evohealth

January 2024

Changing lives:

Improving access to blood cancer treatments in Australia

Evohealth acknowledges that we work on the traditional lands of many Aboriginal clans, tribes, and nations.

We commit to working in collaboration with Aboriginal and Torres Strait Islander communities and peoples to improve health, emotional and social well-being outcomes in the spirit of partnership.

About **Evohealth**

The delivery of healthcare is complex.
Our focus is not.

Better health for all.

CHANGING LIVES:
IMPROVING ACCESS TO BLOOD CANCER TREATMENTS IN AUSTRALIA

CONTENTS.

ABOUT THIS REPORT

BACKGROUND

Changing lives: Improving access to blood cancer treatments in Australia is an evidence-based and product agnostic report developed between July and December 2023. It was independently authored by Evohealth, a specialist health advisory firm, in partnership with an expert Advisory Committee of clinicians and a patient advocate. This report considers gaps in access to treatments for blood cancer in Australia in the context of the ongoing Health Technology Assessment Policy and Methods Review.

APPROACH

This report focusses on blood cancers and examples of treatment access gaps that currently exist in Australia compared to overseas.

This report was informed by:

- A comprehensive review of published academic literature, grey literature, and clinical guidelines;
- Interviews with Australian clinicians, patients and patient advocates with experience accessing treatments for blood cancer in Australia; and
- The contributions of our expert Advisory Committee members.

While this project received funding from Janssen Australia, Janssen representatives did not participate in the development of the report to ensure the independence of Evohealth and the expert Advisory Committee.

ACKNOWLEDGEMENTS

Evohealth wishes to acknowledge the ongoing support from the individuals and organisations who contributed to this project.

In particular we would like to acknowledge the expert Advisory Committee who provided critical oversight and input to the development of this report. The expert Advisory Committee comprised the following members:

Professor Stephen Mulligan
Royal North Shore Hospital

Professor John Seymour
Peter MacCallum Cancer Centre, and Royal Melbourne Hospital

Sharon Winton
Lymphoma Australia

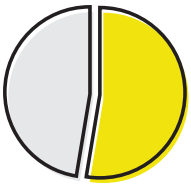
EXECUTIVE **SUMMARY**

A trio of blood cancers are killing Australians

Blood cancers are broadly classed under three main types - leukaemia, multiple myeloma, and lymphoma, but also include other rare and associated disorders. These cancers affect people of all ages and walks of life. Despite improvements in life expectancy, the number of people diagnosed each year continues to grow. [1] As the 135,000 Australians living with blood cancer know all too well – the diagnosis is difficult, and treatment is even more challenging. [1]

AN ADDITIONAL AUSTRALIAN IS DIAGNOSED WITH BLOOD CANCER EVERY **27 MINUTES**. [1]

APPROXIMATELY **2,212** AUSTRALIANS DIED FROM LEUKAEMIA IN 2022. [1]



ONLY **55%** OF PATIENTS ARE ALIVE FIVE YEARS AFTER DIAGNOSIS WITH MULTIPLE MYELOMA. [2]

APPROXIMATELY **7,397** AUSTRALIANS WERE DIAGNOSED WITH LYMPHOMA IN 2022. [3]

The gruelling toll of treatment

Traditional treatments for blood cancer are intensive, debilitating, and long, placing a significant burden on patients, their caregivers, and families. [4, 5] Many treatments come with substantial toxicities and significant side effects that make them almost unbearable. The quality of life for patients undergoing these treatments is poor. [4, 5]

Many of these patients wait in hope as they learn about the potential of exciting new therapies that could improve their prognosis and quality of life as they undergo necessary treatment.

There is hope on the horizon

Many patients treated with newer and novel therapies can expect to live longer with less disease burden than conventional treatment options. [6, 7] Targeted therapies, including chimeric antigen receptor (CAR) T-cell therapy, bispecific antibodies and Bruton's tyrosine kinase (BTK) inhibitors, are changing the treatment paradigm of blood cancers for the better. These treatments offer hope for patients, but only if they can access them within Australia's health system.

> *I don't worry about the science; the drugs are there. What's important is that we have a system that is ready to assess them when they arrive.*
>
> **- Clinical haematologist**

Australian patients are missing out

Our National Medicines Policy (NMP) promises timely availability of safe, effective, and affordable medicines for all Australians. [8] In practice, this means that any Australian, in any location, should be able to access innovative medicines when and where they need them.

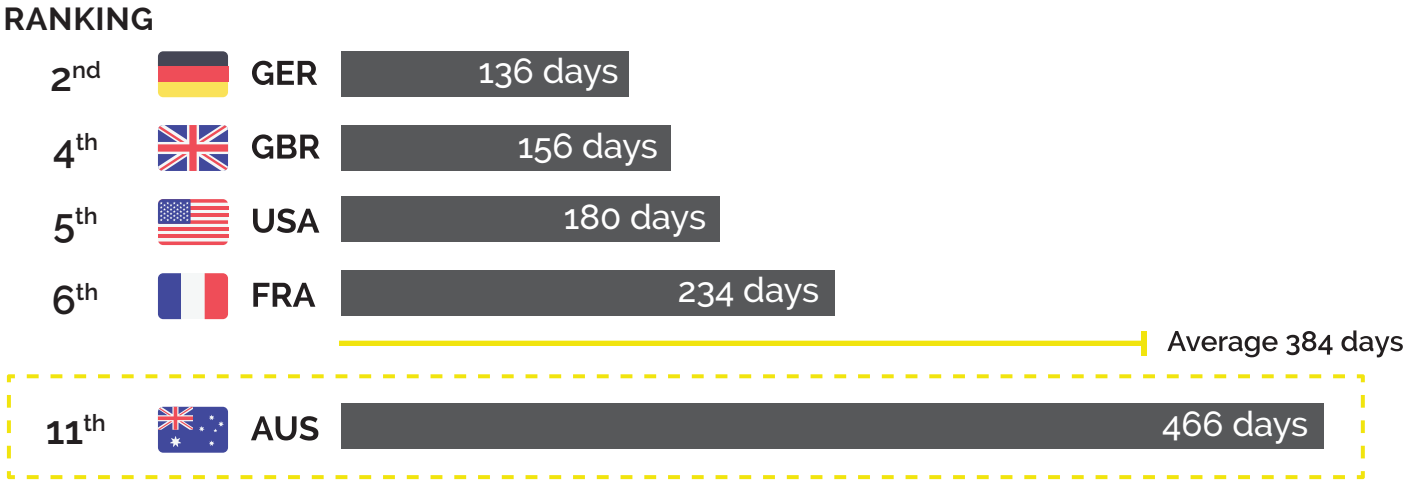
The NMP aligns with the Australian psyche and our pride in having a world-class health system. Whilst this may have been true in the past, for blood cancer, there is increasing evidence that Australians are missing out on access to treatments.

For each of the three main types of blood cancer, Australia has fewer registered therapies compared with Europe and the United States, with the exception of treatments for leukaemia registered via the European Medicines Agency (EMA). What is even more concerning is that for each of the therapies listed on the Australian Register of Therapeutic Goods (ARTG), only 70 per cent are publicly subsidised and therefore available to patients across Australia.

Only **7 out of 10** treatments for blood cancer registered in Australia are funded. [9]

According to Medicines Australia's last *Medicines Matter* report, between 2016 and 2021, the average time from registration to reimbursement for the 20 Organisation for Economic Co-operation and Development (OECD) countries analysed was 384 days, with Australia's average at 466 days (Figure 1). [10]

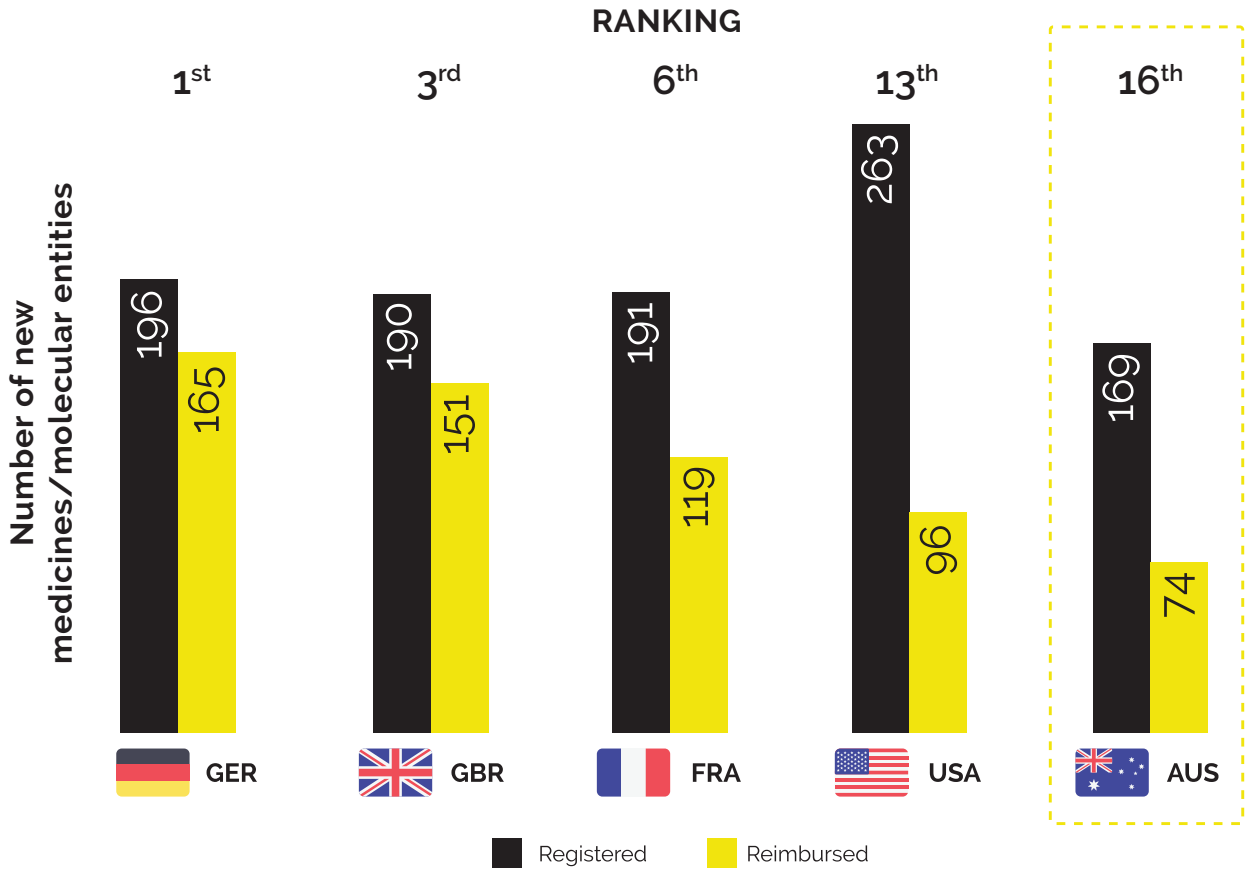
Figure 1: Average time from registration to reimbursement between 2016-2021 [10]'



Adapted from Medicines Australia 'Medicines Matter' report 2022.

