TE AHO O TE KAHU
CANCER CONTROL AGENCY

Te rere o te toto
Understanding blood cancer medicine availability in Aotearoa New Zealand
Full report

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TE AHO O TE KAHU CANCER CONTROL AGENCY

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HE KUPU TAKAMUA
FOREWORD

Tēnā koutou,

Every year in Aotearoa New Zealand, around 2,800 people are diagnosed with a blood cancer. There are no known prevention or screening interventions for blood cancers. For the people diagnosed, cancer medicines are often the principal treatment option. It is incredibly important to all people with cancer, their whānau, and their cancer treatment teams that the most appropriate treatment is available to them, when and where they need it.

For a number of years, there has been concern that Australia has more cancer medicines available than Aotearoa New Zealand. The report *Understanding the Gap: an analysis of the availability of cancer medicines in Aotearoa* was written in 2022 to provide clarity as to the extent and materiality of the difference in medicine availability between Australia and Aotearoa New Zealand. Only medicines that met a minimum threshold of clinical benefit (based on an internationally recognised tool) were identified as a gap in the report.

At the time of the 2022 report, it was not possible to assess the magnitude of clinical benefit for blood cancer medicines funded in Australia but not in Aotearoa New Zealand. Te Aho o Te Kahu made the commitment to complete that part of the analysis as soon as possible. We are very pleased to now deliver on that commitment and complete this work.

The information in this report will make clear how blood cancer medicine availability in Aotearoa New Zealand is different from Australia, a country we are routinely compared with. We hope the report will contribute further to the understanding of the availability of cancer medicines in Aotearoa New Zealand and that it will be a useful reference for the health system. The insights gained from this report can add to the discourse about access to medicines in this country and be considered alongside the many other sources of evidence and advice that inform decisions about medicines funding.

Cancer medicines are an important part of providing quality cancer care, but they are just one of a broad range of approaches needed to combat cancer. Coordinated efforts across the entire cancer continuum are required to ensure the system functions as efficiently and equitably as possible to deliver the best health outcomes. This includes focusing on prevention activities, identifying and diagnosing people with cancer early (including through screening), and ensuring there is adequate workforce and infrastructure to support high-quality care (including surgery and radiation therapy) and quality-of-life supports (including palliative and end-of-life care). The full health benefits of cancer medicines can only be realised if all parts of the cancer care continuum are working well and adequately resourced.

People with cancer, and their whānau, must always remain at the centre of any conversation about cancer treatments. While this report is technical, it has been written with those people in mind.

I would like to thank all those who provided their expertise to support this report, including the staff at Te Aho o Te Kahu and the wider project team of clinical pharmacists and haematologists who are at the front line of care delivery. The release of this report brings to completion over three years of work for this group.

It is my hope that this report will provide additional clarity and insights to all those invested in ensuring there are fewer cancers, better survival, and equity for all.

Mauri ora

Rami Rahal
Chief Executive and National Director of Cancer Control
Te Aho o Te Kahu - Cancer Control Agency

NGĀ MIHI
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Jo-Anne Wilson
Pharmacist

We also are grateful to Pharmac staff for their input to develop this work.

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mā te kite ka mōhio,
mā te mōhio ka mārama.

Seek and discover,
discover and know,
know and become
enlightened.

HE WHAKARĀPOPOTONGA
EXECUTIVE SUMMARY

What this report is about

This report summarises the similarities and differences in the publicly funded medicines used in the treatment of blood cancers between Australia and Aotearoa New Zealand.

Why are we interested in this?

Cancer medicines are a key part of providing quality clinical cancer treatment along with radiation therapy and surgery. People with cancer, their whānau, and cancer clinicians expect the appropriate medicines to be available when needed.

It is often acknowledged that Aotearoa New Zealand has lower access to cancer medicines than other high-income countries like Australia and the United Kingdom. This report set out to improve understanding of the difference in availability of publicly funded blood cancer medicines between Australia and Aotearoa New Zealand. In addition, it sought to describe the magnitude of clinical benefit or opportunity that might be realised if these medicines were funded and available in Aotearoa New Zealand.

We think this information will be useful and informative to the public and policy makers. It is not intended to inform medicine funding decisions in isolation of a range of other factors being considered.

