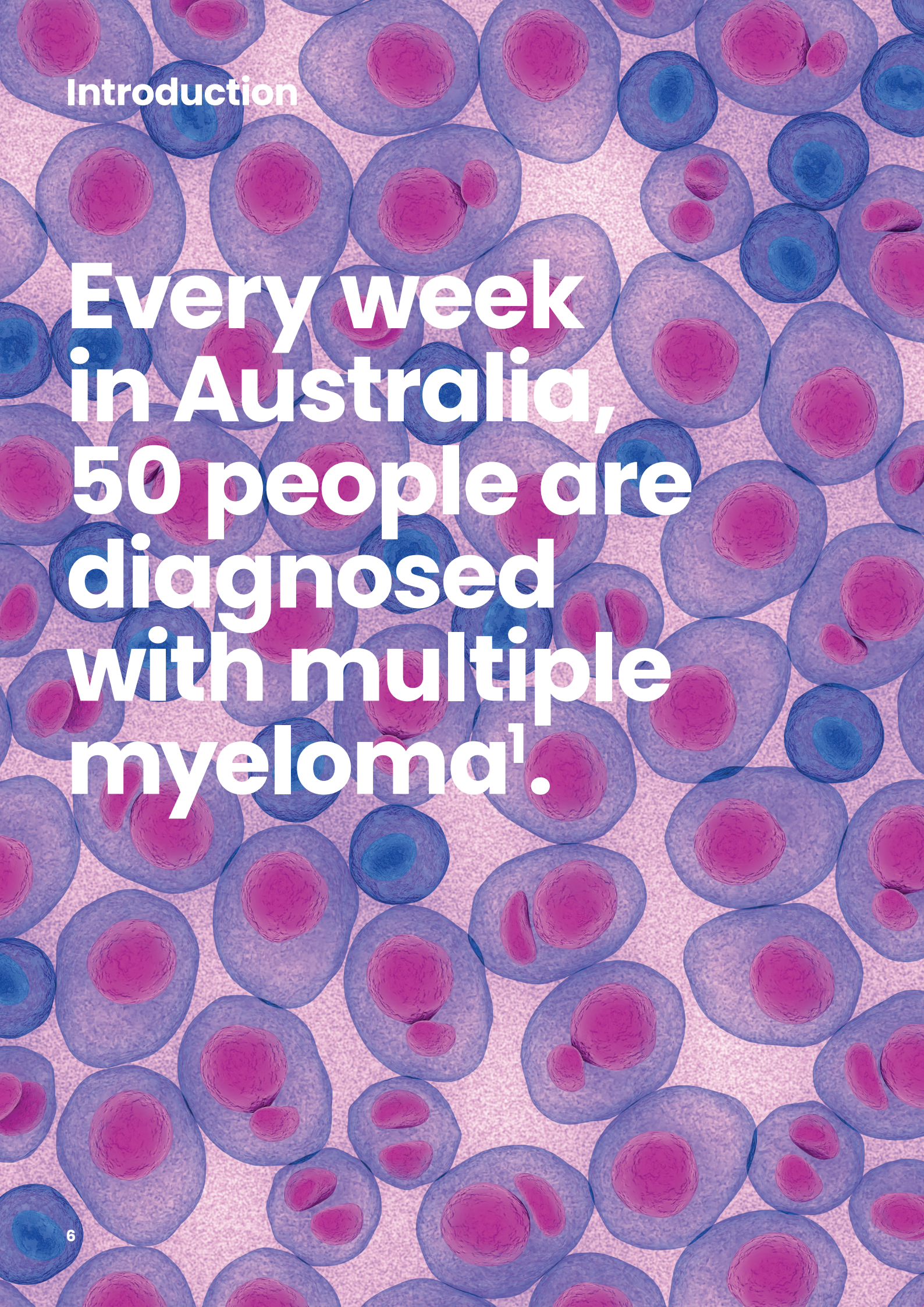
The basic problem is that often a new therapy (referred to as an add-on) for multiple myeloma is used in combination with another therapy (also known as the backbone treatment) that cannot be demonstrated to be cost-effective, despite their obvious clinical benefits.

The result is that companies often see their submissions for funding of their therapies rejected multiple times by the PBAC, or they cannot even see a way forward to apply to have their therapies considered for funding in the first place.

The situation is particularly concerning since other countries, such as the UK and Canada, have found ways to fund these therapies, while Australia has not.

Urgent action needed now

The challenge of how to fund combination medicines is not new, and not unique to multiple myeloma, but the time has come to urgently address it. With an average life expectancy of 5 years from diagnosis, Australians living with multiple myeloma do not have the luxury of waiting years for this economic policy impasse to be resolved.	As an immediate first step, a stakeholder workshop should be convened between relevant companies, the Department of Health and Aged Care, clinicians, and patient advocacy groups as a matter of priority. This is needed to review possible policy options and agree on a way forward.
Previous efforts have failed to resolve the problem and have not gotten the attention or policy priority they deserve. This needs to change.	**The purpose of this discussion paper is to explore and quantify the extent of the problem, with a call for action for all stakeholders to work together to resolve it. If we do not address the lack of innovative combination treatments available in Australia today, the problem will only get worse.**
Urgent action is also needed now because even more new therapies for multiple myeloma are coming to the market in the next few years and are likely to be delayed or not come to Australia unless these issues can be fixed.	Australians living with multiple myeloma, and their family and friends, should not have to wait any longer than they already have for action. They do not have time left to wait.



Every week in Australia, 50 people are diagnosed with multiple myeloma[1].

The goal of treatment is to control the disease, maximise quality of life and reduce the risk of early mortality.[2] Combination therapy improves outcomes for patients in terms of progression free survival and overall survival via a synergistic or an additive manner. By combining agents with different mechanisms of action, combination therapies are considered the most effective option for achieving such remission from newly diagnosed patients through to relapsed or refractory multiple myeloma.