Further, when it comes to reimbursement, between 2016 and 2021, Australia ranked 16th among these OECD nations for the number of new molecular entities or new medicines reimbursed. [10] For a nation that prides itself on a world-class health system, this is a disappointing result for patients (Figure 2).

Figure 2: Number of new medicines registrated and reimbursed between 2016-2021 [10]



Adapted from Medicines Australia 'Medicines Matter' report 2022

Even when treatments are available it does not always mean that access is guaranteed. Complicated treatment sequencing and restrictions for Pharmaceutical Benefits Scheme (PBS) subsidised access, as well as the inability of our health technology assessment (HTA) system to value combination treatment, has significant treatment implications for clinicians and their patients daily in Australia.

A system under reform

Yet, there is much to be hopeful for. In late 2023, the Government released its much-anticipated response to the *The New Frontier – Delivering better health for all Australians* report. [11] This report, released in 2021, provided 31 recommendations for improving patient access via evolution of Australia's HTA system. Much of the Government response acknowledges that solutions will be developed alongside the concurrent HTA Policy and Methods Review.

Also of relevance is the mid-term review of the National Health Reform Agreement (NHRA). [12] The NHRA commits the Australian Government and all State and Territory Governments to work together to improve health outcomes for all Australians and ensure sustainability of the health system. [13] With some treatments for blood cancers considered specialised, high-cost therapies and funded under the NHRA, this review is of critical importance to patients in Australia. [14]

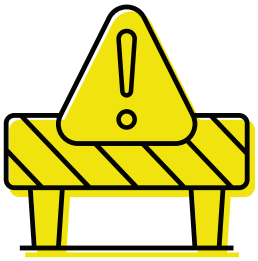
Taking a step back, we need to make substantial changes [to our HTA system]. It's our climate change moment.

- Clinical haematologist

Access to innovative blood cancer therapies has been in entropy for too long. However, with a government that isn't opposed to reform, the time is right for real and lasting change. Bold reform that provides access to the best treatments available is what we need to improve the lives of our fellow citizens.

We have identified six key barriers to best practice blood cancer care access in Australia. Each of these barriers are ripe for reform in the context of both the HTA Policy and Methods review and NHRA mid-term review.

The barriers are:



1. Application for registration in Australia is unattractive.
2. Lengthy delays in achieving funding.
3. No clear HTA pathway.
4. Focus on budgetary impact.
5. Complex prescribing restrictions that are not aligned with best practice care.
6. Inability to effectively value combination therapy.

Investment in best practice treatment for blood cancer is an **investment in the hope of a future for Australian patients.**

With deaths from blood cancer ranked third of all cancers in Australia, our citizens expect timely access to treatments that support them to live longer and better despite a blood cancer diagnosis. [15]

To ensure equitable, timely, safe, and affordable access to treatments for blood cancer in Australia, we must reduce barriers to accessing these therapies. This report aims to explore the extent of the problems hindering access and pose options and solutions for how to address them. Getting this right and improving access to blood cancer treatments for Australian patients has the potential to change lives.

RECOMMENDATIONS

We provide seven evidence-based recommendations informed by research, as well as our analysis of registration and reimbursement data from Australia, Europe, and the United States. These recommendations are crafted to fit within the scope of both the review of Australia's HTA system and the NHRA.

To change lives and improve access to life-saving treatments for blood cancer in Australia, we need to:

RECOMMENDATION 1

Enhance incentives offered for ARTG registration in Australia to ensure that, as a country, our regulatory process is commensurate with similar advanced economies and health systems.

RECOMMENDATION 2

Establish a separate authority outside of the scope of HTA committees that considers price and budget impact.

RECOMMENDATION 3

Leverage the policy imperative from the mid-term review of the NHRA, and current HTA review, to deliver a single HTA body to evaluate all therapies, inlcuding high-cost and highly specialised treatments.

RECOMMENDATION 4

Establish a single source of Federal funding for high-cost therapies as part of the mid-term review of the NHRA.

RECOMMENDATION 5

Conduct a comprehensive review of restrictions for PBS-subsidised blood cancer therapies to ensure alignment with contemporary best-practice clinical care.

RECOMMENDATION 6

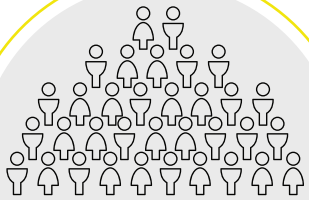
Within the current HTA review, ensure that flexible pricing and payment models are included that adequately capture the value that combination therapy can deliver to patients with blood cancer.

RECOMMENDATION 7

Embed an ongoing five-year review process into Australia's HTA framework following the outcomes of the current HTA review.

BLOOD CANCERS IN **AUSTRALIA**

Blood cancers are the **third biggest** cause of cancer deaths in Australia. [16]



By 2035, more than **35,000 Australians** per year are expected to be diagnosed with blood cancer. [3]

An additional Australian is diagnosed with blood cancer every **27 minutes.** [1]

2,212 Deaths

Approximately **2,212** Australians died from leukaemia in 2022. [1]

Approximately **7,397** Australians were diagnosed with lymphoma in 2022. [3]

only 55%

of patients are alive five years after diagnosis with multiple myeloma. [2]

AUSTRALIAN PATIENTS ARE **MISSING OUT**

On average Australia takes **466 days** from registration to reimbursement for new medicines, which is **82 days longer than average** for OECD countries. [10]

AUSTRALIA **RANKS 16TH**

among the OECD nations for the number of new molecular entities or new medicines reimbursed. [10]

Only **7 out of 10** treatments for blood cancer registered in Australia are funded. [9]

41%

of TGA-approved combinations for multiple myeloma are not listed on the PBS. [17]

THE WAIT FOR **ACCESS TO TREATMENTS**

Lenalidomide for multiple myeloma took over **450 days** to be PBS listed from the time it was registered with the TGA. During this time patients had to pay **$200,000** to access **a single course of treatment.** [18, 19]

Venetoclax used to treat chronic lymphocytic leukaemia took over **550 days** to be funded on the PBS after it was registered with the TGA. [21, 22]

Brexucabtagene autoleucel

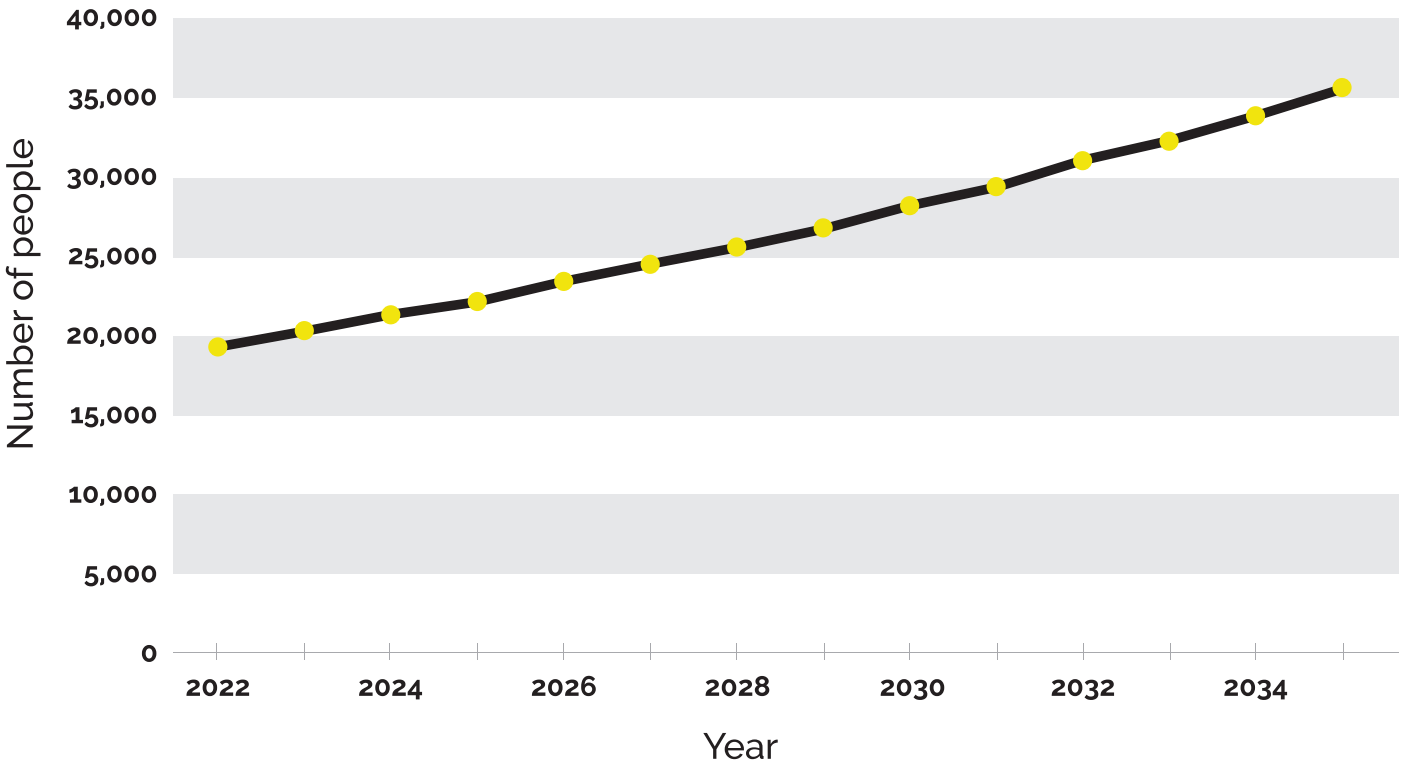
has not yet been funded for the treatment of relapsed of refractory mantle cell lymphoma despite receiving a positive MSAC recommendation **over two years ago** in July 2021. [20]

MODERN MEDICINE, **LEGACY SYSTEMS**

Every **27 minutes**, someone in Australia is diagnosed with blood cancer. [1]

Blood cancer is a condition that can impact individuals across all age groups, but is particularly prevalent among children and older adults (Figure 3). In 2023, blood cancers collectively constituted approximately 12 per cent of all cancer cases in Australia, affecting nearly 20,000 individuals who received a diagnosis. [15] Regrettably, the occurrence of blood cancers is on the rise, despite notable advancements in life expectancy. [1]

Figure 3: Projections for incidences of all blood cancers in Australia to 2035. [3]



Adapted from 'Leukaemia Foundation, State of the Nation: Blood Cancers in Australia' report 2023.