What we did

We compared all the blood cancer medicines that are publicly funded in Australia through the Pharmaceutical Benefit Scheme with those publicly funded in Aotearoa New Zealand through Pharmac's Pharmaceutical Schedule. This identified what blood cancer medicines were available only in Australia, only in Aotearoa New Zealand, or in both countries.

We looked at medicine availability in terms of:

- the number of individual medicines
- the number of medicine-indication pairs (one medicine might have multiple specific uses (indications); 'medicine-indication pairs' refers to each specific indication for a medicine's use)
- regimen-indication pairs (a regimen requires multiple medicines to be used together for a specific treatment of an indication).

For medicines only funded in Australia, we assessed the clinical benefit they would provide if they were funded in Aotearoa New Zealand. We used a scoring system called the European Society for Medical Oncology – Magnitude of Clinical Benefit Scale for Haematological Malignancies (ESMO-MCBS: H). These scores were classified into substantial or not substantial magnitude of clinical benefit.

What we found

13 blood cancer medicines were publicly funded in Aotearoa New Zealand but not in Australia

58 blood cancer medicines were publicly funded in both Aotearoa New Zealand and Australia

24 individual blood cancer medicines were funded in Australia but not in Aotearoa New Zealand

42 blood cancer medicine-indication pairs

12 had a substantial magnitude of clinical benefit

37 blood cancer regimen-indication pairs

11 had a substantial magnitude of clinical benefit

Who will be interested?

We expect the scale and magnitude of clinical benefit of medicine gaps in Aotearoa New Zealand will be of interest to people with cancer and their whānau, the health sector, Pharmac, the New Zealand Government, non-governmental organisations, and the general public.

In conclusion

This report highlights areas where cancer medicines could be used more effectively to deliver quality, timely cancer care.

Cancer medicines are an important part of providing quality cancer care, yet they do not exist in isolation. The full health benefits of cancer medicines can only be realised if all parts of the cancer care continuum are working well and equitably. This includes ensuring people can access funded medicines and other treatments in a timely way (ideally through early diagnosis) and close to home. This relies on having a resourced workforce, and services across the whole cancer system, including nurses, clinicians, haematologists, pathologists, labs and imaging.

Te Aho o Te Kahu remains committed to our vision of fewer cancers, better survival, and equity for all, supported by a reliable, modern and consistent health care system. We will continue working with our sector partners to continually strengthen the cancer system as a whole, including medicines.

KŌRERO O MUA
BACKGROUND

Cancer medicine availability

We know that timely access to cancer medicines is a central part of cancer treatment for many New Zealanders. We also know that the public funding of medicines, including cancer medicines, is complex due to the considerable number of medicines available, the increasing cost of medicines and limited budgets. Although these factors are not unique to our country, it is generally established that Aotearoa New Zealand has access to fewer cancer medicines than countries we like to compare ourselves to, including Australia, the United Kingdom and Canada.

In 2022 Te Aho o Te Kahu published *Mārama ana ki te Āputa: he tātari i te wāteatanga o ngā rongoā mate pukupuku i Aotearoa | Understanding the Gap: an analysis of the availability of cancer medicines in Aotearoa* (Te Aho o Te Kahu 2022; hereafter referred to as 'the 2022 report'). The 2022 report described the medicine gaps between Australia and Aotearoa New Zealand for solid tumour and blood cancer medicines. However, the report was only able to describe the magnitude of clinical benefit for solid tumour medicines funded in Australia but not in Aotearoa New Zealand. The magnitude of clinical benefit for identified gaps was not able to be presented for blood cancer medicines because the assessment tool – the European Society for Medical Oncology – Magnitude of Clinical Benefit Scale (ESMO-MCBS) – was not validated for use with blood cancer medicines. In mid-2023, a validated ESMO-MCBS was released specifically for the assessment of clinical benefit of blood cancer medicines. Therefore, this analysis and report is a follow-on from the 2022 report that aims to complete the understanding of medicines availability by re-assessing the gaps in publicly funded blood cancer medicines between Australia and Aotearoa New Zealand and determine the likely magnitude of clinical benefit if the identified gaps were publicly funded in Aotearoa New Zealand.