Australians with multiple myeloma are missing out on the latest innovative combination treatments consisting of triplet combinations and four drug combinations.

Nearly 1 in 4 medicines approved by the TGA for multiple myeloma have never been submitted to the PBAC.

The purpose of this discussion paper is to explore and quantify the extent of the problem with an immediate call for action to the Department of Health and Aged Care, clinicians, patient advocacy groups, and industry. If we do not address the lack of innovative combination treatments available in Australia today, the problem will only get worse.

Multiple myeloma in Australia

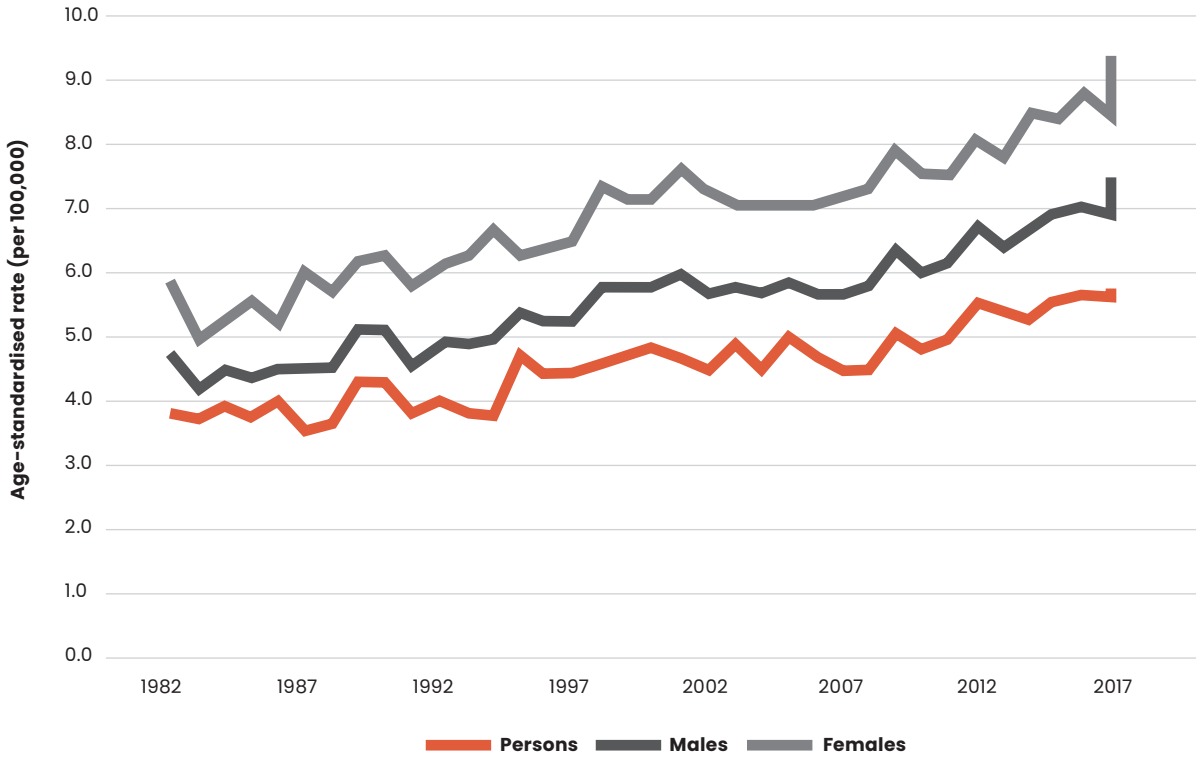
Multiple myeloma accounts for about 10% of haematological cancers in Australia.

There are around 6,500 Australians living with multiple myeloma at any one time.

More than 2,600 Australians are diagnosed with multiple myeloma every year and around 1,000 die from it each year.[4]

The incidence of multiple myeloma in Australia is increasing over time (Figure 2).

Figure 2. Age-standardised incidence rates for multiple myeloma, 1982 to 2018, by sex



The promise of longer life expectancy through better healthcare with more effective treatment options is demonstrated in the rising multiple myeloma survival rate in Australia. The most recent data available shows that Australians diagnosed with multiple myeloma have a 55% chance of living 5 years from the point of diagnosis compared with the general Australian population (**Figure 3**).

Improvements still need to be made. The 55% 5-year relative survival rate for multiple myeloma patients compares less favourably with the 70% rate for all cancers in Australia[5].

4 Cancer Australia. "Multiple myeloma in Australia statistics", Australian Government, 18 August 2022, https://www.canceraustralia.gov.au/cancer-types/myeloma/statistics, accessed 1/9/2022.
5 Cancer Australia, "All cancers in Australia", Australian Government, https://www.canceraustralia.gov.au/impacted-cancer/what-cancer/cancer-australia-statistics, accessed 1/9/2022.

What is the problem?

Combination therapy, where two or more therapeutic agents are combined, is a cornerstone of cancer therapy. While combination therapy is proven to be clinically effective, it is challenging for sponsors to demonstrate cost-effectiveness under Australia's approach to health technology assessment (HTA).

In the case of multiple myeloma, several combination regimens, registered for use in Australia – and funded in other countries – are not available in Australia via the PBS.

As summarised in **Figure 1**, medicines and indications TGA-approved for multiple myeloma are (i) not being submitted to the PBAC, and (ii) PBAC submissions are not resulting in PBS listings. Of the multiple myeloma indications that are TGA-approved, 41% are not PBS listed.