These striking figures position blood cancer as the second most frequently diagnosed cancer and the third leading cause of cancer-related deaths nationwide. [16]

Australia boasts a world-class health system. We have a life expectancy of 85.4 years for females and 81.3 years for males. [23] In the 2022-2023 financial year, we spent over $17 billion providing subsidised access for Australians for medicines via the PBS. [24] Yet for clinicians treating patients with blood cancer, their ability to use the best therapies available is becoming increasingly challenging.

The concerning reality is that Australian patients diagnosed with blood cancer are not only entering a terrifying and life-changing period, but also encounter significant obstacles in accessing optimal treatment. This deficiency is a result of a combination of clinical, policy and technical failures accumulated over recent decades.

Adding to the gravity of the situation is the notable disparity in the number of registered blood cancer treatments between Australia and our largest overseas counterparts.

A closer examination of each of the three primary types of blood cancer reveals that Australia consistently trails behind Europe and the United States in terms of registered therapies, apart from leukaemia treatments approved by the EMA (Table 1).

Remarkably, the data also underscores that of the therapies listed on the ARTG, only 70 per cent receive public subsidisation, limiting their availability to patients nationwide.

Only **7 out of every 10** blood cancer treatments registered in Australia receive subsidised funding. [9]

Table 1: Comparison of therapies registered for blood cancer in the US, EU, and Australia, and reimbursed in Australia [9]

		NUMBER OF THERAPIES			
		Registered			Reimbursed
		FDA	EMA	TGA	PBS + Other
BLOOD CANCER	Leukaemia	58	32	42	30
	Multiple myeloma	24	22	20	14
	Lymphoma	58	62	49	34

Key: ***FDA:*** *United States Food and Drug Administration;* ***EMA:*** *European Medicines Agency;* ***TGA:*** *Therapeutic Goods Administration;* ***PBS:*** *Pharmaceutical Benefits Scheme.*

Source: Evohealth

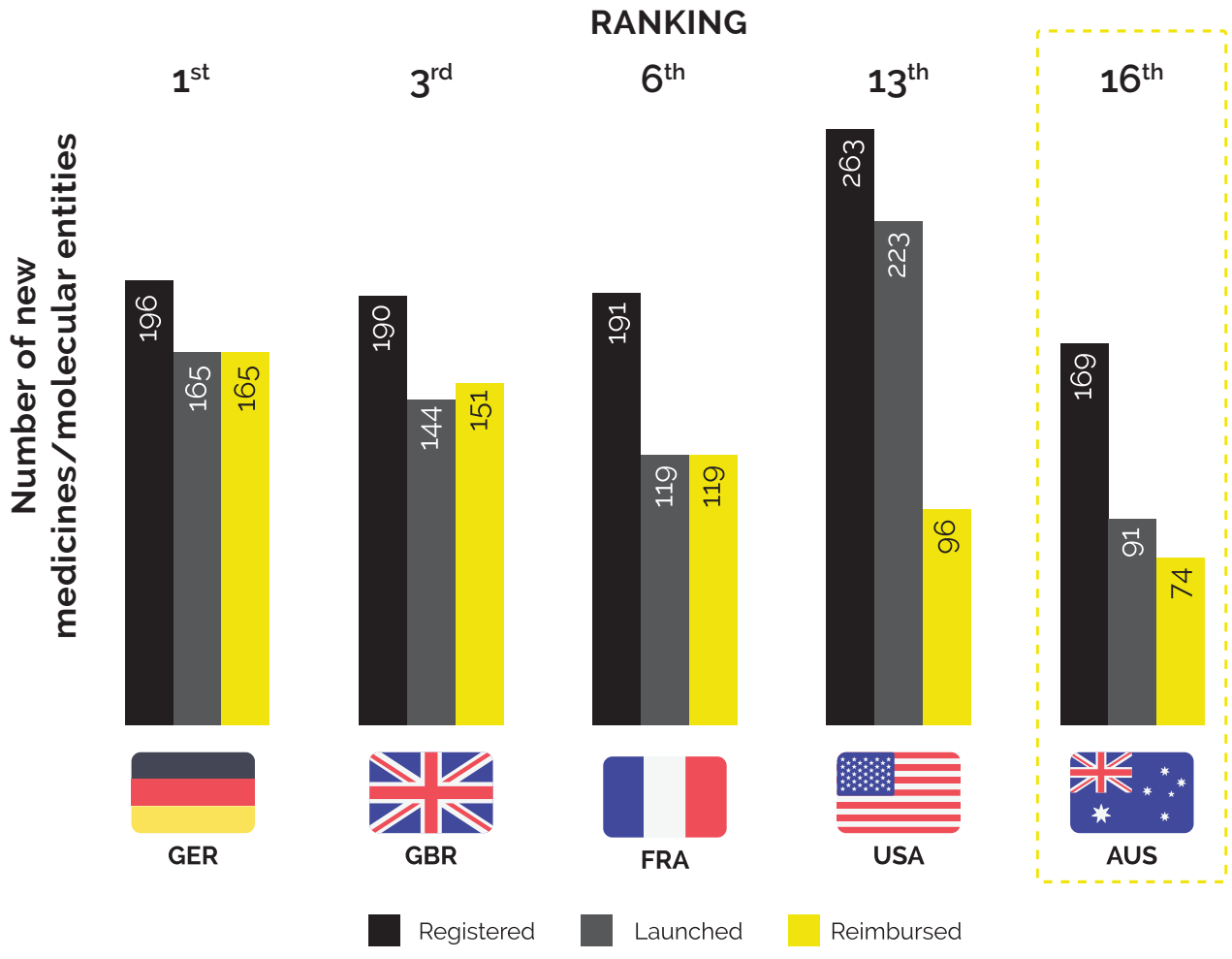
This is only part of the story. Of those therapies that are reimbursed, eligibility is connected to complicated lines of therapy and treatment sequencing that often bears little resemblance to best practice patient care. This has major treatment implications for blood cancer patients every day in Australia.

It is critical then, that questions are asked as to how we have ended up with sub-standard access to clinical care and that solutions are developed to improve access to treatment that not only extends but improves quality of life for blood cancer patients. This report details the result of extensive research and analysis into the very reasons that many Australians have no, or limited, access to the latest innovations in blood cancer care and proposes solutions to address this shortfall.

Why are there gaps in access to best practice care?

There are many reasons why patients are unable to access best practice blood cancer treatment in Australia. As revealed earlier, many therapies are simply not seeking registration in the first place, and of those that do, the HTA path is fraught with challenges and barriers. When it comes to reimbursement, between 2016 and 2021, Australia ranked 16th among the OECD nations analysed for the number of new molecular entities or new medicines reimbursed (Figure 4). [10] This outcome is disheartening for a country that values its top-tier healthcare system.

Figure 4. Number of new medicines reimbursed in OECD nations (2016-2021) [10]



Adapted from Medicines Australia 'Medicines Matter' report 2022

We have identified six critical issues with Australia's registration and reimbursement process that ultimately impedes clinicians from delivering best practice care to patients with blood cancer. These are summarised below:

1 REGISTRATION IN AUSTRALIA IS UNATTRACTIVE

As discussed, many treatments are not even registered in Australia. Without registration, a therapy cannot be made available for therapeutic use, either subsidised, or via private or compassionate access. We cannot determine with absolute certainty why these therapies are not applying for registration in Australia. However, we do know that amongst sponsor companies there is a strong perception of the difficulty in securing appropriate listing and reimbursement, deeming Australia as a less favourable option for registering a therapy in the first place.

2 LENGTHY DELAYS IN ACHIEVING FUNDING

Between 2016 and 2021, the average time from registration to reimbursement for 20 OECD countries was 384 days, with Australia's average at 466 days. [10] Further, the 2021 Inquiry into approval processes for new drugs and novel medical technologies in Australia also identified significant issues in our HTA system, resulting in reduced or no subsidised access to appropriate and best practice patient care. [11]

3 NO CLEAR HTA PATHWAY

Our HTA system is inherently rigid and inflexible in its ability to consider novel and new therapies. The obvious example of this was when CAR T-cell therapy first applied for evaluation in Australia. As a Class 4 biological therapy it was unable to be considered by the Pharmaceutical Benefits Advisory Committee (PBAC), a committee more adept at considering clinical and cost-effectiveness of such an intervention. Ultimately, CAR T-cell therapy was assessed by the Medical Services Advisory Committee (MSAC), which although is ably placed to evaluate medical services, had little or no experience with the required economic, price and funding negotiations. This continues to be an issue with two committees beholden to the legislative remit of an earlier era.

4 FOCUS ON BUDGETARY IMPACT

Submission to Australia's HTA committees, PBAC and MSAC, include provision of detailed evidence of anticipated budgetary impact over the following six-year period. This information is considered alongside safety, clinical and economic data. Since 2010, multiple reforms and policies have been implemented, including a cross-Government policy that ensures any investment in health includes cost offsets, to limit the fiscal growth in the portfolio. This has created a focus on managing and mitigating budget impact, especially for high-cost therapies, within both PBAC and MSAC processes.

5 COMPLEX PRESCRIBING RESTRICTIONS THAT ARE NOT ALIGNED WITH BEST PRACTICE CARE

Eligibility to prescribe and treat patients under PBS criteria and following MSAC recommendation can be rigid and inflexible. In a climate of focus on budgetary impact, they are also often developed to limit fiscal uncertainty and not aligned to best practice treatment guidelines.

Further, the complexity of these restrictions with stringent, detailed lines of therapy cause confusion, or worse, apathy for clinicians when applying for subsidised treatments.

6 INABILITY TO EFFECTIVELY VALUE COMBINATION THERAPY

Many treatments for blood cancer are utilised in combination with two or more other therapies. Australia's HTA system includes assessing this treatment where clinical benefit is deemed to be similar, or better to comparative care.

This creates challenges for valuing these combinations when price setting is rigid and inflexible, thus not allowing sufficient value to be attributed to the second or subsequent agent(s).

> *It's incredibly challenging for a patient if [they are aware] a treatment exists, and they can't access it.*
>
> **- Patient advocate**

We have identified six critical issues with Australia's registration and reimbursement process that ultimately impedes clinicians from delivering best practice care to patients with blood cancer. These are summarised on the next page (Table 2).