The 2022 report found 72 individual cancer medicines that were available in Australia but not in Aotearoa New Zealand.[1] This included medicines that were available in Aotearoa New Zealand but for the treatment of a different cancer than they are used for in Australia. The 72 individual medicines translated to 126 different treatment uses, called indications, 98 of which were for solid tumour cancers and 28 for blood cancers. This decreased to 88 regimens for solid tumour cancers and 26 for blood cancers when medicines used in combination were taken into account (that is, when two or more medicines are used at the same time as part of one treatment). Three of the identified gaps were likely to be associated with substantial clinical benefit in a curative clinical setting, and 17 additional gaps were likely to be associated with substantial clinical benefit in a non-curative setting. Since the publication of the 2022 report, five of the identified 20 have been funded by Pharmac and are publicly available in Aotearoa New Zealand.

[1] In this report, 'available medicines' refers to publicly funded medicines. For Aotearoa, this means medicines funded by Pharmac.

Cancer has a significant impact on the health and wellbeing of New Zealanders

Cancer is the leading cause of death in Aotearoa New Zealand, and a major contributor to health loss (Te Aho o Te Kahu 2021). Each year, approximately 27,000 people are diagnosed with cancer and around 9,000 people die of cancer in Aotearoa New Zealand. The majority of people diagnosed with cancer have a solid tumour, with the most common solid tumour cancers being breast, lung, prostate and colorectal. However, around 10% of cancer diagnoses and deaths in Aotearoa New Zealand are due to blood cancers, most commonly non-Hodgkin's lymphoma, acute leukaemias and multiple myeloma.

Cancer does not impact everyone equally. The burden of cancer disproportionally impacts Māori, who are more likely to be diagnosed with cancer, get cancer at a younger age, to be diagnosed with more severe disease, and have poorer survival than non-Māori (Gurney, Robson et al 2020; Gurney, Stanley et al 2020; Te Aho o Te Kahu 2021). Other inequities in cancer are evident, with high rates of cancer incidence and cancer death being experienced by Pacific peoples, disabled people and those living in the most deprived areas of Aotearoa New Zealand (Te Aho o Te Kahu 2021). These inequities in cancer are unjust and unfair and are the result of many factors, including differential access to the social determinants of health; differential exposure to cancer risk factors; poorer access to cancer screening and diagnostic services; and the accessibility, timeliness and cultural safety of subsequent care (Te Aho o Te Kahu 2021; Vaccarella et al 2019).

When combined, blood cancers are the fourth most commonly diagnosed cancer for Māori, the sixth most commonly diagnosed for non-Māori and the third most common cause of cancer death for all New Zealanders. Around 1,000 New Zealanders die from a blood cancer each year (Te Aho o Te Kahu 2021). For blood cancers specifically, Māori have higher age-standardised rates of incidence and have lower survival rates (Gurney, Robson et al 2020; Gurney, Stanley et al 2020).

Cancer medicines are a critical part of cancer treatment and high-quality care

Access to appropriate and effective cancer medicines is central to providing high-quality cancer care and improving cancer outcomes. While some people with blood cancer may receive radiation therapy, and some may need surgery, these other treatment modalities play a much more critical role in the treatment of solid tumours. Access to medicines is critically important in the treatment of blood cancers.

Cancer medicines are most often administered as a series of infusions in a hospital setting, but some medicines can be taken orally as tablets or capsules. Cancer medicines typically have a fixed treatment duration or are taken until the cancer

progresses or unacceptable medicine toxicity occurs. Cancer medicines may be used with an aim of curing cancer, extending survival and/or improving quality of life. For many New Zealanders impacted by cancer, and their whānau, even small improvements in longevity and quality of life can be important.

Ensuring cancer medicines are available and accessible when needed can be challenging

People with cancer, their whānau, and health professionals who provide cancer care expect to have the medicines they need funded and available when they need them. Worldwide, countries are struggling to meet this expectation. The gap between medicines that are funded and medicines that are approved to treat a particular stage and type of cancer is an increasing issue globally. Medicine availability is an understandably emotive topic for people with cancer, their whānau, health professionals providing cancer care and advocacy groups.