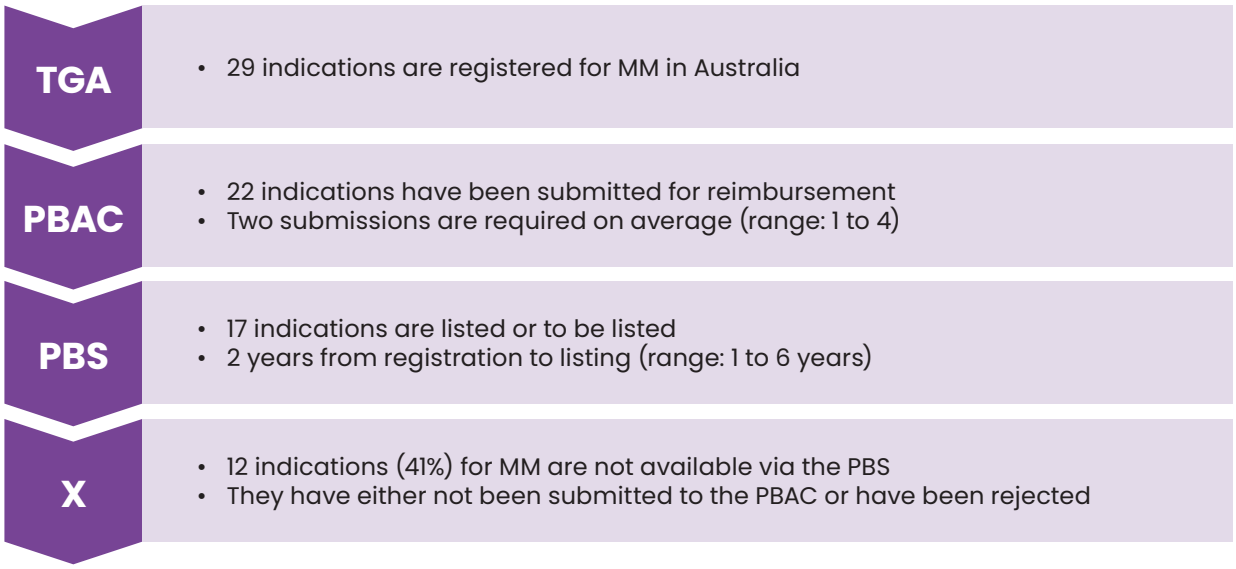
Several innovative combination regimens have never been submitted for funding (n=7/29; 24%). The result is that clinically effective therapies for multiple myeloma are not Government-funded. This means that patients miss out altogether.

An example is isatuximab in combination with pomalidomide and dexamethasone for the treatment of relapsed/refractory multiple myeloma patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor. It was registered with the TGA on 6 May 2020 and has never been submitted to the PBAC. Median progression free survival (PFS) for the triple combination is 11.53 months versus 6.47 months for pomalidomide in combination with dexamethasone. This represents an increase of 78.2%.

Some of the latest treatments have been rejected multiple times for PBS listing. On average, it takes two PBAC submissions to gain a positive recommendation (range: 1 - 4). This means that Australians wait on average 2 years from TGA registration to PBS listing (range: 290 days to 6 years). One example is elotuzumab in combination with lenalidomide and dexamethasone in relapsed/refractory multiple myeloma patients who have received at least one prior therapy. It took two submissions to secure a positive recommendation and close to 6 years from TGA registration to PBS listing and 18 months from the date of the initial PBAC meeting to PBS listing.

Another example is daratumumab in combination with bortezomib and dexamethasone in relapsed/refractory multiple myeloma patients who have received at least one prior therapy. It required four submissions to the PBAC and more than 3 years to PBS listing from TGA registration.

Figure 1. Access to multiple myeloma treatments in Australia (1 May 2022)



Is this a new problem?

No. The problem has existed for years without resolution, despite various attempts by companies, the Department of Health, clinicians, and patient advocacy groups.

Other countries, like the UK and Canada, have found ways to fund these medicines and provide timely patient access while they resolve the technical complexities in their reimbursement systems. A case in point is the UK's Cancer Drugs Fund (CDF). Before the introduction of the CDF, it took on average more than 4 years for multiple myeloma treatments to be funded following registration (range: 243 days to 12 years). This has reduced to 16 months for combinations funded via the CDF (range: 172 days to 2 years).

For example, the funding of daratumumab in combination with bortezomib and dexamethasone in the UK took approximately 2 years from registration compared with 3 years in Australia. Other examples include the funding of ixazomib in combination with lenalidomide and dexamethasone and isatuximab in combination with pomalidomide and dexamethasone via the Cancer Drugs Fund. At the time of writing, neither ixazomib nor isatuximab are available via the PBS in Australia. It is time Australia found a way to fund and provide timely access to these innovative combinations as soon as possible. Too many Australians have been denied treatment.

Without urgent reform, the problem is likely to get worse as more triple and four-drug combination treatments for multiple myeloma become available on the market in the coming years.

What needs to happen?

The Minister for Health and Aged Care, the Department of Health and Aged Care and the PBAC should commit to resolving this issue as soon as possible.

As an early first step, the Department of Health and Aged Care should immediately convene a stakeholder meeting to work through the issues with clinicians, patient advocacy groups and industry to identify a way forward as a matter of priority. It should then advise the Minister on the best way to resolve the issue.

This problem has dragged on for far too long. Australia's 6,500 multiple myeloma patients and their families deserve a solution.

1 https://www.canceraustralia.gov.au/cancer-types/myeloma/statistics; Estimated number of new cases of multiple myeloma diagnosed in 2022: 2,625 divided by 52 weeks equals 50.48 cases every week
2 https://www.myeloma.org/frontline-treatment-options
3 Mokhtari RB, et al. Oncotarget. 2017; 8:38022-43.

