June 2023

Reference Committee
Health Technology Assessment Policy and Methods Review
Department of Health and Aged Care
GPO Box 9848
Canberra ACT 2601

Via email: htareviewconsult@health.gov.au

Dear Reference Committee

Re: HTA Review Consultation 1

Thank you for the opportunity to provide a submission to the *Health Technology Assessment Policy and Methods Review – Consultation 1.*

The Leukaemia Foundation is the only national organisation representing all Australians with blood cancer. For over 45 years we have provided a variety of supports and services, and funded life-changing research. We provide evidence-based policy advice and amplify the voices of those affected by blood cancer.

This submission draws on an evidence base that includes but is not limited to:

- our recent *State of the Nation: Blood Cancers in Australia Report 2023*, including a survey of over 4,600 Australians living with blood cancer, plus interviews with other stakeholders,
- Australia's first ever *National Strategic Action Plan for Blood Cancer* (2020),
- our Leukaemia Foundation Consumer Engagement Group, and
- our ongoing interactions with, and support for, the patients receiving our services.

In line with the consultation documentation and survey questions, this submission sequentially addresses features of HTA policy and methods that:

1. are working effectively
2. may act as current or future barriers to earliest possible access
3. may act as current or future barriers to equitable access
4. detract from person-centredness

Thank you for your consideration of the issues highlighted in this submission. We would be happy to discuss further and can be contacted at ctanti@leukaemia.org.au.

Sincerely,

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Chris Tanti
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Context: The imperative to improve blood cancer outcomes

This year 19,403 Australians will be newly diagnosed with a blood cancer. This is equivalent to **53 people every day** or one person every 27 minutes.

Over the past 10 years, the **incidence of blood cancer has increased by 47%**, and 135,000 Australians are now living with a blood cancer. Sixteen Australians will lose their life to blood cancer each day and 1 in 3 people diagnosed with a blood cancer will not survive five years after their diagnosis.

Blood cancers require, in many instances, highly specialised and complex care throughout the treatment period. Many blood cancers can have repeated acute episodes of treatments, remission and relapse.

Some blood cancers can become refractory to current treatments, leaving patients with very limited options. Treatments are often aggressive, highly toxic and can result in debilitating lifelong side effects.

The health and social imperatives for action are underlined by an economic imperative. By 2035, blood cancer will **cost the economy $71.9 billion each year**. Myeloma and leukaemia are the first and third most expensive cancers for our health system to treat.[1] Around 43% of individuals report out-of-pocket expenses, and more than one in three of these incur more than $A5,000 in cost.

1. HTA system features that are working effectively

'God Bless the PBS' – Blood cancer patient[2]

Recognition that patients are both funders and recipients of listed medicines

Australia's Health Technology Assessment (HTA) system is fundamentally underpinned by a social contract.

Taxpayers fulfill their end of the social contract by paying taxes. The government, as the custodian of public funds, has the responsibility to allocate tax revenues efficiently and effectively.

Our system currently recognises – and should always recognise – the fundamental right of patients and taxpayers to have access to medicines and healthcare interventions funded by taxpayers.

This social contract is a dynamic relationship. As needs evolve, innovation occurs, and circumstances change, so too should those subsidy arrangements.

We support this underlying principle of equity behind Government subsidisation of therapeutics. It should remain an integral pillar and ongoing driver of our subsidisation system.

[1] Merollini, K.M.D., Gordon L.G., Ho, Y.M., et al., 2022, Cancer Survivors' Long-Term Health Service Costs in Queensland, Australia: Results of a Population-Level Data Linkage Study (Cos-Q), Int J Environ Res Public Health, 19(15), 9473, doi: 10.3390/ijerph19159473.
[2] Blood cancer survey, *State of the Nation 2023.*

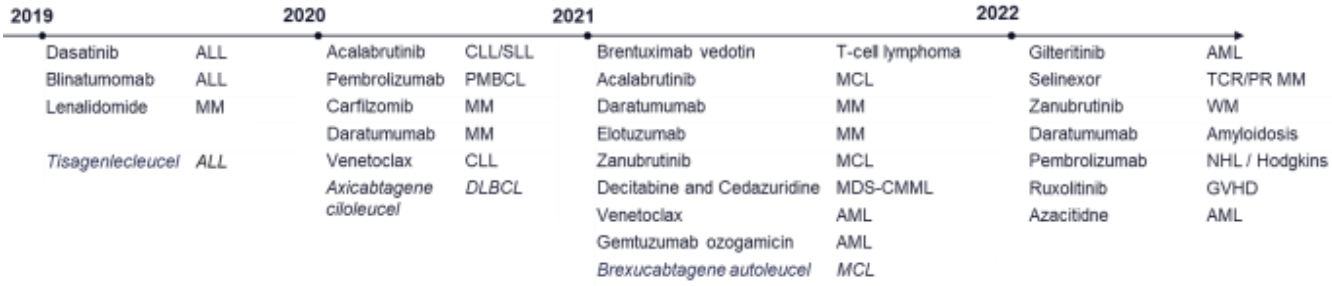
Comparative safety, clinical and cost effectiveness

Clinical efficacy, the quality use of medicines and medicines safety are established fundamentals of Australia's healthcare system. The Federal Government's ongoing commitment to these are reinforced in a range of policy documentation[3].