While optimising the availability of cancer medicines and their role in improving health outcomes for people with cancer is particularly important, medicine availability cannot be considered in isolation. Coordinated and prioritised action across the entire cancer care continuum is required to ensure outcomes for New Zealanders with cancer improve to the greatest extent possible. The wider cancer health system, which works to prevent cancer and provide access to diagnosis and treatment across the cancer continuum, must be functioning well.

There are many reasons why Aotearoa New Zealand and other countries globally are struggling to ensure cancer medicine availability meets cancer need. Four reasons are described below.

Cancer medicines are developing rapidly.

The population is growing and people are living for longer, which means more people are developing cancer, and the need for cancer treatments is increasing. Additionally, scientific and technological research and developments are occurring at pace, rapidly increasing our understanding of how cancer works and how cancer treatments could be developed to target specific cancers more effectively. As a result, more and more cancer medicines are being developed and becoming available, many with very specific clinical indications. Progress in cancer medicine development and improvements in cancer survival also mean that many more lines of therapy are required and available for patients than there have been historically.

Cancer medicine spend is increasing.

While the number of cancer medicines is growing, the cost of cancer medicines is also increasing. New cancer medicines are costly and increasingly unaffordable for health care systems and patients.

Cancer medicines are often more expensive than other medicines, and they are also more rapidly increasing in price (Bach 2009; Savage et al 2017). There is growing concern that the cost of some medicines does not align with the health benefit those medicines

provide (Hwang et al 2022; Vivot et al 2017; Vokinger et al 2020). Pharmaceutical companies argue that the high prices reflect the high cost of developing effective medicines. Ultimately, this makes it difficult for countries to fund all available cancer medicines (World Health Organization 2018). The impact that cost has on medicine availability varies by country due to different funding pathways. For example, countries like the United States provide cancer medicines through insurance policies where some of the cost can be passed on to the insurer and onto patients, whereas there will be different medicine accessibility in countries like Aotearoa New Zealand and Australia that cover the full cost of medicines through a limited public health budget.

It is increasingly difficult to determine what the value-add of some new medicines will be.

Evaluation of the benefit of a new cancer medicine is conducted through clinical trials. The most useful clinical trials aim to demonstrate a new cancer medicine has an increased duration of survival or improved quality of life compared to currently available treatments. Sometimes direct comparison trials are not possible and single-arm clinical trials are conducted, usually for rare cancers. Many clinical trials measure outcomes using surrogate markers – that is, markers intended to indicate that increased survival and/or improved quality of life will be achieved sometime in the future. In practice, surrogate markers do not always correlate with improved clinical outcomes.

Common examples of surrogate markers include progression-free survival (the length of time during and after treatment where the cancer is still present but does not get worse) and disease-free survival (the length of time after treatment that a patient survives without signs or symptoms of cancer). While these measures demonstrate that medicines have an impact on the biological progression of cancer, they do not always translate into improved quality of life or overall survival. That is, although biologically the cancer might not be worsening, there may not be any change to how a person feels physically or how long they will live for.

Accelerated approval pathways for medicines, using early evidence based on surrogate markers, are increasingly used internationally, including by the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA). This can have a negative impact on the global understanding of medicine benefits, with minimal emphasis placed on assessment of whether surrogate markers translate into positive health outcomes (Akhade et al 2022). In the long term, accelerated medicine approval disincentivises investment in longer-term trials that are more costly but necessary to demonstrate that a medicine meaningfully improves quality of life and/or survival outcomes (Akhade et al 2022). It is important to be able to consistently evaluate the quality of the literature and studies that have led to the approval of a new cancer treatment. It is for this reason the European Society for Medical Oncology (ESMO) developed the Magnitude of Clinical Benefit Scale (MCBS).

The benefit of medicines can only be realised if the health system is able to support the provision of high-quality care to all those in need of care.