Australians are missing out on new multiple myeloma treatments

The clinical pathway for multiple myeloma is complex. As the disease progresses, patients relapse and become refractory to current treatments. The treatment landscape is evolving at a rapid pace and Australia's standard of care is not in line with international best practice and what would be suggested by real-world evidence.

It is well recognised today that anti-cancer treatments are often most effective when used in combination[6]. The treatment area is seeing "clinical development programs increasingly focused on combining different immunotherapies or pairing them with other types of anti-cancer treatments"[7].

The main reason for combining one or more treatments is primarily one of efficacy. Typically, additive benefits such as longer-life expectancy are observed. Additional benefits, however, include a reduced likelihood of treatment resistance developing, and increased options for multiple lines of treatment.

There are several combination treatments that have received approval for use in Australia by the regulator, the TGA (n=29 indications for multiple myeloma; **Figure 1**). A number of these approved treatments have not been recommended by the PBAC for reimbursement on Australia's PBS, while several other treatments have not even been submitted by companies for reimbursement due to uncertainties and technical barriers in the PBS assessment system. Twelve indications have either never been submitted to PBAC or have been rejected to date (**Figure 1**).

This means that there are innovative combination treatment options in Australia that have been shown to be safe and effective in terms of increased progression-free survival and overall survival but are not subsidised and made accessible to Australian patients.

Multiple myeloma patients thus already experience delays and significant wait times for those treatments that are funded through the PBS, while there are a range of other treatments that are not funded, either due to PBAC rejections or because companies do not feel they can submit their treatments for evaluation due to little prospect of success given technical issues in the system.

Tragically, for a disease where the average life expectancy on diagnosis is 5 years, such challenges with reimbursement compromise and cut short precious time a patient can have with loved ones.

6 Gilad, Y.; Gellerman, G.; Lonard, D.M.; O'Malley, B.W. Drug Combination in Cancer Treatment— From Cocktails to Conjugated Combinations. Cancers 2021, 13, 669, http://dx.doi.org/10.3390/cancers13040669, accessed 12/1/2021.
7 SYNEVI. 2019. Assessing & Evaluating Combination Medicines, A report for Medicines Australia, August, Sydney, p. 9.

The system is not working for Australian multiple myeloma patients

Crucially, the delays and restrictions on access to the latest and most clinically effective combination treatments are not due to questions about whether they work. There is agreement among clinical experts that there is demonstrable benefit for multiple myeloma patients in receiving such treatments.

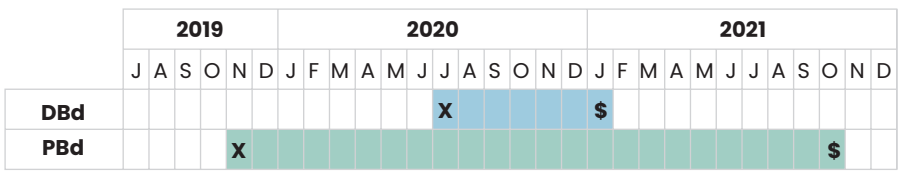
The issue with access lies in the framework of the evaluation system for reimbursement. The result is that current clinical treatment practice for multiple myeloma in Australia is behind international best practice. While various treatments have problems in securing government funding, the roadblocks that often prevent companies even attempting to obtain funding are particularly acute with new innovative add-on therapies designed to be given in combination with a backbone. 'Backbone' and 'add-on' therapies may be owned by the same manufacturer, or the therapies may be owned by different manufacturers where one owns the 'backbone' therapy, and another owns the new innovative 'add-on' therapy (**Table 1**).

Consider the examples shown in **Table 1**, where two combinations utilise the same 'backbone' (bortezomib) and 'add-on' therapies with the same (daratumamab) and different (pomalidomide) manufacturers. The listing of pomalidomide in combination with bortezomib and dexamethasone, with different manufacturers for the 'backbone' and 'add-on' therapy occurred on 1 October 2021. This is nearly 2 years from when it received a positive PBAC recommendation at the November 2019 meeting (Figure 4). In contrast, the listing of daratumumab in combination with bortezomib and dexamethasone, with the same manufacturer for both the 'backbone' and 'add-on' therapy occurred on 1 January 2021. This listing only took 6 months from the positive PBAC recommendation at the July 2020 meeting (**Figure 4**).

Table 1. Examples of 'backbone' and 'add-on' therapies with the same and different manufacturers

Indication	Backbone	Sponsor	Add-on	Sponsor
Daratumamab in combination with bortezomib and dexamethasone in RRMM patients who have received at least one prior therapy	Bortezomib	Janssen	Daratumumab	Janssen
Pomalidomide in combination with bortezomib and dexamethasone in RRMM patients who have received at least one prior therapy	Bortezomib	Janssen	Pomalidomide	BMS

Figure 4. Time from PBAC recommendation to PBS listing for 'backbone' and 'add-on' therapies with the same and different manufacturers



KEY

DBd	Daratumumab in combination with bortezomib and dexamethasone
PBd	Plmalidomide in combination with bortezomib and dexamethasone
R	Registration: TGA approval
X	Positive PBAC recommendation
$	PBS listing

Source: Maestro Database. Accessed 1/9/2022.