Table 2. Examples of therapies and the perceived barriers to access in Australia

			BARRIER TO ACCESS					
THERAPY	THERAPY TYPE	INDICATION	Registration in Australia is unattractive	Lengthy delays in achieving funding	No clear HTA pathway	Focus on budgetary impact	Complex prescribing restrictions	Inability to value combination therapy
LEUKAEMIA								
Brexucabtagene autoleucel	CAR T	ALL			×	×		
Venetoclax	BCL-2 inhibitor	CLL		×		×		
Dabrafenib and vemurafenib	BRAF inhibitor	HCL			×			
MULTIPLE MYELOMA								
Idecabtagene vicleucel	CAR T	Multiple myeloma	×			×		
Ciltacabtagene autoleucel	CAR T	Multiple myeloma			×	×		
Lenalidomide	IMiD	Multiple myeloma		×		×		
Daratumumab + lenalidomide + dexamethasone	Combination	Multiple myeloma				×		×
LYMPHOMA								
Brentuximab vedotin	CD30-directed antibody-drug conjugate	Hodgkin's lymphoma					×	
Pirtobrutinib	BTK inhibitor	MCL	×					

Key: ***ALL:*** *Acute lymphoblastic leukaemia;* ***BCL-2****: B-cell lymphoma 2;* ***BTK:*** *Bruton's tyrosine kinase;* ***CAR T:*** *Chimeric antigen receptor T-cell therapy;* ***CLL:*** *Chronic lymphocytic leukaemia;* ***HCL:*** *Hairy cell leukaemia;* ***IMiD:*** *Immunomodulatory imide drug;* ***mAb:*** ***MCL:*** *Mantle cell lymphoma.*

DELIVERING ON THE **PROMISE OF HTA**

Patients are inherently and appropriately impatient and most blood cancer patients cannot afford to wait. Successive delays in access to blood cancer care has prevented access to treatment readily available overseas, and in some cases cost the lives of Australians. This has been the case for both novel and innovative care, as well as combinations of existing traditional therapies. For example, many of the more recent innovations in practice, including certain CAR T-cell therapies, bispecific monoclonal antibodies and BTK inhibitors, are improving blood cancer care overseas for some indications, but as yet are unavailable in Australia.

The path to access is a difficult one to navigate. For decades, Australia has relied on a HTA framework to assess and manage safe, equitable and affordable access to new therapies. For a time, this system was the envy of the world. However, it was designed for a different era.

Limitations in HTA were acknowledged in the 2021 Inquiry into approval processes for new drugs and novel medical technologies in Australia. The outcome of this inquiry and extensive stakeholder consultation was the report, *The New Frontier – Delivering better health for all Australians*, detailing 31 recommendations for improving patient access via evolution of Australia's HTA system. [11]

Prior to the Government's response to this report in late 2023, there was recognition of the urgent need to begin work on examining our HTA framework. [25] The current HTA Policy and Methods Review commenced in 2022 and offers an opportunity to find our way back to providing critical access to innovative therapies for our fellow citizens if key issues are adequately addressed. [26]

The HTA Policy and Methods Review provides a **once-in-a-generation opportunity** for the Australian Government to ensure that Australian patients can access the treatments they need.

Incentivising registration

Australia's rigorous regulatory framework is critical to ensuring the quality and safety of the treatments available to Australian patients. [27] As recipients of these therapies, we put our trust in this system to evaluate every application with a high level of scrutiny and detail, a process that takes time.

The challenge is striking the right balance between necessary rigour and timely access while also not setting the bar too high for treatments, such as those that treat rare blood cancers in small patient populations.

The Australian market for pharmaceuticals is relatively small compared to overseas markets such as the United States and Europe, accounting for only one per cent of the total global sales. [28] However, market size does not need to impede registration if there are creative mechanisms to encourage sponsors to bring their innovation to Australia.

In all markets, regardless of size, but even more so in Australia, incentives to pursue market authorisation can be critically important. This is particularly true for certain therapies for rare blood cancers. Special designations that streamline regulatory processes and reduce development costs such as orphan drug, fast track, and priority review designation have proven to be an effective approach for sponsor companies to create and introduce therapies for rare diseases with unmet clinical needs in overseas markets. [29]

The United States and Europe offer a range of these incentives for therapies granted orphan designation, encouraging sponsors to seek registration of their therapies to these markets.

These incentives include protocol assistance, administrative support, priority review, data exclusivity to protect clinical trial data, and extended market exclusivity. [30, 31] Australia's incentives for orphan drugs designation are limited to a waiver of the registration application and evaluation fees. [32]

Favourable provisions and pathways for market authorisation can encourage sponsor companies to seek registration for their products. Restrictive and onerous pathways, on the other hand, can create barriers that disincentivise approaches and delay decisions. Examples of therapies such as **idecabtagene vicleucel** (see CASE HIGHLIGHT ONE) and **pirtobrutinib** (see CASE HIGHLIGHT TWO) highlight that accelerated approval pathways in the United States and orphan designation incentives in the European Union (EU) are more attractive for sponsors to apply for market authorisation than those available in Australia. As a result, early access to life-changing therapies is provided in other regions, while Australian patients with blood cancer miss out.

CASE HIGHLIGHT ONE: Registration in Australia is unattractive

Idecabtagene vicleucel for multiple myeloma

Place in therapy: Idecabtagene vicleucel is a CAR T-cell therapy indicated for treatment of patients with relapsed or refractory multiple myeloma. It was the first CAR T-cell therapy approved for multiple myeloma in the United States and Europe. [33, 34]

International: In April 2017, the EMA assigned orphan drug status to idecabtagene vicleucel and in August 2021 granted conditional registration approval as fourth line treatment for adults with multiple myeloma. [35, 36] In the approval EMA stated that it demonstrated clinically meaningful responses for relapsed or refractory multiple myeloma. [34]

In March 2021, the United States FDA also permitted market authorisation to idecabtagene vicleucel as fourth line treatment for adult patients with relapsed or refractory multiple myeloma. [33]

Australia: Idecabtagene vicleucel is yet to receive registration status in Australia and remains a significant gap in the treatment options available to Australian patients with multiple myeloma.

CASE HIGHLIGHT TWO: Registration in Australia is unattractive

Pirtobrutinib for mantle cell lymphoma

Place in therapy: Pirtobrutinib is a highly selective noncovalent inhibitor of Bruton's tyrosine kinase (BTK) with demonstrated resistance to kinase mutations and a better safety profile than comparators. It is used for the treatment of mantle cell lymphoma (MCL).

International: In 2021, the EMA granted orphan designation approval for pirtobrutinib to treat MCL after treatment with another BTK inhibitor. [37] In April 2023, the EMA granted conditional registration stating that it would have been unlikely this therapy would have been developed without the orphan designation incentives. [38] In January 2023, the United States FDA granted accelerated approval for pirtobrutinib, under its accelerated approval pathway, to treat relapsed or refractory MCL (third line). [39]

Australia: Pirtobrutinib has yet to receive registration status in Australia and remains a significant gap in the treatment options available to Australian patients with MCL.

Pathways for therapies that treat rare cancers

Undoubtedly, Australia's robust regulatory framework ensures access to safe and efficacious treatments. However, the disadvantage of this rigour is that it can create barriers to approving therapies with small patient numbers unable to seek registration for minor indication changes without the requisite data. **Dabrafenib** and **vemurafenib** (see CASE HIGHLIGHT THREE) provide two good examples of our regulatory system creating significant barriers for what should be minor indication extensions.

CASE HIGHLIGHT THREE: No clear HTA pathway

Dabrafenib and vemurafenib for hairy cell leukaemia

BRAF gene mutations can cause cancer or cause it to grow more quickly. Inhibitors of the B-Raf enzyme gene, including dabrafenib and vemurafenib, are used to treat patients with a broad range of cancers including melanoma, non-small cell lung cancer and thyroid cancer. [40, 41]

There is strong data to support use of these therapies in orphan rare diseases including BRAF-mutated hairy cell leukaemia (HCL) and histiocytic disorders. [42-44] Unfortunately, due to HCL being a rare form of leukaemia, there are no phase 3 randomised trials to support registration.

These therapies demonstrate a clear example where niche or orphan molecular categories of agents with broad approval can only be used 'off-label' for haematological malignancies where the same molecular abnormalities occur.

Reducing time to reimbursement

Every Australian taxpayer can appreciate that wise and sensible use of our finite funding resources is essential. However, if the balance is not right and we are too frugal with these resources, then this can disincentivise sponsors from considering a submission for market access in Australia. Worse still, a co-dependency exists where if the barriers to funding are too significant, some sponsors may not even consider registering their therapy in the first place.

The *National Health Act 1953* legislates that the PBAC may only recommend the funding of a therapy that they are satisfied is cost-effective. [45] Unfortunately, Australia's willingness to pay for therapies seems to be set at a lower threshold than comparable countries overseas. [45]

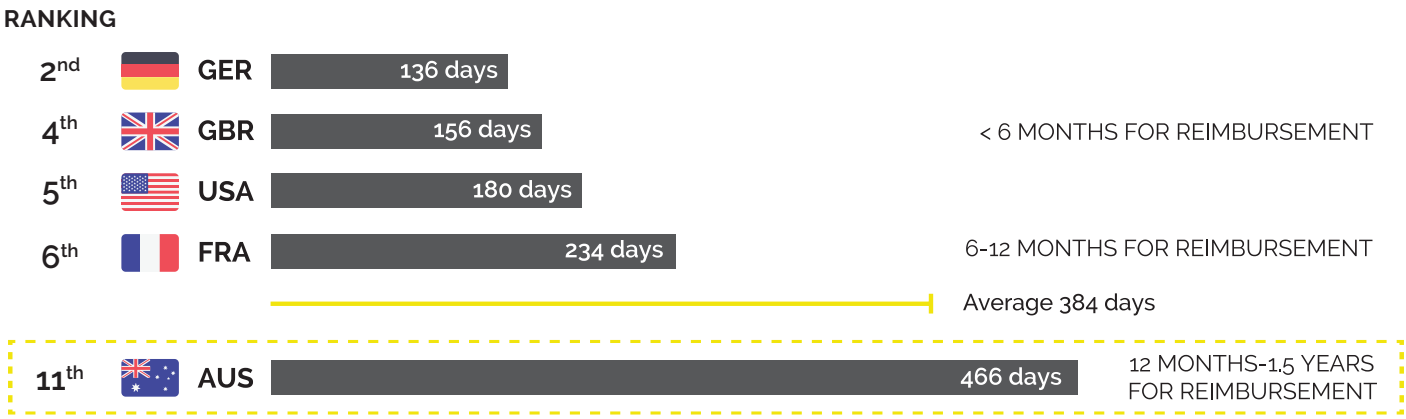
In the United Kingdom, the National Institute for Health and Care Excellence (NICE) states that its implicit cost effectiveness threshold is in the range of £20,000 to £30,000 (approx. AUD$37,000 to $56,000) per quality adjusted life year (QALY) gained, unless for end-of-life treatment where a higher price is acceptable. [46] Unlike NICE, Australia's HTA system does not explicitly state an acceptable incremental cost effectiveness (ICER) threshold. This lack of transparency has led studies assessing previous PBAC decisions to estimate Australia's willingness to pay for therapies to remain between AUD$15,000–$75,000 per QALY gained. [47] A threshold that has barely shifted from the previously estimated AUD$50,000 in the late 1990s. [46, 47]

Without an implicit threshold companies can only speculate the likelihood their treatment will be funded at an acceptable price and this likely pushes Australia lower on the priority list for the launch of newer more expensive treatments. [46] The inflexibility of this willingness to pay metric makes it challenging to evaluate novel treatments that deliver significant improvements in patient outcomes that are often more costly.