For funded cancer medicines to be effective, the health system must ensure the medicines are truly accessible to people who need them. The health care system must have capacity to provide all the care associated with the treatment regime. This includes sufficient health workforce (including nurses, haematologists, oncologists, pharmacists, laboratory and imaging specialists, allied health services, and administrators),

appropriate infrastructure (such as infusion sites, laboratories, pharmacies, radiology services and clinic rooms) and all other required services and equipment. For example, a patient receiving intravenous systemic anti-cancer therapy (chemotherapy) every 3 weeks for a blood cancer will require:

- multiple interactions with their haematologist, who will decide what medicine they need and will monitor the ongoing effects of treatment on the patient and their cancer
- a pharmacist to check and make up the individual medicine doses each time the patient has an infusion
- multiple blood tests and imaging tests to determine how the patient's cancer, and body generally, is responding to cancer treatment – these tests need to be completed, reviewed, interpreted and communicated across a range of health professionals
- an administrator to schedule the patient's infusion appointments and follow-up clinical appointments
- multiple interactions with nursing staff who are likely to administer the infusions and monitor the patient during the treatment
- possible interactions with the patient's General Practitioner (GP)or emergency department staff if adverse events or side effects occur
- support from allied health services and psychosocial services
- on occasions, liaising with the blood bank, and the subsequent administration of blood products.

Therefore, providing cancer care and administering medicines safely to those who need them requires a significant amount of resource that is additional to the cost of funding the actual medicine itself. Health systems, in Aotearoa New Zealand and internationally, are grappling with workforce shortages and pressures to reduce hospital expenditure, which in turn is impacting the health system capacity. This is a growing challenge with rising health care costs in the context of growing and aging populations.

Investment in any new medicines must be considered alongside the resources and services needed to ensure patients and whānau receive timely, effective and safe cancer treatment.

Deciding what medicines are funded publicly is complex

All countries must assess the value of new medicines and choose which medicines to fund. The way this is achieved varies between countries, but the assessment and decision-making process is always complex. There are benefits and drawbacks to all approaches.

Funding available for health systems is limited, and there is an increasingly wide spectrum of health conditions, which is associated with an increasing number of people requiring care, many with complex needs. One part of this challenge globally is determining how much resource should be put towards cancer. There are multiple ways

to assess the trade-offs that go into making these decisions, and there is no 'right' amount to spend on cancer or public medicines.

Decisions about which medicines are publicly funded in Aotearoa New Zealand are made by Pharmac. Pharmac is an independent Crown entity tasked with publicly funding medicines that secure the best health outcomes that can reasonably be achieved within the fixed pharmaceutical budget it is allocated by the Government.

Budget constraints, combined with the high cost of many medicines, mean Aotearoa New Zealand, like other countries, cannot fund every medicine on the market. This requires prioritised decisions about the medicines that can be funded in Aotearoa New Zealand.

Pharmac uses a framework called the Factors for Consideration to evaluate the benefit of a proposed new medicine and how this compares to other proposed new medicines. The Factors for Consideration include:

- the health need of the patient population
- the health/clinical benefits of the new medicine compared to what is already available
- the cost implication of funding this new medicine, including potential savings
- how suitable the new medicine is, compared to what patients receive now.

The Factors for Consideration and the Pharmac decision-making process also specifically consider the health outcomes of population groups experiencing health disparities, the impact of the medicine on Māori areas of focus, and Māori health outcomes.

Using the Factors for Consideration, Pharmac creates a list of medicines in priority order that it would fund if/when budget is available. This is the Options for Investment (OFI) list. Additional budget to fund new medicines primarily arises due to:

- savings Pharmac achieves in payment for medicines it already funds
- additional budget provided by the Government.

As of June 2024, there are 140 medicines on the OFI list that Pharmac would fund if it had available budget. Fifty-seven are for the treatment of cancer generally, with 17 specifically for blood cancers.

In this report, we are comparing the availability of blood cancer medicines in Australia with their availability in Aotearoa New Zealand.

Table 1 provides a high-level summary of some of the differences between how medicines are funded in Aotearoa New Zealand compared with Australia. This provides useful context to consider when interpreting the results of the availability analysis.