In addition to regulatory HTA processes that ensure the safety and efficacy of health technologies permitted to be sold in Australia, HTA in the reimbursement context has helped ensure robust assessment of the comparative safety, clinical and cost effectiveness of technologies proposed for Government subsidy.[4]

Encouragingly, this is occurring while newer therapies are still being approved. For example, in the past several years there has been approval and funding for 19 new blood cancer therapies, including three CAR T-cell therapies. The Pharmaceutical Benefits Advisory Committee (PBAC) has made more than 16 positive recommendations for PBS listing of blood cancer treatments.[5]

Figure 1: Listings of blood cancer therapies[6]



Ways of further improving access to therapies are explored in section 2.

"I know that through wonderful research my treatment is new, and the treatment cost only came on the PBS list in January this year. If this research had not found this treatment my diagnosis would have given me only 2-3 months to live."

Blood cancer patient – State of the Nation 2023[7]

"As a 30 year survivor of a BT for myelofibrosis and an active advocate for greater access to effective therapies for those of us with MPNs, I was blown over when my haematologist offered me Jakavi (ruxolitinib phosphate) for my chronic GVHD and found that it was already listed on the PBS for this purpose. Thank goodness for those who have kept their eyes on the ball in recent years and extended the range of this drug from its original use in treating MF. Now just let's hope it works!"

Blood cancer patient – LF Consumer Engagement Group

Importance of consumer-centricity

In principle, the importance of putting the patient at the centre is well-established in Australia's HTA system.

[3] For example, the National Medicines Policy, https://www.health.gov.au/sites/default/files/2022-12/national-medicines-policy.pdf.
[4] Review of health technology assessment in Australia, 2009 https://www.health.gov.au/sites/default/files/documents/2022/03/review-of-health-technology-assessment-in-australia.pdf
[5] State of the Nation, pp.71-72 - https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf
[6] State of the Nation, pp.71-72 - https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf
[7] Blood cancer survey, *State of the Nation 2023.*

This is also reflected in other key policy documentation, including recent and fundamental frameworks such as the National Medicines Policy (NMP):

- "The NMP acknowledges the fundamental role of consumers in achieving the policy aim by placing the individual at the centre, and by focusing on and responding to the needs of Australia's diverse population."[8]

The importance of consumer-centricity should remain a fundamental part of HTA processes. There are opportunities to further strengthen what this looks like in practice (see Section 4).

2. Current or future barriers to earliest possible access

Current evidence requirements

Current restrictions around the use of evidence in HTA processes are delaying access for patients.

A lack of evidence of benefit, or uncertainty in the evidence, may prevent the listing of a new medicine, device, or service on the PBS or MBS.

Uncertainty in evidence increases as the volume of sample data decreases (i.e. with fewer patients). Many blood cancers are rare and therefore uncertainty of benefit is often high.

Further, rapid advances in genomic profiling are enabling even more accurate subtype diagnosis.

The potential benefits of better diagnosis using genomics are demonstrable and profound. It allows clinicians to improve survival outcomes by more precisely matching patients to targeted therapies.[9] Our recent 'State of the Nation' report also contains new data showing 31 per cent of blood cancer patients who had a genomic test had their diagnosis and treatment plan altered.[10]

However, smaller patient populations challenge traditional evidence generation models.

Conducting traditional randomised controlled trials is consistent with best practice, evidence-based medicine, yet smaller populations mean trials are more difficult to recruit for.

It can also reduce pharmaceutical company incentives to seek PBS or MBS listings for new medicines, devices, or services and in turn, could impede clinicians' access to novel and specialised therapies for blood cancer patients.[11]

Lack of evidence to support public subsidy – and/or a clear pathway or incentive for listing – can also have the unintended consequence of increasing 'off-label' prescribing. This can lead to inadequate generation of the evidence required to support listings, with outcomes not always reported to relevant clinical registries (e.g. bendamustine, indicated for lymphoma and CLL, is used off-label for myeloma).[12]

As a result, many potentially life-saving therapies available overseas are not available in Australia. **Appendix A** identifies many blood cancer treatments and diagnostics that are used overseas but not in routine clinical practice in Australia.