Prolonged assessment times are also reported as a disincentive when applying for reimbursement of new therapies in Australia. Despite having mechanisms for parallel registration and reimbursement assessment, Australia's average time from registration to reimbursement is 466 days, while for 20 comparable OECD countries the average is 384 days (Figure 5). [10] Further, it often takes multiple PBAC submissions to receive a positive recommendation, with 1.7 submissions required on average. [47] This affects newer therapies

in particular with one analysis finding that between 1 July 2021 and 30 June 2022 only four out of 37 (11 per cent) of submissions seeking a higher price over the existing alternative(s) were recommended on the first submission. [48] The requirement for repeat submissions costs the sponsor company, disincentivising applications and delaying access for patients.

Figure 5. Average time from registration to reimbursement in OECD nations (2016-2021) [10]



Adapted from Medicines Australia 'Medicines Matter' report 2022.

A further challenge of our current system is the time taken for some treatments to be funded after receiving a positive recommendation by the PBAC. Following a positive PBAC recommendation, several processes must occur to list the medicine, including negotiation and agreement of price with the sponsor company, any restrictions on use and any special pricing agreements or deeds. An analysis of positive PBAC recommendations and subsequent PBS listing between 2010 – 2018 found this process to take between 187–245 days, [47] with a more recent report from March 2021 to 2023 finding this time ranges between 110–138 days depending on the submission type. [48]

In theory a medicine could be reimbursed within 60 days of Therapeutic Goods Administration (TGA) registration if no delays occur at any step of the process and parallel processing is conducted. However, this very rarely occurs and with post PBAC processes taking over three months on average it is no surprise that only 17 per cent of new therapies were reimbursed in Australia in less than six months between 2016 – 2021, placing us a disappointing 13th for timeliness compared to other OECD nations. [10, 48] While these processes are important for judicious use of resources, in reality, each delay experienced as a result of our reimbursement assessment processes creates another patient access gap.

Historical examples such as **venetoclax** (see CASE HIGHLIGHT FOUR) and **lenalidomide** (see CASE HIGHLIGHT FIVE) highlight the lengthy time it can take for a treatment to receive a positive recommendation for funding (17 and 15 months respectively). Unsurprisingly, this wait has significant impact on patients physically, emotionally, and financially.

CASE HIGHLIGHT FOUR: Lengthy delays in achieving funding

Venetoclax for chronic lymphocytic leukaemia

Venetoclax is a BCL-2 inhibitor used to treat chronic lymphocytic leukaemia (CLL), one of the most prevalent forms of leukaemia. It was registered in Australia in December 2015, but was not listed on the PBS until May 2017. [21, 22]

As one of the more common forms of blood cancer, this example highlights how many patients with CLL were forced to pay out of their own pocket for this treatment if they could afford it.

CASE HIGHLIGHT FIVE: Lengthy delays in achieving funding

Lenalidomide for multiple myeloma

For years patients with multiple myeloma faced financial challenges accessing a treatment they knew could be life changing. Lenalidomide was first registered for patients with multiple myeloma in November 2015. [18] These patients knew that this therapy could lead to remission of their disease, but most could not afford to pay for it out of their own pocket as it cost almost $200,000 to access a single course. This life-saving treatment wasn't listed on the PBS until February 2017. [19]

This example highlights how the few patients who received lenalidomide during this time were forced to use their life savings to access treatment despite its proven safety and efficacy.

RECOMMENDATION 1

Enhance incentives offered for ARTG registration in Australia to ensure that, as a country, our regulatory process is commensurate with similar advanced economies and health systems.

Cell therapies for blood cancer

In 2021, our landmark white paper *Cell and gene therapies: Rising to the challenge* forecast considerable challenges that our HTA system would face in assessing the true benefit of these complex and specialised treatments. [49] This included a failure to recognise the transformative value of short-term treatments in our current methodologies. Indirect costs are also not included during evaluation in Australia, which is different to other countries such as France and Germany, where overall access to therapies is considerably higher than in Australia. [10]

Two years on from our first report, we revisited Australia's preparedness for cell and gene therapies (CGTs) in our *Cell and gene therapies: Rising to the Challenge Scorecard 2023*. [50] Progress on HTA reform for CGTs was one of the key indicators we measured and was subsequently rated as 'Some Progress' after our extensive analysis of reforms since 2021 (Figure 6).

Figure 6. 'HTA process for CGTs has been reviewed' was rated as 'Some progress'. [9]

The Minister for Health to establish a cross-functional working group including Department of Health (both Federal and State/Territory), industry, patients, and academics to consider current Health Technology Assessment (HTA) for CGTs.

Indicator	Progress
HTA Processes for CGTs have been reviewed	● ○ ○

○○○ Not Achieved ●○○ Some progress achieved ●●○ Partially achieved ●●● Fully Achieved

Source: Evohealth

The arrival of modern treatments like CAR T-cell therapies in Australia has been system-changing, not only in terms of how it is implemented logistically, but also with regards to impact on our health budget. There is no denying that the financial impact of these therapies will be significant, but so too can be their effect on the lives of patients. CAR T-cell therapy will change the treatment of blood cancers in Australia if we can prioritise national reimbursement. [51] However, decades of reform coupled with intermittent tinkering intended to mitigate and manage budgets have left us with a system that no longer supports the interest of Australian patients.

Ciltacabtagene autoleucel (see CASE HIGHLIGHT SIX) provides an example of a CAR T-cell therapy that Australian patients continue to miss out on due to uncertainty compared to other therapies and a lack of evidence that they provide value for money. Australia's HTA systems must find ways to assess therapies that do not fit neatly into our current processes.

CASE HIGHLIGHT SIX: No clear HTA pathway

Ciltacabtagene autoleucel for multiple myeloma [52-55]

In June 2023, TGA approved ciltacabtagene autoleucel, a CAR T-cell therapy, for registration in Australia as fourth line treatment for relapsed or refractory multiple myeloma. This is the same registration criteria as EMA and even less restrictive than the United States where patients must have failed four prior lines of therapy.

However, MSAC did not support funding this treatment through the NHRA due to high uncertainty in terms of clinical safety and efficacy compared to other treatments and a lack of evidence that it provided good value for money.

The sponsor's application was scheduled to be considered again at the November 2023 MSAC meeting, with the minutes not yet published at the time of writing this report.

Managing budget impact

It is entirely appropriate that Australia's HTA committees are tasked with considering clinical effectiveness and cost-effectiveness of medicines, vaccines, and other therapies. As a committee comprised primarily of clinicians, with some health economists, it is unusual that they are also tasked with considering budget impact of health interventions. The whole of Government cost offset policy and requirement for Cabinet approval for PBS listing of a medicine that will cost more than $20 million per year has led to fiscal concerns about overall cost overshadowing other elements of decision-making, at times. Our HTA committees should be able to focus on making recommendations that optimise health outcomes, leaving budget and decisions on investment to Government. [56]

It is apparent that while many HTA systems worldwide use overlapping criteria, reimbursement decisions only sometimes align, even for economically similar countries. [57] Australia's HTA decision-making could be improved by learning from systems in other countries, enhancing transparency in how decisions are made and the nuances of how criteria are assessed, including benchmarks for PBS listing timelines.

Progressively, PBAC decisions are extending beyond the realm of cost-effectiveness evaluation to encompass considerations for budgetary cost containment. The integration of conservative HTA decisions with budgetary apprehension has led to the unfortunate consequence of Australian patients being deprived of access to essential therapies. [26]

Stakeholders agree that the evaluation of the effectiveness of a treatment should remain distinct from affordability concerns. Incorporating budgetary impact into the overall treatment value erroneously implies that addressing pharmaceutical expenditure alone will resolve systemic affordability challenges, overlooking the presence of various inefficiencies within healthcare systems. [26] To actively consider the value that reflects the impact of a treatment on patient outcomes, their quality of life and long-term healthcare costs, separation of traditional HTA and budget impact is required.

RECOMMENDATION 2

Establish a separate authority outside of the scope of HTA committees, that considers price and budget impact.

CAR T-cell therapy triggered an evolution of public hospital funding for high-cost therapies. In 2021, an addendum to the NHRA established the means for the Commonwealth and States and Territories to fund new high-cost, highly specialised therapies. [58] The Addendum does not specify individual therapies but sets out the conditions under which "new high-cost specialised therapies" will be funded through the NHRA. Funding of specific therapies is under the auspice of the Independent Health and Aged Care Pricing Authority (IHACPA) under instruction from the Commonwealth Minister for Health.

The addendum has two sub clauses that specify the basis to fund such therapies, namely: [13, 59]

- C11a - The Commonwealth will provide a contribution of 50 per cent of the growth in the efficient price or cost (including ancillary services), instead of 45 per cent; and
- C11b - They will be exempt from the national funding cap for a period of two years from the commencement of service delivery of the new treatment.

New high-cost therapies are considered for funding once the Minister has accepted the MSAC recommendation for funding.

This approach to funding has created yet another layer of complex negotiations, as States and Territories are required to contribute 50 per cent of the cost. This has led to further negotiation with sponsor companies resulting in yet more delay and anguish for patients (see CASE HIGHLIGHT SEVEN).

CASE HIGHLIGHT SEVEN: Focus on budgetary impact

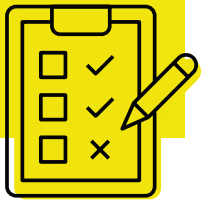
In July 2021, MSAC expressed support for public funding of **brexucabtagene autoleucel**, a treatment for relapsed or refractory mantle cell lymphoma (RR MCL). As of the July 2023 MSAC meeting, there had been no progress in the funding process, however, the sponsor company had submitted a pricing proposal – the first since the original 2021 advice. [20]

Despite a variance between the proposal and the initial advice, MSAC carefully considered the pricing proposal. Ultimately, the committee reaffirmed its support for public funding. MSAC also highlighted the importance of comprehensive data collection through a registry accessible to all stakeholders. Furthermore, they outlined plans for a thorough review of clinical effectiveness, cost-effectiveness, and budget impact within three years post-commencement of public subsidy for CAR-T cell therapy for RR MCL. [20]

In late 2023, the mid-term review of the NHRA was released, including consideration of the Addendum. Amongst the recommendations is a call for a unified national HTA process for the assessment and delivery of high-cost, highly specialised therapies, rather than a response to reducing funding barriers, which is much more within its remit and keeping with feedback from stakeholders during the consultation process. [26]

RECOMMENDATION 3

Leverage the policy imperative from the mid-term review of the NHRA, and current HTA review, to deliver a single HTA body to evaluate all therapies, including high-cost and highly specialised therapies.