Table 1: Comparison of medicine funding processes between Australia and Aotearoa New Zealand

	Australia*	Aotearoa New Zealand
Payer	The Australian Government subsidises or fully covers the cost of many medicines through the Pharmaceutical Benefits Scheme (PBS).	The New Zealand Government subsidises or fully covers the cost of many medicines through the Pharmaceutical Budget, which is managed by the government agency Pharmac.
Patient costs	Patient co-payments for hospital and community medicines range from AU$6.80–$42.50. Patient co-payments for medicines in 2020–2021 was AU$1.4 billion.	The patient co-payment on the majority of publicly funded medicines administered in the community is $5.[†] Medicines administered in a hospital setting do not have a patient co-payment.
Budget	Expenditure on medicines funded through the PBS is uncapped, meaning new medicines can be added and funded as demand grows. Future expenditure is therefore expected to increase but with the intention that it will stay in line with 0.7% of Australia's gross domestic product.	The Pharmaceutical Budget in Aotearoa New Zealand is fixed and is allocated each year as part of the annual Budget cycle (Vote: Health). Pharmac is legislated to work within a fixed budget. Pharmac generates some additional budget from savings generated by the annual tender (negotiation of better prices for medicines Pharmac already subsidises) or the introduction of generic/biosimilar products upon patent expiry.
Expenditure 2022/23 (net)	Spent $16.7 billion[‡]	Spent $1.177 billion[§]
Population 31 Dec 2022	26,268,359[¶]	5,151,600[#]
Expenditure per person	$636	$343
Medicines regulator	Therapeutic Goods Administration (TGA). Medicine safety approval and funding can be considered in parallel.	Medsafe. Medicine safety approval and funding can be considered in parallel.

	Australia*	Aotearoa New Zealand
Method of new medicine approval	Medicines are evaluated for approval by the Pharmaceutical Benefits Advisory Committee (PBAC), an independent expert body appointed by the Government. PBAC's assessment of the value of a new medicine includes consideration of cost, clinical effectiveness, safety, quality and efficacy, and cost-effectiveness of the medicine compared to other treatments for the same condition. A medicine must be given a positive recommendation by PBAC to be funded in Australia, after which the medicine supplier must negotiate the listing, including pricing, with the Department of Health. Decisions under $20 million per year are made by the Minister of Health. Investments over $20 million require Cabinet approval. Not all medicines are given a positive recommendation by PBAC. Some may be declined, and some may be deferred until additional information is available.	Applications for new medicines are received and assessed by Pharmac with input from clinical advice committees. Pharmac assesses the value of a new medicine using the Factors of Consideration Framework, which considers the health need, health benefit, costs/savings and suitability of a new medicine compared to what is already available. These factors are considered at a patient, whānau and health system level. Using the Factors of Consideration, Pharmac prioritises new medicine applications against each other to form the OFI list. The OFI list represents a prioritised list of medicines that Pharmac would fund if there was an available budget. Not all assessed medicines are ranked on the OFI list. Some may be recommended for decline and others may be ranked on an 'Only if cost neutral/cost-saving' list. Medicines ranked on the latter are those that provide similar benefit to medicines that are already available so will only be funded if the cost of the medicine or to the health system is the same as what is already available.

* Parliament of Australia (2022).

† The $5 patient co-payment for community pharmaceuticals in Aotearoa New Zealand was removed between 1 July 2023 to 1 July 2024. During this time period there was no patient co-payment for community pharmaceuticals.

For further information on how medicines are funded in Aotearoa New Zealand, see page 9 of the 2022 report or Pharmac's web page titled 'The funding process' (**pharmac.govt.nz/medicine-funding-and-supply/the-funding-process**).

For further information on how medicines are funded in Australia, see Parliament of Australia (2022).

‡ Australian Government Department of Health and Aged Care (2023).

§ Pharmac (2023).

¶ Sourced from Australian Bureau of Statistics.

Sourced from Stats NZ.

What this analysis sets out to achieve

This report aims to compare the current state of publicly funded blood cancer medicine availability in Aotearoa New Zealand with publicly funded blood cancer medicine availability in Australia. For blood cancer medicines identified as being available in Australia but not in Aotearoa New Zealand, the magnitude of clinical benefit of the identified medicine gaps is described using the European Society for Medical Oncology – Magnitude of Clinical Benefit Scale for Haematological Malignancies (ESMO-MCBS:H).

The analysis was designed to establish a system-level understanding of the medicine availability between the countries to inform public discourse.

NGĀ TUKANGA
METHODS

The primary purpose of this analysis was to complete the original objective of the 2022 report by conducting an analysis comparing the availability of publicly funded blood cancer medicines in Australia with the availability of publicly funded blood cancer medicines in Aotearoa New Zealand. For the blood cancer medicines that were identified as being available in Australia but not in Aotearoa New Zealand, the analysis also determines the materiality of the gap by assessing the magnitude of clinical benefit.