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[8] *National Medicines Policy*, https://www.health.gov.au/sites/default/files/2022-12/national-medicines-policy.pdf
[9] National Strategic Action Plan for Blood Cancers, 2020, https://www.leukaemia.org.au/wp-content/uploads/2020/09/National-Strategic-Action-Plan-for-Blood-Cancer_June-2020.pdf
[10] *State of the Nation: Blood Cancers in Australia Report 2023*
[11] Submission to *Inquiry into approval processes for new drugs and novel medical technologies in Australia*, p.5.
[12] Blood Cancer Taskforce, 2020, *Rapid Review of Evidence*, Table 5.3, pp.189-190. Available at https://www.leukaemia.org.au/wp-content/uploads/2020/09/National-Strategic-Action-Plan-for-Blood-Cancer_Review-of-Evidence-for-Action-1.pdf

'It is frustrating when I know there is a better medication for my PV but it is not available in Australia. Besremi is readily available overseas. Why do we always have to wait for the best treatments?'

Blood cancer patient – State of the Nation 2023

"When it comes down to the wire for patients, the lengthy approval/denial/repeat process in Australia is devastating. Especially when new drugs and procedures have been approved and are successfully in use overseas (usually the US and Europe), such as, lately, CAR-T and bi-specific antibodies.

Clinical trials for RRMM in Australia are few and far between, and oligo and nonsecretory myeloma patients are excluded from these trials as they do not have easily measurable disease markers (ie blood indicators). Being told 'there's nothing else we can do' is tough, especially when you know that there is, just that it's only there for the wealthy few who could afford to travel overseas and pay for it."

Blood cancer patient – LF Consumer Engagement Group

Case study – Matt

After running out of proven, effective treatment options in Australia for his rare type of leukaemia, 56-year-old Matt stumbled across a clinical trial in America recruiting people to test ibrutinib, which wasn't available in Australia at the time.

Matt says he had access to the treatment options of his choice after he was diagnosed in 2004, but each time was unable to achieve full remission.

He felt his only option left was to try ibrutinib via Australia's compassionate access program.

However, his application was declined because **"there wasn't enough evidence to prove ibrutinib could successfully treat this type of blood cancer".**

After discovering the trial on Google, Matt made contact with the trial in the US himself and was able to access the drug in the US through that trial.[13]

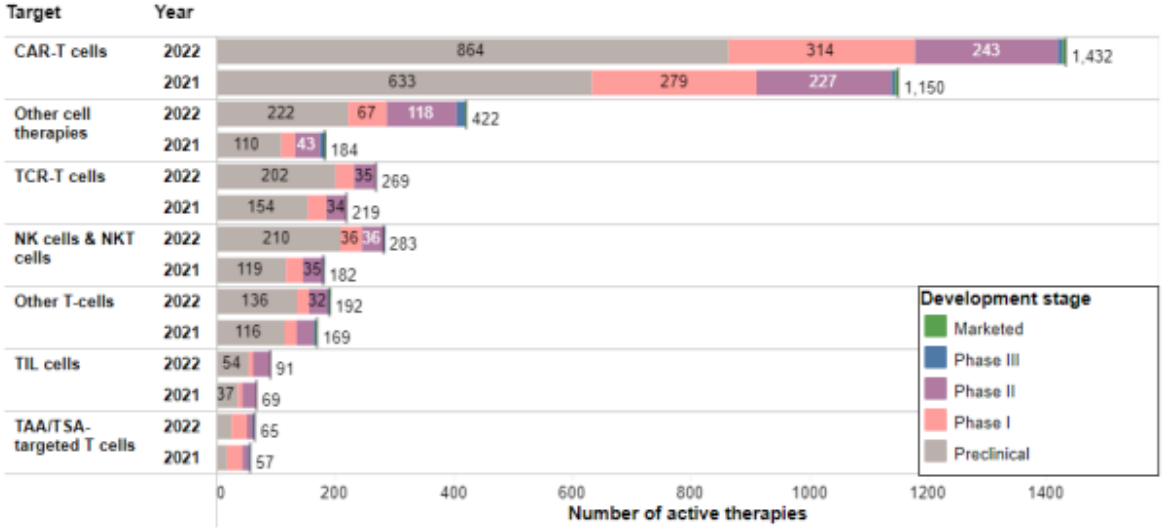
HTA requires greater responsiveness to newer therapies

These access gaps may be magnified by new, high-cost cellular therapies such as immunotherapies.[14]

There is a significant pipeline of cell and gene therapies being developed globally, ultimately attempting to enter mainstream clinical practice.

[13] https://www.leukaemia.org.au/stories/matts-story/
[14] *State of the Nation: Blood Cancers in Australia Report 2023*, p.78.