RECOMMENDATION 4

Establish a single source of Federal funding for high-cost therapies as part of the mid-term review of the NHRA.

Reducing complexity in care

Cruelly, even when a therapy is registered and reimbursed in Australia, access is not always guaranteed for patients with blood cancer. Complex treatment sequencing requirements can limit a clinician's available treatment options, and rigid PBS eligibility criteria creates an inflexible paradigm that hinders a clinician's ability to adhere to best practice guidelines. With specific treatments only accessible once in a patient's lifetime, the dreadful news that their cancer has returned can be even harder to bear.

Narrow indications permitted by the PBS and complicated restrictions on eligibility for line of therapy limit treatment utility by preventing access to specific therapies until patients have used other treatments that are potentially less effective.

Further, despite going against what would be considered 'best practice' guidelines, patients can even be penalised because a particular therapy was not used in a specific order in their treatment, and some treatments can only be used once in a patient's lifetime and are no longer available to be considered for their treatment if needed in the future.

> *[Australia's PBS criteria] is a minefield of navigation to use [treatments] in the correct sequence so that you don't lose out on an entire treatment option.*
>
> **- Clinical haematologist**

Myeloma conferences in the United States present new and exciting innovation, however it bears virtually no relationship to what is accessible in Australia.

- Clinical haematologist

Brentuximab vedotin (see CASE HIGHLIGHT EIGHT) provides an example where narrow approval and complicated line of therapy eligibility limits patient access by restricting the use of a treatment. Clinicians are forced to carefully plan and sequence a patient's treatment in advance with the limited options available to them and no knowledge of how the patient may respond.

This is not patient centric, and ultimately, they will continue to miss out on treatments as clinicians struggle to navigate the system.

CASE HIGHLIGHT EIGHT: Complex prescribing restrictions

Brentuximab vedotin frontline for Hodgkin's lymphoma

Place in therapy: Brentuximab vedotin is a combination of an antibody that binds to the CD-30 receptor linked to the cytotoxic drug monomethyl auristatin E. The monoclonal antibody delivers the drug molecule to the CD30-positive cancer cells and stops them dividing. [60]

International: The United States FDA and EMA have both approved Brentuximab vedotin first line for advanced HL (stage III and IV) in combination with chemotherapy for patients who have been previously untreated. [60, 61]

Australia: Australian clinicians can only use Brentuximab vedotin for RR HL in patients who have previously undergone an autologous stem cell transplant (ASCT) or two prior therapies when ASCT is not an option. Patients also cannot receive more than 12 cycles of this treatment in a lifetime. [62]

This case highlights the significantly more restrictive use of Brentuximab vedotin in Australia.

RECOMMENDATION 5

Conduct a comprehensive review of restrictions for PBS subsidised blood cancer therapies to ensure alignment with contemporary best practice clinical care.

Valuing combination therapies

In medical oncology, combination therapy is common practice to ensure ongoing evolution and optimisation of care. Patients deserve to receive access to the most effective combination treatments at the appropriate time in the treatment algorithm. Yet combination therapies in cancer continue to present significant problems for affordability and value for money in health systems worldwide. [17] The lack of solutions for combination treatment extends to other areas of oncology beyond blood cancer and into other disease areas as well.

Both the Bellberry *Challenges in valuing and paying for combination regimens in oncology* forum held in 2019 and *The New Frontier – Delivering better health for all Australians* report raise valuing combination therapy within our HTA framework as a key and critical issue, citing significant challenges that must be overcome, including the need for: [11, 63]

- common regulatory definitions and clarity in terminology and regulatory pathways;
- increased collaboration between manufacturers, HTA agencies and payers, particularly when products in a combination are owned by different sponsor companies;
- value attribution frameworks and increased flexibility in pricing negotiations; and
- innovative clinical trial design and optimisation of combination product treatment regimens.

Yet, issues with access to combination treatments continue to exist, particularly in countries such as Australia, where the HTA system focuses on added clinical benefit. Such is the fate of combination therapies under evaluation that some treatments are not being deemed cost-effective even when the additional therapy was added at no cost. [17]

Daratumumab, combined with **lenalidomide** and **dexamethasone** (see CASE HIGHLIGHT NINE), provides an example where reimbursement of combination regimens using current HTA systems can be challenging.

CASE HIGHLIGHT NINE: Inability to value combinations

Daratumumab + lenalidomide + dexamethasone combined therapy for transplant ineligible, newly diagnosed multiple myeloma. [32, 64]

Daratumumab is a monoclonal antibody use to target the CD38 protein found on myeloma cells, lenalidomide is an immunomodulatory drug used to modulate the immune system, and dexamethasone is a corticosteroid that reduces inflammation. Combined, these treatments can have a powerful synergistic effect that exceeds the sum of their parts.

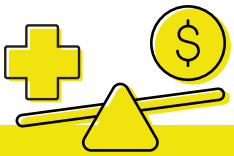
In March 2023 a submission was made to PBAC requesting the listing of this combination therapy on the PBS Section 100 Schedule. The combination had previously been considered for the treatment of RR multiple myeloma.

PBAC did not recommend this combination for reimbursement, citing several concerns. It was also noted "that a substantial price reduction would be required to ensure daratumumab was cost-effective, and that a risk sharing agreement (RSA) would be required to mitigate the high likelihood of use in the transplant eligible population."

With new therapies often patented and owned by different companies, a collaborative approach between all stakeholders will be needed to take necessary steps towards improving patient access to combination therapies. There must also be a willingness for flexibility in pricing and payment mechanisms between sponsor companies and funders to ensure appropriate patient access to clinically effective combination therapies.

As newer treatments emerge there will only be increased potential and demand for combination therapies. If double and triple therapy combinations are already testing the system, how will we account for quadruple or even more therapies when they inevitably arrive?

Australia's HTA system must find ways to value and pay for combination treatment regimens. New frameworks that account for uncertainty and possible long-term benefits of combinations are needed for their practical and meaningful evaluation, including the potential for developing new evaluation methods for combination therapies that are demonstrably superior to single treatments. Fortunately, there is no shortage of support for improving patient access to combination therapies. Industry representatives, HTA agencies, policymakers, payers, and other stakeholders must collaborate to prioritise potential policy options and agree on a critical path to overcome these challenges.



RECOMMENDATION 6

Within the current HTA review, **ensure that flexible pricing and payment models are included** that adequately capture the value that combination therapy can deliver to patients with blood cancer.

FROM SYMPTOMS **TO SOLUTIONS**

Australia's HTA journey began three decades ago when we became one of the first countries to require the submission of evidence for the evaluation of new treatments being assessed for reimbursement. [65] What began as a mechanism to manage affordable access to new medicines in an environment of rising healthcare costs has seen iterative adjustments and updates to enable ongoing assessments to continue as new and innovative health technologies have emerged. Since then, the landscape of health technologies has transformed dramatically. A one-size-fits-all approach to treatment is a blunt instrument that is failing Australian patients with blood cancer. A future where precision and personalised therapy delivers the right therapy to the right patient at the right time based on their unique genetic, biological, and environmental factors is on our doorstep. However, Australian patients are missing out and will continue to do so – unless we can find solutions.

> *"Taking a step back, we need to make substantial changes [to our HTA system]. It's our climate change moment."*
>
> **- Clinical haematologist**

Australian patients with blood cancer need access to optimum treatment, and Australia's clinicians must be able to deliver best-practice medicine to treat them. Our HTA systems must encourage sponsor companies to register their therapies in Australia without fear of prohibitive restrictions or lengthy processes to expand eligibility or introduce new indications.

We must also find ways to reduce the complexity and administrative burden for prescribers by streamlining complex patient PBS eligibility criteria. Only then can clinicians prescribe the therapy they need to treat their patients with the best therapies available.

Achieving this will require monitoring and evaluating the policy impact (both positive and negative) to enable agility in adapting to the impact of implemented changes and course correcting when observations reveal unintended consequences of a policy decision. By doing so, brave and bold policy can be confidently implemented and tested, with measurable goals to track progress towards improving access to cutting-edge blood cancer treatments. Regular feedback on the effectiveness of implemented policy changes can enable adjustments as required to ensure continuous improvement.

HTA review is not enough; we need reform

Calls from industry, academia and the public that Australia's HTA system is 'good but not good enough,' and 'don't let perfect get in the way of good' have been heard by the Australian Government with a commitment to action demonstrated in the ongoing HTA Policy and Methods Review. The HTA review presents an opportunity to address current access gaps such as those outlined in this report and prevent future gaps in access to treatments. While the review offers a significant opportunity for change, ongoing review will be critical in ensuring our system keeps pace with continued advancements in health technologies.

It has taken three decades to achieve a wholesale review of Australia's HTA system. Like the recently reviewed NMP, a formalised five-yearly review process must be adopted for our HTA system. Modern medicine is advancing too quickly. Medical knowledge has been expanding exponentially. Where it doubled every 50 years in 1950, it was predicted that it would take only 73 days to double by 2020, and this was before the current wave of advances in Artificial Intelligence. [66] Innovation and the pace of change is only increasing, and Australia's HTA system needs to keep up. Patients cannot afford to wait another 30 years while the next life-saving treatments are within touching distance.

RECOMMENDATION 7

Embed an ongoing five-year review process into Australia's HTA framework following the outcomes of the current HTA review.

RECOMMENDATIONS

Summary of recommendations

To capitalise on the opportunity to reform our HTA systems and ensure Australian patients can access appropriate, innovative therapies now and in the future, we must embrace the willingness for change. We must seize this opportunity to make the necessary adjustments so that Australia's health system can once more become a model for the rest of the world.

We present seven tangible recommendations for system reform. Our recommendations have been informed by a comprehensive review of academic and grey literature, review of registration and reimbursement data, interviews with policymakers, clinicians, and a patient advocate, and the contributions of our project Advisory Committee.

RECOMMENDATION 1

Enhance incentives offered for ARTG registration in Australia to ensure that, as a country, our regulatory process is commensurate with similar advanced economies and health systems.

This report has surmised that there are a range of reasons why Australians with blood cancer miss out on innovative care. These included Australia's relatively small market, costly submission process and protracted assessment timelines.