The 2022 report did list the gaps in blood cancer medicine availability between Australia and Aotearoa New Zealand but did not comment on any likely clinical benefit of the identified gaps. This was because the tool used to measure the magnitude of clinical benefit (the ESMO-MCBS) was not validated for use with blood cancer medicines at that time. In mid-2023, a variation of the ESMO-MCBS specific to blood cancer medicines – the ESMO-MCBS:H – became available.

Because this analysis is a continuation of the 2022 report, this analysis utilised the same methodology that was outlined in the 2022 report. A high-level summary of the methodology is explained here. For further information, please refer to the 2022 report (Te Aho o Te Kahu 2022).

Why did we compare medicine availability in Aotearoa New Zealand with that in Australia?

Australia was selected as a comparator country for the following reasons.

- Australia has a broadly similar health system and approach to pharmaceutical funding.
- Information on which medicines are publicly funded is clear and easily accessible.
- Comparisons between Australia and Aotearoa New Zealand with respect to health care outcomes and health care availability, particularly for cancer, are relatively common in public discourse. Australia is a country Aotearoa New Zealand often compares and benchmarks itself against.

How did we determine differences in medicine availability?

In this report, we compared the list of medicines for the treatment of blood cancers that are publicly funded in Australia with those that are publicly funded in Aotearoa

New Zealand. From this comparison we were able to determine which blood cancer medicines are available in:

- both Australia and Aotearoa New Zealand
- Australia but not in Aotearoa New Zealand
- Aotearoa New Zealand but not in Australia.

A list of medicines publicly funded in Australia is available through the Pharmaceutical Benefits Scheme (PBS), which is a part of Australia's Department of Health and Aged Care. A list of medicines publicly funded in Aotearoa New Zealand is available through Pharmac's Pharmaceutical Schedule. We compared blood cancer medicine availability between the two lists as of 1 January 2024.

What was considered a gap?

One cancer medicine may be used in the treatment of more than one cancer type or clinical circumstance. The specific clinical circumstance a medicine is used for is called the **indication**. An example of this is the blood cancer medicine called pembrolizumab, which can be used for two indications: one being relapsed or refractory Hodgkin's lymphoma and the other being relapsed or refractory primary mediastinal B-cell lymphoma. Some cancer treatment consists of more than one cancer medicine being used at the same time (ie, used in combination) for a specific indication. The combination of treatments to treat a single indication is called a **regimen**.

This report defines gaps in medicine availability between Australia and Aotearoa New Zealand in three ways:

1. **Individual medicine gaps (eg, azacitidine)**

   'Individual medicine gaps' refers to individual medicines that are funded in Australia but not in Aotearoa New Zealand irrespective of the specific clinical circumstance the medicine is used for (indication) or whether it needs to be used with another medicine at the same time (regimen).

2. **Medicine-indication pair gaps (eg, azacitidine for patients who are unfit for intensive chemotherapy)**

   'Medicine-indication pair gaps' refers to medicines that are funded in Australia but not in Aotearoa New Zealand, with reference to each specific and different indication for the medicine's use. One medicine might be funded for several indications and all the identified indications would need to be funded to close the gap.

   Medicines that are part of medicine regimens and are funded in Australia but not in Aotearoa New Zealand will be counted as medicine-indication pair gaps individually. For example, if medicine A was available in Australia (but not in Aotearoa New Zealand) for indication X and indication Y, this would be counted as two separate medicine-indication pair gaps. In addition, if medicine B was used in combination with medicine C for indication Z this would be counted as two separate medicine-indication pair gaps: Medicine B for indication Z would be one gap and medicine C for indication Z would be a separate gap.

3. **Regimen-indication pair gaps (eg, azacitidine with venetoclax for patients who are unfit for intensive chemotherapy)**

   'Regimen-indication' pair gaps' refers to the situation where more than one medicine will be required for a particular treatment and that all those medicines need to be funded to close that particular treatment gap.

   If two separate medicines are part of the same regimen for the same indication, this will be counted as a single regimen-indication pair gap to reflect that both these medicines will need to be funded to close the identified gap. For example, if medicine B was used in combination with medicine C for indication Z, this would be considered a single regimen-indication pair gap.