Figure 2: A wave of CAR T-cell therapies on the horizon[15]



The healthcare regulatory and reimbursement eco-system must also cope with the speed at which we are becoming able to differentiate between different blood cancer types through genomics. This is underscored by a recent (March 2023) MSAC recommendation for NGS gene panel testing for genetic variants associated with blood cancers. Importantly, MSAC noted that 'genetic testing is now standard of care for patients with these types of malignancies."[16]

System fragmentation

As the *National Health Reform Agreement (NHRA) Long-term Health Reforms Roadmap* acknowledges:

- "The current approach to HTA to inform policy investment and disinvestment decisions in Australia is fragmented. It does not support coordinated and timely responses to rapidly changing, emerging, and disruptive technologies, including high-cost and highly specialised therapies and services.

  Separate HTA processes exist across all levels of the health system, and across levels of government. This duplicates effort, creates inefficiencies and inconsistent advice, and delays access to innovative and emerging technologies."[17]

For example, CAR T-cell therapies are reliant on a complicated funding mix from both the Federal and state and territory governments. Eight centres provide CAR T-cell therapy in Australia, but are concentrated in NSW (4 centres), Victoria (2 centres) and Queensland (2 centres), with an unclear process for establishing sites.[18] To date, funding for these services has been based on the National Health Reform Agreement (50% state and 50% Federal).

[15] https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf, p.83.
[16] *MSAC Public Summary Document: Application No. 1684 – Genetic testing for variants associated with haematological malignancies*, http://www.msac.gov.au/internet/msac/publishing.nsf/Content/0E3364FCF94B9002CA25874F00283CE5/$File/1684%20Final%20PSD-Nov%202022.pdf, p.4.
[17] *National Health Reform Agreement (NHRA) – Long-term Health Reforms: Roadmap*, https://www.health.gov.au/sites/default/files/documents/2021/10/national-health-reform-agreement-nhra-long-term-health-reforms-roadmap.pdf, p.7.
[18] *State of the Nation: Blood Cancers in Australia Report 2023*, p.78.

'Disparity between states on availability of CAR T [has been an issue], also cut-off ages for treatments varies between states.'
Blood cancer patient – State of the Nation 2023

Workforce

While not specific to HTA processes, improving access to therapies will also necessitate ensuring we maintain a skilled and well-resourced workforce. This reflects one of the four central pillars of the new *National Medicines Policy* (NMP): "Collaborative, innovative and sustainable medicines industry and research sectors with the capability, capacity and expertise to respond to current and future health needs."[19]

This is particularly important for newer therapies. Consultation undertaken as part of *State of the Nation 2023* showed that clinician stakeholders feel today's workforce is not adequately resourced to deliver novel medicines and CAR T-cell therapies.[20]

Suggestions for improvement

Right to Trial

The Leukaemia Foundation proposes the creation of a 'Right to Trial' program. It would aim to support systematic evidence development and provide a mechanism for the more systematic evaluation of off-label use and re-purposing of drugs.[21]

The House of Representatives' *Inquiry into approval processes for new drugs and novel medical technologies in Australia* supported the Leukaemia Foundation's recommendation for a 'Right to Trial Fund'. It recommended:

- "Federal Government…establish a fund to support patients, clinicians and non-profit organisations to sponsor registration and reimbursement applications where there is no realistic prospect of a company serving as sponsor, and where the Department of Health is otherwise supportive of the application (Recommendation 9)."

Case study: Right to Trial program

A Right to Trial program could enable:

a) *Improved access* – access to new therapies and building evidence about their effectiveness in a documented, regulated clinical trial setting. Potentially this could be used as the basis for a submission or a larger clinical trial.

b) *Support for submissions* – more systematic evidence development and clinician-led or patient-led submissions for new therapies. This would provide a mechanism for the more regular and systematic use and evaluation of off-label medicines, and could reduce dependence on industry to conduct the research needed to advance potentially curative therapies.

[19] *National Medicines Policy*, https://www.health.gov.au/sites/default/files/2022-12/national-medicines-policy.pdf
[20] *State of the Nation: Blood Cancers in Australia Report 2023*, p.53.
[21] LF submission to *Inquiry into approval processes for new drugs and novel medical technologies in Australia*, 2020.

The Right to Trial Program would need to be developed to ensure that therapies accessed through the program met required eligibility criteria, such as the criteria used to determine off-label use, or applications for compassionate access, where safety criteria can be prescribed and met, and are in routine use already today.

In addition, there would need to be clear entry and exit timelines to limit potential unintended consequences vis-a-vis the PBS. This would provide a more systematic and scientific mechanism for the evaluation of medicines that are used off-label and more equitable access to emerging therapies.

Such a program, properly designed, would reduce inequities of access to therapies where evidence is in development.