We must actively work to remove these barriers and align with similar countries when it comes to timely patient access. One area for noticeable improvement is access to orphan drugs. Australia should follow the lead of authorities such as the EMA and the FDA and increase incentives for sponsors to bring orphan drugs to Australia. The United States and Europe offer a range of incentives for medicines that are granted orphan designation, encouraging sponsors to seek registration of their medicines in these markets, including protocol assistance, administrative support, and extended market exclusivity. For a market as small as Australia's, we need to offer more than a fee waiver to register orphan drugs.

RECOMMENDATION 2

Establish a separate authority outside of the scope of HTA committees that considers price and budget impact.

It is entirely appropriate that our HTA committees consider the clinical and cost-effectiveness of blood cancer care. However, when it comes to managing investment in health as a nation, the process must be removed from HTA assessments. Decisions are currently weighted heavily towards economics, and the value that reflects the impact of treatment on patient outcomes and associated improvements to their quality of life needs to be adequately considered. Separating these functions will enable recommendations to be made to the Minister for Health based on the expertise of the relevant committee while still allowing the Australian Government to remain fiscally responsible.

RECOMMENDATION 3

Leverage the policy imperative from the mid-term review of the NHRA, and current HTA review, to deliver a single HTA body to evaluate all therapies, inlcuding high-cost and highly specialised treatments.

CAR T-cell therapy triggered an evolution of funding for high-cost therapies in Australia's public hospitals. While the addendum to the NHRA attempted to address the funding challenges, the approach created additional complexity for all parties involved, resulting in significant delays to patient access.

The mid-term review of the NHRA has called for the progression of a unified national approach to the framework for HTA assessment and delivery of these high-cost and highly specialised therapies. It is critical that the response to the review from all levels of Government is swift and positive to enable timely and sustainable access to novel therapies as a priority. Patients are dying while they wait. Australians deserve better.

RECOMMENDATION 4

Establish a single source of Federal funding for high-cost therapies as part of the mid-term review of the NHRA.

With countless innovative therapies on the horizon, high-cost and highly specialised therapies are here to stay. Timely, equitable and affordable access to novel treatments will only be possible with forward planning of health expenditure, workforce, and infrastructure at current and future treatment sites. These innovations can and will revolutionise the treatment of blood cancers in Australia. However, the current funding mechanisms are already creating a barrier due to a need for a coordinated approach. There must be increased accountabilities for all stakeholders to encourage timely decisions that do not penalise patients.

The Cancer Drugs Fund (CDF) in England provides an exemplar for how such a funding source could work. The CDF offers early access to promising new cancer treatments while gathering data for informed funding decisions and broader availability.

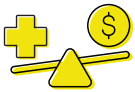
Australian patients need faster access to cutting-edge treatments, and they need it now. The debacle that is the current funding stalemate for CAR T-cell therapy highlights significant issues in our current system. Federally funded access to high-cost therapies, including cell therapies, will give patients the access they are entitled to without delay.

RECOMMENDATION 5

Conduct a comprehensive review of restrictions for PBS-subsidised blood cancer therapies to ensure alignment with contemporary best-practice clinical care.

The Australian Government spent over $17 billion providing subsidised access to medicines via the PBS in the 2022-2023 financial year. Yet restrictive PBS eligibility criteria and complicated treatment sequencing requirements still limit the treatment options available to clinicians and their ability to adhere to best practice clinical guidelines.

The PBS is not a substitute for evidence-based clinical guidelines for blood cancer. Due to budget impact and uncertainty, restrictions are too often developed to limit use. Conducting a comprehensive review and aligning how blood cancer patients access subsidised therapies with best-practice care will ensure that clinicians can provide evidenced-based care for all blood cancer patients who will potentially benefit from an intervention. Following an initial review, ongoing review will also be necessary to support continuing flexibility with changing practice.



RECOMMENDATION 6

Within the current HTA review, ensure that flexible pricing and payment models are included that adequately capture the value that combination therapy can deliver to patients with blood cancer.

It is widely accepted that addressing evaluation and funding challenges of combination therapies is critical, yet the complexities involved have proven difficult to solve for many years in Australia and worldwide.

The HTA review provides an opportunity to fundamentally change how this issue is managed once and for all so that treatment protocols with multiple agents are not penalised and less effective monotherapies are not preferentially subsidised for patients who would benefit from these clinically superior combinations. Patient care should not be compromised because their best treatment option includes a combination of therapies from different sponsor companies that are subject to differing RSAs.

RECOMMENDATION 7

Embed an ongoing five-year review process into Australia's HTA framework following the outcomes of the current HTA review.

The HTA Policy and Methods Review is a welcome opportunity to modernise Australia's HTA system to ensure equitable access, optimal value, and continuous improvement. However, one review in 30 years is not enough. With the fast pace of medical innovation, reviewing the methods and approaches to HTA every five years is the minimum goal we should strive for. This timeframe also aligns with the anticipated ongoing reviews of Australia's NMP.

ABBREVIATIONS

Abbreviation	Description
ALL	Acute lymphoblastic leukaemia
ARTG	Australian Register of Therapeutic Goods
ASCT	Autologous stem cell transplant
B-ALL	B-cell acute lymphoblastic leukaemia
BCL-2	B-cell lymphoma 2
BTK	Bruton's tyrosine kinase
CAR	Chimeric Antigen Receptor
CDF	Cancer Drugs Fund
CGT	Cell and Gene Therapy
CLL	Chronic lymphocytic leukaemia
DLBCL	Diffuse large B-cell lymphoma
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
HCL	Hairy cell leukaemia
ICER	Incremental cost effectiveness ratio
IHACPA	Independent Health and Aged Care Pricing Authority
IMiD	Immunomodulatory imide drug
HTA	Health Technology Assessment
MCL	Mantle cell lymphoma
mAb	Monocolonal antibody
MSAC	Medical Services Advisory Committee
NICE	National Institute for Health and Care Excellence
NHRA	National Health Reform Agreement
NMP	National Medicines Policy
OECD	Organisation for Economic Co-operation and Development
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
QALY	Quality adjusted life year
RR	Relapsed and/or refractory
RSA	Risk share agreements
TGA	Therapeutic Goods Administration

REFERENCES

1. Leukaemia Foundation. *Blood cancer facts and figures*. 2023; Available from: https://www.leukaemia.org.au/blood-cancer/understanding-your-blood/blood-cancer-facts-and-figures/.
2. Cancer Australia. *Multiple myeloma in Australia statistics*. 2022; Available from: https://www.canceraustralia.gov.au/cancer-types/myeloma/statistics.
3. Leukaemia Foundation. *State of the Nation: Blood Cancers in Australia*. 2023 [cited 2023 Dec 1]; Available from: https://www.leukaemia.org.au/how-we-can-help/advocacy-and-policy/state-of-the-nation/.
4. Leukaemia Foundation. *Chemotherapy is a common treatment for many blood cancers*. 2020 [cited 2023 Sept 25]; Available from: https://www.leukaemia.org.au/blood-cancer/journey/active-treatment/treatment-options/chemotherapy/.
5. Leukaemia and Lymphoma Society. *Side effects* 2023 [cited 2023 Sept 27]; Available from: https://www.lls.org/leukemia/acute-myeloid-leukemia/treatment/side-effects.
6. Dickinson, M. *Expert Series interview: Associate Professor Michael Dickinson discusses CAR T-cell therapy*. 2021.
7. Peter MacCallum Cancer Centre. *CAR-T Cell Therapy*. 2023 [cited 2023 Sep 20]; Available from: https://www.petermac.org/patients-and-carers/treatments/haematological-treatments/cellular-therapies-program/car-t-cell-therapy.
8. Department of Health and Aged Care. *National Medicines Policy 2022*. 2022 [cited 2023 Sept 5]; Available from: https://www.health.gov.au/sites/default/files/2022-12/national-medicines-policy.pdf.
9. Evohealth. *Analysis and comparision of registered and reimbursed blood cancer treatments in Australia, United States of America, United Kingdom and European Union*. . 2023.
10. Medicines Australia. *Medicines Matter 2022: Australia's Access to Medicines 2016-2021*. 2022 [cited 2023 Oct 20]; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/04/Medicines-Matter-2022-FINAL.pdf.
11. Australian Government. *The New Frontier - Delivering better health for all Australians*. 2021 [cited 2023 15 December]; Available from: https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/Newdrugs/Report.
12. Rosemary Huxtable. *Mid-Term Review of the National Health Reform Agreement Addendum 2020-2025 – Final Report*. 2023 [cited 2023 Dec 12]; Available from: https://www.health.gov.au/resources/publications/nhra-mid-term-review-final-report-october-2023?language=en.
13. Department of Health and Aged Care. *2020–25 National Health Reform Agreement (NHRA)*. 2023; Available from: https://www.health.gov.au/our-work/2020-25-national-health-reform-agreement-nhra.
14. Department of Health and Aged Care. *NHRA Mid-term Review Final Report – October 2023*. 2023 [cited 2023 15 December]; Available from: https://www.health.gov.au/resources/publications/nhra-mid-term-review-final-report-october-2023?language=en.
15. Australian Institute of Health and Welfare, *Cancer data in Australia.* 2023, AIHW: Canberra.
16. Cancer Council Victoria. *Blood cancer*. 2023; Available from: https://www.cancervic.org.au/cancer-information/types-of-cancer/blood_cancers/blood_cancer.html#:~:text=through%20blood%20vessels.-,How%20common%20are%20blood%20cancers%3F,with%20a%20form%20of%20leukaemia.
17. Shawview Consulting. *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*. 2022 [cited 2023 15 December]; Available from: https://www.sanofi.com.au/dam/jcr:3f59ee4e-21a4-43f6-9387-985e7a91c93d/Shawview%20No%20Time%20Left%20to%20Wait%20Nov%202022.pdf.
18. Therapeutic Goods Administration, *Australian Public Assessment Report for Lenalidomide*. 2016: Australia.
19. Leukaemia Foundation. *Same cancer, same drug but our access to treatment was anything but consistent*. 2020; Available from: https://www.leukaemia.org.au/stories/three-myeloma-stories/.
20. Medical Services Advisory Committee. *1647– Brexucabtagene autoleucel for relapsed or refractory mantle cell lymphoma*. 2022; Available from: http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1647-public.
21. Therapeutic Goods Administration, *Australian Public Assessment Report for Venetoclax*. 2017: Australia.
22. Pharmaceutical Benefits Scheme, *4.06 VENETOCLAX Tablet 10 mg, 50 mg and 100 mg, Venclexta®, AbbVie Pty Ltd.* . 2017: Australia.