The system is not working for Australian multiple myeloma patients (con't)

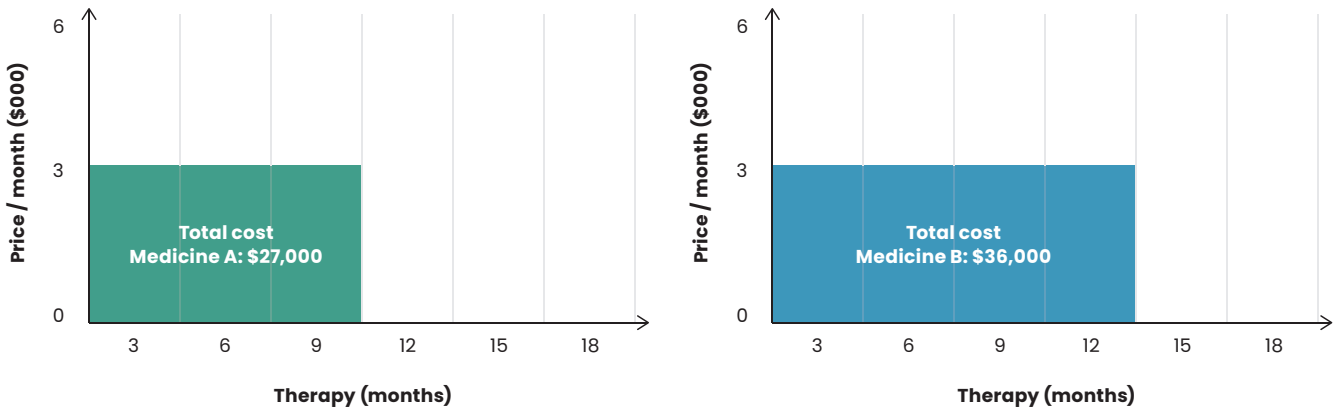
Over the same period, the price of the 'backbone' bortezomib was reduced by 45% on 1 February 2021 due to the removal of the special pricing arrangement, and a further 25% reduction on 1 June 2021 when a second brand listed. This represents a total price reduction of 59% for botezomib, which may have been a factor in the timing of the listing for pomalidomide by improving the cost-effectiveness outcome.

Companies are also currently submitting cost minimisation analyses of their triple combination versus dual therapy. This should be a cause for concern given the basis of cost minimisation submissions is non-inferior efficacy at the equivalent price level. A recent example is elotuzumab in combination with lenalidomide and dexamethasone for the treatment of relapsed or refractory multiple myeloma. The two submissions the company needed to secure a positive PBAC recommendation sought PBS listing on the basis of a cost minimisation analysis versus carfilzomib in combination with dexamethasone.

Ironically, the problems in Australia's medicine evaluation system for combination treatments stem from the fact that such treatments are successful in improving health outcomes for multiple myeloma patients. This is an important outcome for the patient, but the current obstructions in the evaluation and pricing system arise because the new add on treatment extends the duration and cost of treatment beyond the original existing backbone. There is no agreed framework among stakeholders on how to manage this. The result is an impasse and multiple myeloma patients are missing out on treatment options.

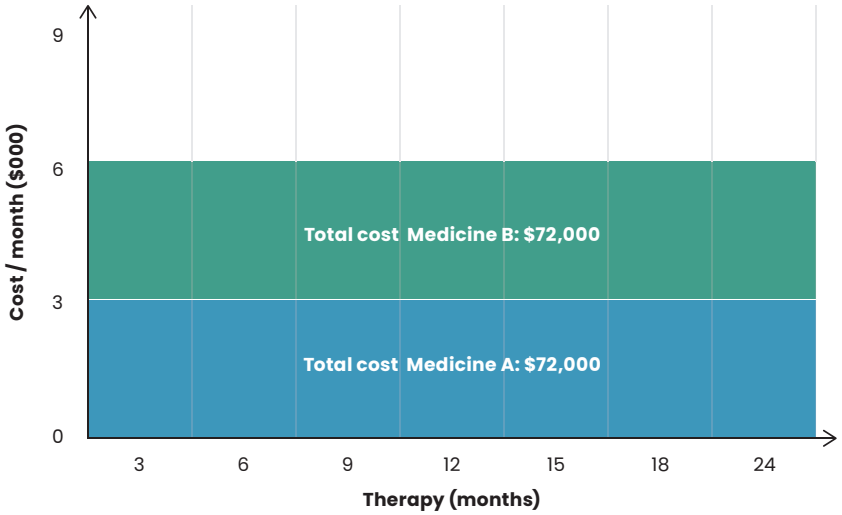
The combination of the backbone therapy together with the add-on therapy can lead to an increase in the duration of treatment for both therapies which leads to increased costs for government. The hypothetical example below (**Figure 5**) highlights the potential impact of two monotherapy treatments being combined for use in a combination treatment that extends a patient's life out to 24 months but increases overall cost to government from $63,000 to $144,000 for that increase in life expectancy. In this example, the use of the individual therapies together in combination leads to an increase in cost of treatment for the patient of $81,000 for an additional 12 months of life (**Figure 6**), leading to budgetary issues and potential breaches of the PBAC's accepted cost-effectiveness thresholds.

Figure 5. Cost and therapy duration of hypothetical monotherapies for cancer treatment



Source: SYNEVi. 2019. Assessing and Evaluating Combination Medicines, White Paper prepared for Medicines Australia, 23 August, Chatswood.

Figure 6. Cost and therapy duration of hypothetical combination treatment for cancer treatment



Source: SYNEVi. 2019. Assessing and Evaluating Combination Medicines, White Paper prepared for Medicines Australia, 23 August, Chatswood.

This can lead to circumstances in which such new combination treatments are not deemed cost-effective even where the new add-on therapy has a zero price.

The issue of how combination treatments are not well handled in the Australian health system was highlighted in the recent Parliamentary Inquiry by the House of Representatives Standing Committee on Health, Aged Care and Sport into approval processes for new drugs and novel medical technologies in Australia. The report, The New Frontier – Delivering better health for all Australians, identified the need to improve how combination treatments are assessed and funded in Australia[8]. The House of Representatives Committee called on the Australian government to review how it assesses the cost-effectiveness and value of combination treatments and make changes. The report notes that the current system was developed before combination treatments were commonplace as is becoming the case today. In its submission to the inquiry, Medicines Australia noted that "recent attempts to examine and resolve these ongoing concerns have made little progress"[9].