Moreover, while the program could be piloted for blood cancers it could easily be extended to a wider range of conditions over time; it need not be blood cancer specific"[22]

See **Appendix B** for a case study of a LF-funded clinical trial that embodies many of these characteristics – the Blood Cancer Genomics Trial (MoST-LLy) co-funded by LF and Tour de Cure.

Additional reimbursement pathways

As articulated in *State of the Nation 2023*, Australia should broaden and add to its reimbursement pathway options.

Australia has a managed entry scheme for drugs where the extent or value of the clinical effect is uncertain, but this is not well-used.[23]

Additional pathways could include:[24]

- pathways that allow for the use of earlier and more varied clinical data, including international data such as through Project Orbis. PBAC could consider and recommend reimbursement for a product based on early results, such as the ZUMA-1 or CARTITUDE-1 study, and then revise the rate of reimbursement based on updated results.
- rolling review of confirmatory clinical trials or real-world data
- increasing use of international data and real-world evidence.

A harmonised, national approach to cellular and genetic therapies

Australia needs a national policy for the commissioning, funding and governance of CAR T-cell and other cellular and genetic therapies.

These therapies could be beneficial for many patients, but collaboration among the Federal and State and Territory Governments is required to develop a policy that:

- ensures a coordinated national approach to supporting the development of cellular and genetic therapies
- overcomes challenges caused by current funding arrangements, e.g. as seen with CAR T-cell therapies.

[22] *State of the Nation 2020*, https://www.leukaemia.org.au/wp-content/uploads/2020/06/State-of-the-Nation-Blood-Cancer-in-Australia_Leukaemia-Foundation.pdf, p. 100.
[23] *State of the Nation 2023*, https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf, p.81.
[24] *State of the Nation 2023*, https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf, p.81.

- draws from international initiatives, such as the FDA's Regenerative Medicine Advanced Therapy Designation.

3. Current or future barriers to equitable access

There is an access 'postcode lottery'

There remains inconsistent access to diagnostics and novel and specialised therapies across Australia – leading to a 'postcode lottery' of blood cancer outcomes. Research demonstrates that this contributes to potentially preventable loss of life, poor quality of life, and inequitable outcomes across patient groups.[25]

Not all patients are able to afford or physically access the alternatives if a therapeutic is not listed for subsidy – fund the therapy personally, find a clinical trial, or be granted access through a compassionate access scheme.

Many newer diagnostics/treatments/therapies are available either only through clinical trials (which are mostly available at major metropolitan treatment centres) or at the patient's own expense. This can limit access to people in regional/remote areas or those who cannot afford to access non-PBS treatments.

Many genomic diagnostic services are not publicly subsidised. This privately funded model not only limits uptake, but also means that uptake is inequitable.[26]

The need for consideration of these issues is underpinned by the new NMP, which has as the first of its four pillars:

- "Equitable, timely, safe and reliable access to medicines and medicines-related services, at a cost that individuals and the community can afford."

Moreover, the NMP subsequently commits the Commonwealth to "Deliver national health programs and regulatory functions that ensure equitable, timely, affordable, safe and reliable access to medicines and medicines-related services."[27]

It's very stressful knowing this drug is available overseas and patients are having excellent results from it, however, I can't access it in Australia because of the cost.
– Blood cancer patient[28]

I travelled to Germany to take part in a clinical trial for a new leukaemia drug. It cost us $100,000, which we paid for by fundraising. After three years, I'm still disease free. It saved my life; I had no other option, but wait to die.
– Blood cancer patient[29]

There are about 800 of us in Australia with Waldenström's Macroglobulinaemia (WM), a rare subtype of non-Hodgkin lymphoma. Our overwhelming concern is getting access to emerging treatments available to WM patients worldwide and having them funded by the PBS. Due to the years of approval for PBS, accessing new treatments may involve a personal cost of as much as $100,000.
– Blood cancer patient[30]

[25] *State of the Nation: Blood Cancers in Australia Report 2023*, p.xvii.
[26] *State of the Nation: Blood Cancers in Australia Report 2023*, p.84.
[27] *National Medicines Policy*, https://www.health.gov.au/sites/default/files/2022-12/national-medicines-policy.pdf
[28] Leukaemia Foundation submission to *Availability of new, innovative and specialist cancer drugs in Australia*, 2015.
[29] Leukaemia Foundation submission to *Availability of new, innovative and specialist cancer drugs in Australia*, 2015.
[30] Leukaemia Foundation submission to *Availability of new, innovative and specialist cancer drugs in Australia*, 2015.

Case study – Katrina's delay in diagnosis and accessing affordable treatment

Katrina's delay in diagnosis was followed by an agonising six-month wait for a drug she needed but couldn't afford – one that was eventually made available to her on compassionate grounds.

"I used to lie in bed at night and imagine I could feel my body just multiplying these horrible little cancer cells," recalls Katrina.