23. Australian Bureau of Statistics. *Life tables*. 2022; Available from: https://www.abs.gov.au/statistics/people/population/life-tables/latest-release.
24. Department of Health and Aged Care. *Pharmaceutical Benefits Scheme (PBS) Expenditure & Prescriptions Report 1 July 2022 to 30 June 2023*. 2023 [cited 2023 Dec 23]; Available from: https://www.pbs.gov.au/statistics/expenditure-prescriptions/2022-2023/PBS-Expenditure-prescriptions-report-2022-23.pdf.
25. Department of Health and Aged Care. *Inquiry into approval processes for new drugs and novel medical technologies in Australia*. 2023 [cited 2023 Dec 16]; Available from: https://www.health.gov.au/resources/publications/inquiry-into-approval-processes-for-new-drugs-and-novel-medical-technologies-in-australia.
26. Department of Health and Aged Care. *Health Technology Assessment Policy and Methods Review – Consultation 1*. 2023; Available from: https://ohta-consultations.health.gov.au/ohta/hta-review-consultation1/consultation/published_select_respondent.
27. Therapeutic Goods Administration. *TGA regulatory framework*. 2020 [cited 2023 Sept 27]; Available from: https://www.tga.gov.au/tga-regulatory-framework.
28. Medicines Australia. *Facts book 2021 Fifth Edition* 2021 [cited 2023 Oct 20]; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2021/06/Medicines-Australia-Facts-Book-2021.pdf.
29. Michaeli, D.T., et al., *Special FDA designations for drug development: orphan, fast track, accelerated approval, priority review, and breakthrough therapy.* Eur J Health Econ, 2023.
30. Food and Drug Administration. *Designating an Orphan Product: Drugs and Biological Products*. 2023; Available from: https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/designating-orphan-product-drugs-and-biological-products.
31. European Medicines Agency. *EU/3/22/2581: Orphan designation for the treatment of diffuse large B-cell lymphoma* 2023; Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu-3-22-2581.
32. Department of Health and Aged Care. *PBAC Public Summary Document - March 2023 PBAC Meeting*. 2023 [cited 2023 15 December]; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2023-03/files/daratumumab-psd-03-2023.pdf.
33. Food and Drug Administration. *FDA approves idecabtagene vicleucel for multiple myeloma*. 2023; Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-idecabtagene-vicleucel-multiple-myeloma.
34. European Medicines Agency, *Abecma (idecabtagene vicleucel)*. 2021.
35. European Medicines Agency, *Public summary of opinion on orphan designation*. 2017.
36. European Medicines Agency. *First cell-based gene therapy to treat adult patients with multiple myeloma*. 2021; Available from: https://www.ema.europa.eu/en/news/first-cell-based-gene-therapy-treat-adult-patients-multiple-myeloma.
37. European Medicines Agency. *EU/3/21/2450: Orphan designation for the treatment of mantle cell lymphoma*. 2021; Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu-3-21-2450.
38. European Medicines Agency. *Jaypirca*. 2023; Available from: https://www.ema.europa.eu/en/medicines/human/summaries-opinion/jaypirca.
39. Food and Drug Administration. *FDA grants accelerated approval to pirtobrutinib for relapsed or refractory mantle cell lymphoma*. 2023; Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-pirtobrutinib-relapsed-or-refractory-mantle-cell-lymphoma.
40. Johns Hopkins Medicine. *BRAF Mutation and Cancer*. 2023; Available from: https://www.hopkinsmedicine.org/health/conditions-and-diseases/braf-mutation-and-cancer.
41. Drugbank. *Dabrafenib*. 2023; Available from: https://go.drugbank.com/drugs/DB08912.
42. Cross, M.J., et al., *Dabrafenib Is a Safe and Effective Therapy in Relapsed/Refractory Classical Hairy Cell Leukemia.* Blood, 2020. **136**(Supplement 1): p. 7-8.
43. Dietrich, S., et al., *BRAF Inhibition in Refractory Hairy-Cell Leukemia.* New England Journal of Medicine, 2012. **366**(21): p. 2038-2040.
44. Park, J.H., et al., *Vemurafenib and Obinutuzumab as Frontline Therapy for Hairy Cell Leukemia.* NEJM Evidence, 2023. **2**(10): p. EVIDoa2300074.
45. Medicines Australia. *Funding innovative medicines*. 2022 [cited 2023 Sep 2023]; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2022/11/HTA-DP-Funding-Innovative-Medicines-.pdf.
46. Wang, S., D. Gum, and T. Merlin, *Comparing the ICERs in Medicine Reimbursement Submissions to NICE and PBAC-Does the Presence of an Explicit Threshold Affect the ICER Proposed?* Value Health, 2018. **21**(8): p. 938-943.
47. Lybrand, S. and M. Wonder, *Analysis of PBAC submissions and outcomes for medicines (2010–2018).* International Journal of Technology Assessment in Health Care, 2020. **36**(3): p. 224-231.

48. Medicines Australia. *A Healthcare System for the 21st Century*. 2023 [cited 2023 Oct 20]; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/08/20230606-sub-Medicines-Australia-HTA-Review-Consult-1-FINAL.pdf.
49. Evohealth. *Cell & Gene Therapies: Rising to the challenge* 2021; Available from: https://www.evohealth.com.au/wp-content/uploads/2023/09/Evohealth_Cell_and_gene_therapies_rising_to_the_challenge_FA.pdf.
50. Evohealth. *Cell and gene therapies: Rising to the challenge Scorecard 2023*. 2023; Available from: https://www.evohealth.com.au/wp-content/uploads/2023/09/Evohealth.Risingtothechallenge.Scorecard2023.pdf.
51. Evohealth. *CAR T-cell therapy: Is Australia ready, willing and able?* 2022 [cited 2023 Sep 23]; Available from: https://www.evohealth.com.au/insights/car-t-cell-therapy-is-australia-ready-willing-and-able/.
52. Department of Health and Aged Care. *CARVYKTI (Janssen-Cilag Pty Ltd)*. 2023; Available from: https://www.tga.gov.au/resources/prescription-medicines-registrations/carvykti-janssen-cilag-pty-ltd.
53. European Medicines Agency. *Carvykti*. 2023; Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/carvykti.
54. Food and Drug Administration. *FDA approves ciltacabtagene autoleucel for relapsed or refractory multiple myeloma*. 2023; Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ciltacabtagene-autoleucel-relapsed-or-refractory-multiple-myeloma.
55. Medical Services Advisory Committee. *1690.1 – Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T cell to treat refractory or relapsed multiple myeloma*. 2023; Available from: http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1690.1-public.
56. Alex Grove. *The Pharmaceutical Benefits Scheme: a quick guide*. 2016 [cited 2023 Dec 12]; Available from: https://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/pubs/rp/rp1516/Quick_Guides/PBS.
57. Jenei K , R.A., Bayle A, et al.,, *Health technology assessment for cancer medicines across the G7 countries and Oceania: an international, cross-sectional study.* Lancet Oncology,, 2023. **24**(June): p. 624-635.
58. Federal Financial Relations. *Addendum to National Health Reform Agreement 2020-2025* 2021 [cited 2023 Dec 12]; Available from: https://federalfinancialrelations.gov.au/sites/federalfinancialrelations.gov.au/files/2021-07/NHRA_2020-25_Addendum_consolidated.pdf.
59. Department of Health, *National Health Reform Agreement 2020-2025* 2020.
60. European Medicines Agency. *Adcetris*. 2023 [cited 2023 Dec 21]; Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/adcetris.
61. Food and Drug Administration. *Brentuximab Vedotin*. 2018 [cited 2023 Dec 11]; Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/brentuximab-vedotin.
62. Pharmaceutical Benefits Scheme. *Brentuximab Vedotin*. 2023 [cited 2023 Dec 12]; Available from: https://www.pbs.gov.au/medicine/item/10166C-10171H-10172J-10180T-11067L-11073T-11079D-11080E-11086L-11087M-11089P-11096B-11651F-11660Q-11661R-11664X-12632W-12646N-12656D-12657E.
63. Bellberry limited. *Challenges in valuing and paying for combination regimens in oncology* 2020 [cited 2023 15 December]; Available from: https://bellberry.com.au/wp-content/uploads/Meeting-report-final-draft-May-2020.pdf.
64. Dimopoulos MA, O.A., Nahi H, et al., *Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma.* The New England Journal of Medicine, 2016. **375**: p. 1319-1331.
65. Kim, H., J. Byrnes, and S. Goodall, *Health Technology Assessment in Australia: The Pharmaceutical Benefits Advisory Committee and Medical Services Advisory Committee.* Value in Health Regional Issues, 2021. **24**: p. 6-11.
66. Denson, P., *Challenges and Opportunities Facing Medical Education.* Transactions of the American Clinical and Climatological Association, 2011. **122**: p. 48-58.

DISCLAIMER

This Report has been prepared by Evohealth Pty Ltd (**Evohealth**) on behalf of Janssen-Cilag Pty Ltd (**Janssen**).

This Report has been commissioned by Janssen to develop a product-agnostic report examining all blood cancers and treatment access gaps that currently exist in Australia compared to the United States and countries in the European Union.

This Report is not intended to be, and should not be, used by any person or entity other than a Recipient and Evohealth accepts no duty of care whatsoever to any such other person or entity.

While reasonable efforts have been made to ensure that the contents of this Report are factually correct, this Report is provided by Evohealth on a general basis only. Neither Evohealth nor any of its directors, officers, employees, advisors, consultants, contractors and agents make any representation or warranty, express or implied, as to the currency, accuracy, reliability or completeness of the information referred to or contained in this Report and none of those persons or entities accepts any responsibility or liability (except a liability that cannot lawfully be excluded) for any reliance placed on the contents of this Report by any person. This Report does not purport to be comprehensive or to contain all the information a Recipient may desire or require in respect of its subject matter. The Recipient should make its own enquiries and obtain its own independent advice in relation to the information contained within this Report before making any decision or taking any action based on its contents.

To the maximum extent permitted by law, Evohealth and its directors, officers, employees, advisors, consultants, contractors and agents disclaim and exclude all liability for any loss, claim, demand, damages, costs and expenses of whatsoever nature (whether or not foreseeable): suffered or incurred by any person relying or acting on any information provided in, or omitted from, this Report or any other written or oral opinions, advice or information provided by any of them; or arising as a result of or in connection with information in this Report being inaccurate or incomplete in any way or by reason of any reliance thereon by any person; and whether caused by reason of any negligence, accident, default or however otherwise caused.

Each recipient of this report acknowledges and accepts each of the matters and conditions contained in this Disclaimer.

Date of preparation: January 2024.

Authors: Renae Beardmore, Rhyan Stanley, Deanna Mill and Yukti Sharma.

Report design: Adam Sorgini

Photo Credits: Front cover photo by Janosch Lino on Unsplash
Page 20-21 photo by Christina Victoria on Unsplash
Page 29 photo by Ivan Samkov on Pexels

Suggested citation: Evohealth. 2024. *Changing lives: Improving access to blood cancer treatments in Australia.* Evohealth, Canberra.

January **2024**

(02) 6243 4806

www.evohealth.com.au

Level 9, 2 Phillip Law St,
CANBERRA CITY ACT 2601

evohealth