8 House of Representatives Standing Committee on Health, Aged Care and Sport. 2021. The New Frontier: Delivering better health for all Australians, Parliament of the Commonwealth of Australia, November, Canberra, https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/Newdrugs/Report, accessed 11/12/2021.

9 Medicines Australia. 2021. Submission to House of Representatives Standing Committee on Health, Aged Care and Sport inquiry into approval processes for new drugs and novel medical technologies in Australia, Submission 141, p. 12, https://www.aph.gov.au/DocumentStore.ashx?id=9dada19a-d008-49c7-8038-2bb11faeda6d&subId=695661, accessed 11/12/2021.

A broader evaluation problem in the Australian system

Australia's current medicines evaluation system means that submissions for combination treatments have a limited chance of receiving a positive recommendation if it is even submitted at all.

The lack of a solution or viable way forward for combination treatments is not limited to multiple myeloma, given the problem extends to other areas of oncology and other disease areas.

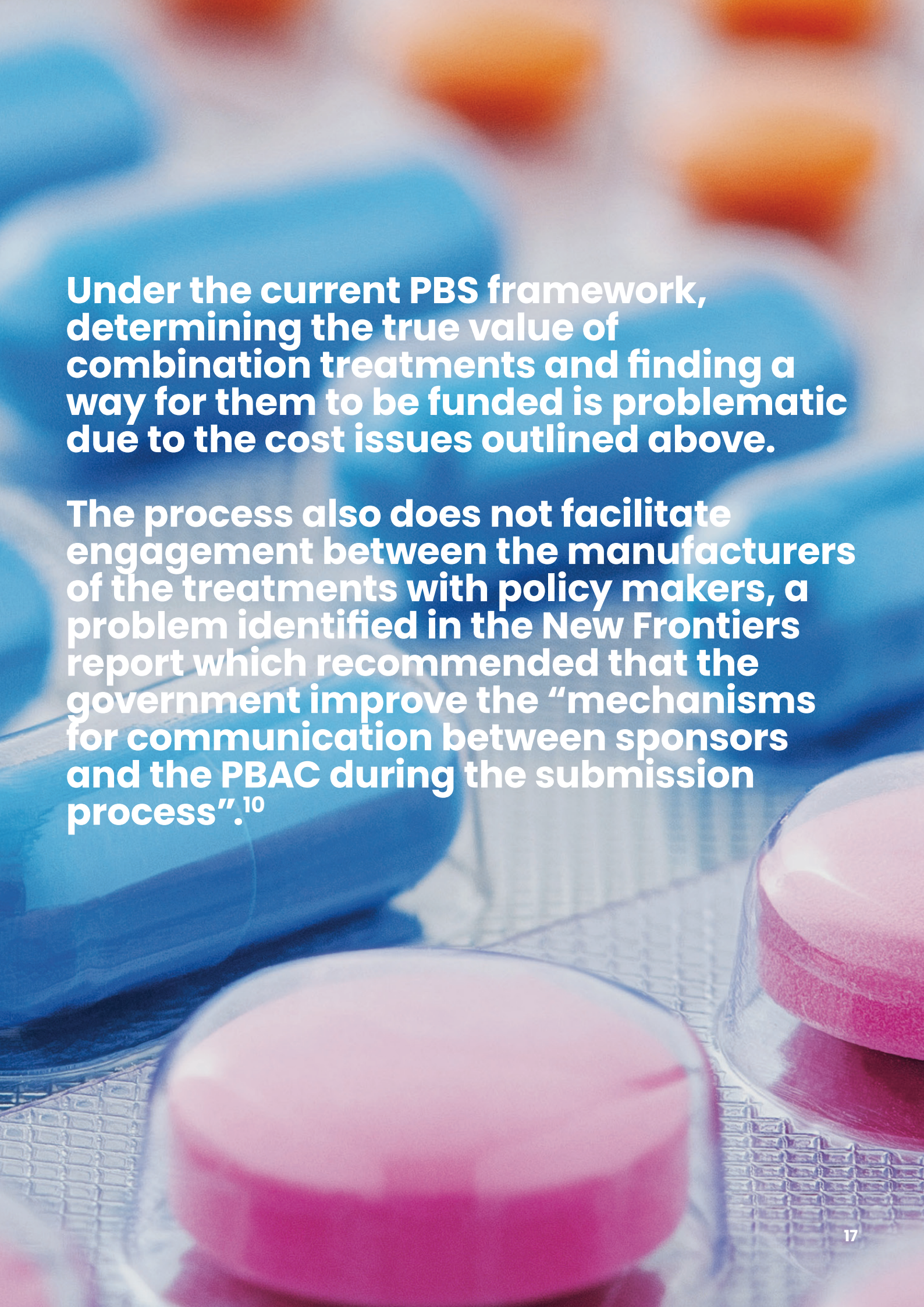
As with other cancers, multiple myeloma patients face a terminal diagnosis while they and their treating physicians are seeing new and effective treatments become standard practice in other countries.

Patients and specialists are united in wanting the Australian system to be modernised to ensure access to the latest clinically and cost-effective medical advances.

While some listings have proceeded, the current evaluation system and funding environment make it very difficult, if not impossible, for companies to proceed with submissions of new combination regimens. The combination of factors such as a lack of flexibility in the evaluation system, problems in the comparison of therapies and the impact of patent expiries and generic price reduction policies all conspire to make an unsustainable environment where companies often cannot bring new therapies to the PBS and Australian patients.