"I'd think, 'This is another day that I haven't had any treatment,' and I'd wonder, 'The longer I wait, is this going to give me less of a chance of a good outcome?"

Two stem cell transplants and a $170,000 treatment later (which she thankfully received financial assistance for) Katrina has been in remission for five years.[31]

System costs

Some newer therapies are compounding existing access gaps due to their high cost.

The high cost of these treatments often leads to negotiations between pharmaceutical companies and reimbursement bodies to determine the reimbursement amount.

The Pharmaceutical Benefits System (PBS) has been a highly scrutinized purchasing program over the recent past. Policy reform was designed to create head room for innovation. We are concerned that potential budget limitations may result in delays to the approval of new innovative medicines, which are of particular concern for the range of rare blood cancers with small populations.

In some cases, the costs are shifted to other areas of the healthcare system, such as hospitals or insurance plans, to accommodate the high price of CAR T-cell therapies.

For example, consultations with stakeholders across the sector during the development of *State of the Nation 2023* found that the establishment of CAR T-cell centres has been ad hoc, complicated by funding models, and affected by cost-shifting and competition.[32]

Case study

"I purchase nivolumab from the pharmaceutical company at full cost. There are no trials in Australia and the cost of the drug is not subsidised.

We begged, borrowed, worked, planned and devoted months of our lives to holding events so that we could have the money for treatment, which has been $130,000 so far.

The result has been that I can have access to this lifesaving treatment so it was all worth it. It has meant that I didn't die. It's as simple as that.

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[31] https://www.leukaemia.org.au/stories/for-mother-of-four-katrina-richards-a-five-year-delay-in-diagnosis-was-followed-by-a-further-wait-for-access-to-treatment/

[32] *State of the Nation 2023*, p.78 – https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf

Because of this drug, I have been able to live, and to live a normal life. This drug not only has had an amazing impact on my lymphoma it has also been significantly easier to tolerate compared to other treatments I have had.

However, I'm still angry and terrified. I constantly think about the fact that people overseas, particularly in the US, have easy access to this drug, and I don't." [33]

– This comment, included in our submission to the previous cancer drugs Inquiry, remains relevant today.

4. Elements and features that detract from person centredness

Opaque processes and difficult-to-understand HTA procedures

Transparency and accountability are crucial to maintaining the social contract underpinning public funding.

From work undertaken to develop the *National Strategic Action Plan for Blood Cancers*, *State of the Nation 2023* and our ongoing engagement with patients and HTA systems, the Leukaemia Foundation notes the following elements and features:

- *Lack of transparency*: Lack of clear and accessible information about the decision-making criteria, methodologies, and evidence considered.
- *Difficult-to-access information*: Relevant documents, reports, and data related to HTA processes are often not easily accessible to the public (inclusive of complex terminology), making it difficult to gain a comprehensive understanding of the assessment process. Pragmatically, HTA-related websites are often very difficult to navigate.
- *Limited stakeholder involvement*: In part due to the two points above, involvement of patients can be limited.
- *Inconsistent communication*: Communication of HTA findings and decisions to the public and stakeholders can be inconsistent, making it hard for individuals and organisations to stay informed about the assessment process and outcomes.
- *Complex evidence evaluation*: The evaluation of clinical and economic evidence can be complex and requires specialized knowledge.
- *Lack of clear decision criteria*: The criteria used to make HTA decisions are not clearly defined or communicated.

Lack of consideration of PROs

Patient Reported Outcomes (PROs) are not adequately used in current HTA processes.

Use of PROs allows the lived experience of patients to be better reflected in healthcare decisions.

Recognising the importance and value of PROs, the NAP called for a national system for patient reported outcomes in blood cancer, and this been adopted in the draft Australian Cancer Plan.

[33] Leukaemia Foundation submission to *Availability of new, innovative and specialist cancer drugs in Australia*, 2015., p.4

In the context of HTA, it can be used to inform research directions by industry and clinicians and investment decisions by governments.

This would be consistent with other recent policy directions. For example, the NHRA Roadmap commits governments to striving to "promote the use of Patient Reported Measures to understand what patients value and improve patient experiences and outcomes."[34]

Potential solutions

Listening to consumers – and generating more evidence for HTA

Norway

One example of how regulators listen to consumers and how this can be used in HTA processes is Norway's approach to the concept of how patients are 'coping.'

After feedback from consumers about what mattered to them, the Norwegian Institute of Public Health (NIPH) has started considered the concept of how patients are coping in the considerations of how to categorise information received.

When applying this in the HTA context, Norway defines coping as “an essential prerequisite for living with a condition, looking at the treatment; does it enable someone to master their life’s challenges?”

Using this concept has allowed Norway to formally categorise information of importance to patients but that can sometimes be difficult to capture, and use this as a different form of evidence.[35]

The United Kingdom

The National Institute for Health and Care Excellence (NICE) in the UK has also made revisions to its HTA processes to better capture consumer views in HTA processes.