Moreover, with Australia falling behind the rest of the world for funded access, will also mean it may become increasingly difficult to conduct clinical trials here. To provide robust evidence, clinical trials need to have comparable patient populations. One important aspect here is the previous treatments that a patient may have received. If Australian patients do not receive "gold standard" treatment options as standard as patients do in other countries, then Australia's base case of evidence and experience may not be sufficient to secure future clinical trials.
In addition, on ethical grounds it will be difficult, if not impossible, for pharmaceutical companies to run clinical trials for multiple myeloma patients in Australia if there is uncertainty about whether new treatments will ever be funded here.

10 House of Representatives Standing Committee on Health, Aged Care and Sport. 2021. The New Frontier: Delivering better health for all Australians, Commonwealth of Australia, November, Canberra, p. xliv, https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/Newdrugs/Report, accessed 11/12/2021



Under the current PBS framework, determining the true value of combination treatments and finding a way for them to be funded is problematic due to the cost issues outlined above.

The process also does not facilitate engagement between the manufacturers of the treatments with policy makers, a problem identified in the New Frontiers report which recommended that the government improve the "mechanisms for communication between sponsors and the PBAC during the submission process".[10]

What is currently available for Australian multiple myeloma patients?

The table below presents all treatments currently approved by the TGA for use in treating multiple myeloma in Australia (**Table 2**). The line of treatment (first to fourth line) and the sponsor of each treatment is presented.

Treatments highlighted in red are those not currently funded in the Australian healthcare system either because they have already been rejected by the PBAC, their sponsoring company has not yet made a submission to PBAC, or the combination therapy has only very recently been recommended and not yet listed on the PBS as in the case of elotuzumab.

Clearly, there are multiple treatments available that have not achieved funding under the PBS, both those where (i) one company owns both the backbone and the add-on therapies and, (ii) where combination treatments involve individual therapies produced by different manufacturers.

There are examples where the combination was only funded on the PBS after the price of the backbone therapy was significantly reduced. More work needs to be done to addressing the reasons why combination therapies face such difficulties and barriers in being reimbursed.

Table 2. PBS listings status of multiple myeloma treatments, as of 1 September 2022

	Treatment	Sponsor	Funded?
1st line	Bortezomib + dexamethasone	Janssen	Yes
	Thalidomide + dexamethasone	BMS	Yes
	Lenalidomide + dexamethasone	BMS	Yes
	Lenalidomide + bortezomib + dexamethasone	BMS+Janssen	Yes
	Daratumumab + bortezomib + dexamethasone	**Janssen+Janssen**	**No**
	Relapse		
2nd line	Bortezomib + dexamethasone	Janssen	Yes
	Thalidomide + dexamethasone	BMS	Yes
	Lenalidomide + dexamethasone	BMS	Yes
	Carfilzomib + dexamethasone	Amgen	Yes
	Daratumumab + bortezomib + dexamethasone	Janssen+Janssen	Yes
	Pomalidomide + bortezomib + dexamethasone	BMS+Janssen	Yes
	Carfilzomib + lenalidomide + dexamethasone	**Amgen+BMS**	**To be funded**
	Daratumumab + lenalidomide + dexamethasone	**Janssen+BMS**	**No**
	Elotuzumab + lenalidomide + dexamethasone	BMS+BMS	Yes
	Ixaxomib + lenalidomide + dexamethasone	**Takeda+BMS**	**No**
	Isatuximab + carfilzomib + dexamethasone	**Sanofi+Amgen**	**No**
	Selinexor + bortezomib + dexamethasone	**Antengene+Janssen**	**No**
	Relapse		
3rd line	Pomalidomide + dexamethasone	BMS	Yes
	Isatuximab + pomalidomide + dexamethasone	**Sanofi+BMS**	**No**
	Daratumumab	**Janssen**	**No**
	Panobinostat + bortezomib + dexamethasone	Novartis+Janssen	Ni
	Relapse		
4th line	**Plitidepsin + dexamethasone**	**Specialised Therapeutics**	**No**
	Selinexor + dexamethasone	**Antengene**	**To be funded**

Future multiple myeloma treatments in the pipeline

There are many more combination treatments for multiple myeloma in the pipeline. Of the 478 phase 2 or phase 3 clinical trials for multiple myeloma currently being undertaken worldwide[11], the vast majority are for new treatments given in combination with other existing treatments. Some of the treatments most likely to make it to market include, but are not limited to:

- **Elranatamab (as monotherapy plus lenalidomide and/or pomalidomide)**
- **Belantamab (plus carfilzomib)**
- **Ibrutinib (plus carfilzomib)**
- **Lisaftoclax (plus pomalidomide)**
- **Venetoclax (plus bortezomib and/or carfilzomib)**
- **Nivolumab (plus pomalidomide and/or elotuzumab), and**
- **Isatuximab (plus lenalidomide and bortezomib plus dexamethasone).**

These treatments may seek regulatory and funding approval soon. It is worth noting that many of the existing backbone treatments that form part of these new combination treatments are not due to go off-patent for some time.

Unless the framework for valuing combination medicines changes, new combination treatments in areas like multiple myeloma may never be submitted to the PBAC for PBS listing. This is in contrast with some of the more recent positive PBAC recommendations where the backbone therapy has been close to patent expiry and, therefore, likely to experience imminent price reductions anyway.
Waiting many years for backbone therapies to lose patent protection and so become cheaper for the newer combination treatments likely to become available is not a sustainable solution. It is not a fair solution for Australian patients with a terminal diagnosis today.

Finally, current problems of listing multiple myeloma combination treatments, including both dual and triple combination treatments, are likely to become more severe as four drug combination treatments become more common in clinical practice. The complexities and rigidities in the evaluation system combined with an increasing number of dual, triple, and four drug therapies risks breaking the system altogether.