The reforms are designed to allow greater flexibility over decisions about value for money and consideration of a broader evidence base.[36]

NICE's reforms include[37]:

- *Adopting new approaches to the evidence* considered by NICE in HTA. This includes greater consideration of real-world evidence from the lived experiences of patients.

  NICE's new "Real-world evidence framework" (June 2022) accepts that "real-world data can improve our understanding of health and social care delivery, patient health and experiences, and the effects of interventions on patient and system outcomes in routine settings."

[34] NHRA Roadmap, https://www.health.gov.au/sites/default/files/documents/2021/10/national-health-reform-agreement-nhra-long-term-health-reforms-roadmap.pdf, p.18.
[35] *Shaping Healthcare Together – Exploring system reform opportunities in the Australian healthcare system*, Bristol Myers Squibb.
[36] https://www.nice.org.uk/news/article/nice-signals-commitment-to-greater-flexibility-in-its-evaluation-of-promising-new-health-technologies-and-making-patient-access-fairer
[37] *Changes we're making to health technology evaluation*, NICE: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation

The Framework acknowledges NICE wants to "use real-world data to resolve gaps in knowledge and drive forward access to innovations for patients."[38]

The Framework, which could be drawn on by Australian HTA authorities, drives better access by:

- "identifying when real-world data can be used to reduce uncertainties and improve guidance
- clearly describing best-practices for planning, conducting and reporting real-world evidence studies to improve the quality and transparency of evidence."[39]

- *Allowing more flexibility for NICE's independent committees* in cases where its particularly difficult to generate enough evidence.

  In acknowledgment of the challenges with generating evidence for some treatments – particularly those regarding children, rare diseases and innovative treatments – NICE's committees will now be able to better manage and consider uncertainty.

  For example, the new *Health Technology Evaluations: The Manual* states:

  - "In these [children, rare diseases and innovative treatments] specific circumstances, the committee may be able to make recommendations accepting a higher degree of uncertainty. The committee will consider how the nature of the condition or technology(s) affects the ability to generate high-quality evidence before applying greater flexibility."[40]

- *Giving additional weight to health benefits* in the most severe conditions, to allow more equitable access to treatments for these conditions (not just end-of-life).

[38] NICE "Real-world evidence framework," https://www.nice.org.uk/corporate/ecd9/chapter/overview
[39] NICE "Real-world evidence framework," https://www.nice.org.uk/corporate/ecd9/chapter/overview
[40] *NICE Manual 2022*, https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741

APPENDIX A: Access gaps in blood cancer diagnosis and treatment

Sub-type	Diagnosis or monitoring testing	First line treatment options	Relapsed and refractory treatment options
ALL	Minimum Residual Disease testing and monitoring which allows for assessment of the depth of remission following therapy and optimise the use of allogeneic stem cell transplantation.	blinatumomab imatinib for Ph-like ALL nilotinib for Ph-like ALL dasatinib for Ph-like ALL ponatinib for Ph-like ALL	CAR T-cell therapy for adults (over 25) Lack of options for relapsed T-ALL
	Lack of funding options for advanced diagnostics (PCR, genomic array, NGS). As a result, several WHO defined ALL sub-entities are not routinely discoverable with current standard of care diagnostics, precluding selection of optimal therapy	PBS restrictions on TKI use beyond 2 years of maintenance	
AML	Lack of funding options for advanced diagnostics (MRD PCR and flow, microarray, NGS), which may impact on transplant decisions.	Many drugs are not funded for inpatient use despite being available on the PBS, which is restricted to outpatient medication use, with major examples including midostaurin, gemtuzumab ozogomycin, venetoclax-azacitidine. gliteritinib (*FLT3* inhibitor) IDH-1 and 2 inhibitors (enasidenib, ivosenib)	Certain MRD monitoring is not undertaken post diagnosis due to the lack of targeted treatment options for some of those markers if they were to relapse/progress. Cell therapy
Lower Risk MDS	Molecular testing unfunded/unavailable	Therapies that improve cytopaenias and /or transfusion dependence are largely unavailable or unfunded (e.g. EPO and luspatercept)	Therapies for relapsed / refractory MDS are nonfunded or unavailable
Intermediate and / or higher risk MDS	Molecular testing unfunded/unavailable and this may change risk and /or allotransplant decisions	Therapies for patients with 10-20% blasts are limited with CR rates<50% and /or significant toxicities for combination therapy (e.g., venetoclax)	Nonfunded or unavailable for MDS phenotype unless patient progresses to AML
CML	-	-	-

CLL	Access to gene array and mutation screening by NGS (e.g. TP53) Frontline young patients no access to novel agents Inequitable access of genetic testing necessary to inform prognosis	acalabrutinib ± obinutuzumab, venetoclax + obinutuzumab for younger patients zanubrutinib ibrutinib	CAR-T cell therapy Triple refractory population- gaps in drug options Richter's Transformation - gaps in drug options Access to venetoclax retreatment Double refractory treatment options pirtobrutinib
Lymphoma	Lack of funding options for advanced diagnostics (NGS	critzotinib (ALK+Lymphoma,	azacitidine (T-Cell)

	and MRD) for lymphomas in general, including MYD88 status in WM, EZH2 status in Follicular lymphoma, P53 in CLL and MCL, Gene Expression Profiles in Diffuse Large B-Cell, (and T-cell) and Whole Exome Sequencing analysis of MYC, bcl 2 and bcl 6. FISH testing used to diagnose HGBL-double hit.	histiocytosis) for first line or relapse BRAF inhibitors for hairy cell leukaemia and histiocytosis. Thiotepa for transplant therapy in primary central nervous system lymphoma bortezomib for abc-DLBCL, and in mantle cell lymphoma polatuzumab for frontline DLBCL	CAR T-cell therapy (Follicular) CAR T-cell therapy (Richter's) CAR T-cell therapy (Mantle cell) Bi-specific antibodies including mosunetuzumab in FL, glofitimab and epcoritimab in DLBCL. tafasitabam and lenalidomide and polatuzumab BR for Diffuse Large B-Cell PD1 inhibitors for extranodal natural killer/T-cell EBV-specific CTL lines for extranodal natural killer/T-cell and other ebv-PTLDs pirtobrutinib in Mantle Cell Lymphoma tazemetostat in EZH2-mutated Follicular Lympohoma
Hodgkin lymphoma		brentuximab vedotin (CD30) in Advanced stage (AAVD)	
Myeloma	CT/PET and whole body STIR MRI skeletal surveys Lack of availability for MRI AND PET means that it is not possible to differentiate between smouldering myeloma and myeloma based on SLIM-CRAB criteria. Lack of funding options for advanced diagnostics (NGS and MRD), including gene expression profile for baseline risk stratification.	bortezomib, lenalidomide, and dexamethasone (VRd) Bendumustine Daratumumab-RevDex for non-transplant eligible patients Specific regimens for high-risk myeloma, such as KCRD-daratumumab daratumumab-VTD induction for some patient cohorts	daratumumab-Pd KPd CAR-T cell therapy (both idecel and ciltacel) BCMA T cell engager - teclistamab

Source: State of the Nation, using data from NCCN, ESMO and NICE clinical guidelines; Department of Health, 2022, Application 1684, Genetic testing for variants associated with haematological malignancies; and National Action Plan for Blood Cancer, Chapters 3 and 5. [41]

[41] https://www.leukaemia.org.au/wp-content/uploads/2023/02/Leukaemia-Foundation_Final-Report_State-of-the-Nation-Blood-Cancers-in-Australia-Report-2023.pdf, pp75-77.

APPENDIX B: Case study – Real-world benefits of genomics for blood cancer patients

The Leukaemia Foundation and Tour de Cure are driving a genomics trial for people living with blood cancer through providing co-funding of $1.8 million towards this program to pilot the screening of 240 patients.

The blood cancer genomics trial links genomic screening of patients who have failed or don't respond to treatment to multiple novel therapeutic combination treatments.

This initial investment has allowed screening and enrollment to open to patients at Royal Brisbane and Women's Hospital, and Royal Adelaide Hospital and SA Pathology providing molecular screening for the program across both states. The trial was awarded additional $2.7 million in funding from the Medical Research Future Fund (MRFF) to expand to other sites.

Below is an account from the family member of a trial participant.

"A huge thank you to LF [and Tour de Cure] for establishing the Blood Cancer Genomics trial as it has resulted in a life-saving treatment for my family member (parent with children).

The family member was diagnosed with T cell prolymphocytic leukaemia in early January (2023) and started standard treatment. Unfortunately, there was no response to the treatment and the condition worsened. It got to the point where even a 15 metres walk was a struggle. Just over a week ago, we were provided the news that our family member only had 3-4 weeks to live. The kids were taken out of school to spend what time they could with their parent.

Fortunately, at a meeting of haematologists immediately after the diagnosis, it was suggested an option was to go on the Blood Cancer Genomics trial as if frontline treatment failed.

The genomic screening provided critical information to commence treatment, and within a few days, the effect on the leukaemia has been nothing short of miraculous.

Within 5 days, lymphocyte count returned to the normal range, and within a week, our family member is better than they have been in months, even being able to ride an exercise bike for 15 minutes.

The effect this has had on our family and the kids is immeasurable, so many thanks for enabling this to happen.