The result is that Australian multiple myeloma patients will miss out even more. Several four drug combination treatments are currently undergoing clinical trial, reinforcing the need to expedite reform of the framework for determining value of combination treatments.

11 Shawview Consulting analysis of www.clinicialtrials.gov, access 9/12/2021.

Urgent change is needed now.

The highest priority is to find a solution quickly for the benefit of Australian multiple myeloma patients and other cancer patients more generally. Without a resolution, this situation will worsen over time, leaving Australia with an outdated treatment landscape unless there is proactive action from government, industry, and other stakeholders.

In a system that does not effectively value and manage these types of emerging innovations, Australian multiple myeloma patients will be left behind compared to patients in other countries. Without urgent action now, many more Australian multiple myeloma patients will miss out on options to extend their lives. They will die before their time.

While the House of Representatives inquiry, **The New Frontier**, has highlighted the issues and the Australian Government's forthcoming HTA Review provides an opportunity for further consideration, time is of the essence. This is particularly so given the amount of time and discussion that has continued over the years with little resolution of the issues.

As an urgent first step, a stakeholder workshop should be convened between relevant companies, patients, carers, patient advocacy groups, clinical groups, the Department of Health and Aged Care and PBAC as a matter of priority This is needed to review possible policy options and agree on a way forward, particularly given the recommendations coming out of the House of Representatives inquiry report.

There has already been much discussion and analysis on this topic with little to show for it. Meanwhile, Australia's multiple myeloma patients are forced to wait for a solution. It is disappointing that there have already been several workshops held in Australia within the last few years that have failed to resolve these issues or ensure the implementation of solutions.

The growing number of combination treatments, the previous failures to solve the issue and the number of Australian multiple myeloma patients who are dying too early while waiting for these administrative issues to be fixed now make this an urgent priority.

Determining what is needed to make progress in this important area in a frank, open workshop between interested parties, to build on previous discussions, evidence to date and the House of Representatives inquiry report is now critical.

Urgent action is needed. Australian multiple myeloma patients have been made to wait too long for improvements, and many have died too early waiting.

Attachment: Time taken to secure PBS listing for multiple myeloma treatments

Technology and sponsor	Indication (combination treatments* in bold)	PBAC Guidance (days to PBS listing from 1st PBAC submission, if applicable)
Thalidomide, THALOMID® *Celgene*	Patients with NDMM who are ineligible for ATSC	Recommended (300)
	In combination with dexamethasone for NDMM that has progressed after one therapy	Recommended (100)
	As monotherapy in RRMM patients	Recommended (852)
Bortezomib, VELCADE®, *Janssen*	In combination with melphalan and prednisone for NDMM not eligible for high dose chemotherapy	Recommended (191)
	As part of combination therapy, for induction therapy prior to high dose chemotherapy with autologous stem cell transplantation for NDMM patients less than 65 years of age	Recommended (334)
	Later-line for patients who have received at least one prior therapy and who have progressive disease	Recommended (685)
	For NDMM with severe acute renal failure with corticosteroid and/or cyclophosphamide	Recommended (262)
Carfilzomib, KYPROLIS® *Amgen*	Later-line, combination with dexamethasone in RRMM patients	Recommended (756)
	Later-line, combination with lenalidomide and dexamethasone in RRMM patients	Recommended March 2022 (Not yet listed)
Lenalidomide, REVLIMID® *BMS (Celgene)*	First-line, combination with bortezomib and dexamethasone in NDMM patients ineligible for ASCT	Recommended (290)
	First-line, combination with dexamethasone in NDMM patients ineligible for ASCT	Recommended (454)
	As maintenance monotherapy in NDMM patients post ASCT	Recommended (805)
	In combination with dexamethasone in RRMM patients	Recommended (683)
	In combination with dexamethasone in NDMM for patients ineligible for ATSC	Recommended (574)
Pomalidomide, POMALYST® *BMS (Celgene)*	In combination with bortezomib and dexamethasone in RRMM patients	Recommended (934)
	In combination with dexamethasone in RRMM patients who have had at least two prior therapies	Recommended (507)
Daratumumab, DARZALEX® *Janssen*	In combination with bortezomib, melphalan and prednisone in NDMM patients' ineligible for ASCT	Rejected
	Later-line, combination with bortezomib and dexamethasone in RRMM patients	Recommended (1,276)
	Later-line, combination with lenalidomide and dexamethasone in RRMM patients	Rejected
	Last-line, monotherapy	Rejected^
Plitidepsin, APLIDIN® *Specialised Therapeutics*	Last-line, combination with dexamethasone in RRMM patients	Rejected
Elotuzumab, EMPLICITI® *BMS*	Later-line, combination with lenalidomide and dexamethasone in RRMM patients	Recommended (546)
Ixazomib, NINLARO® *Takeda*	Later-line, combination with lenalidomide and dexamethasone in RRMM patients	Rejected
Panobinostat, FARYDAK® *Novartis*	Later-line, in combination with bortezomib and dexamethasone in RRMM patients	Not Submitted
Isatuximab, SARCLISA® *Sanofi*	In combination with pomalidomide and dexamethasone in RRMM who have had at least two prior therapies including lenalidomide and a proteasome inhibitor	Not Submitted
	In combination with carfilzomib and dexamethasone in RRMM patients who have had at least one prior therapy.	Not Submitted
Selinexor, XPOVIO® *Karyopharm Therapeutics /Antengene*	Later-line, in combination with bortezomib and dexamethasone in RRMM patients	Rejected

* 'combination' term applied to treatments given in combination with existing treatments that are on-patent and are made by a different manufacturer

^ A condition of the listing for daratumumab in combination with bortezomib and dexamethasone was to provide monotherapy on a compassionate access basis

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