Where a generic or biosimilar product is available in one country and the reference product (often called the originator, innovator, or brand-name product) was available in another, these were considered identical for the purpose of this analysis. Furthermore, if several medicines of the same class for the same indication were available in a jurisdiction, this was only considered once. For example, if medicines E and F are medicines from the same class with the same mechanism of action and were both funded in Australia for indication W, this would only be considered as single gap. This is because only one of medicine E or F would need to be funded in Aotearoa New Zealand to close the identified gap – for example, ibrutinib or zanubrutinib for the treatment of relapsed or refractory mantle cell non-Hodgkin's lymphoma.

How did we measure magnitude of clinical benefit?

Not all gaps in medicine availability offer the same level of benefit. Clinical benefit is primarily driven by the medicine's clinical efficacy (ie, how good the medicine is at its intended purpose) and how much additional benefit the new medicine would provide compared to what patients would get otherwise. Determining the magnitude of clinical benefit for medicines available in Australia but not in Aotearoa New Zealand allows us to understand which gaps are most significant. For example, some medicines may not be available in Aotearoa New Zealand, but a newer or more effective medicine is available instead. This identified gap, therefore, offers no clinical benefit.

The likely magnitude of clinical benefit that could be realised if the medicine gaps were addressed was assessed using the ESMO-MCBS:H.

The ESMO-MCBS and the ESMO-MCBS:H were developed to:

- improve the critical evaluation of medicines
- ensure consistency in evaluation
- reduce the risk of bias that can occur with the interpretation of clinical trial data
- provide a reliable and fair evaluation of the benefit cancer medicines can have to help inform cancer service planning and prioritisation
- reduce unwarranted 'hype' around some new medicines.

We used the ESMO-MCBS:H because:

- it is based on the ESMO-MCBS, which was the tool selected and used in the 2022 report, and it was important to ensure we assessed identified gaps for blood cancers in a comparable manner to the previous assessment of solid tumour cancers
- it is internationally recognised and validated.

The ESMO-MCBS:H aims to highlight those medicines that have a significant positive impact on quality of life and/or survival and distinguish these medicines from those that offer marginal benefits or delay disease progression with no impact on quality of life or survival.

There are several different scoring forms used depending on the clinical trial evidence available and the reported primary endpoints. The ESMO-MCBS:H assesses only the clinical trials that led to the medicine being licensed. Other evidence of medicine efficacy and benefit, including real-world studies, cannot be used in this methodology.

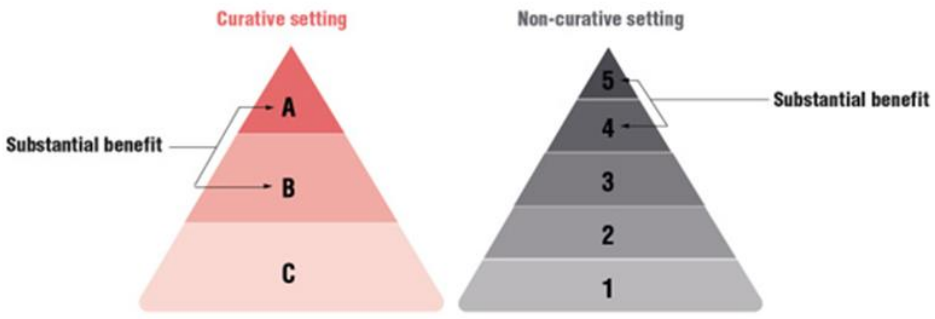
The resulting scores can be:

- A, B or C – these scores indicate medicines that are used with curative intent. Medicines scored with an A or B indicate substantially clinical benefit would be achieved if they were available
- 5, 4, 3, 2 or 1 – these scores indicate medicines that are used in a non-curative setting; that is, they improve quality of life or increase survival but will not cure the cancer. Medicines scored with a 5 or 4 indicate substantial clinical benefit would be achieved if they were available.
- No evaluable benefit (NEB) – These scores indicate that the trial evidence did not provide evidence of benefit.
- Non-scorable – This indicates the trial information was not able to be applied to the ESMO-MCBS:H.

Medicine-indication or regimen-indication pair gaps that were determined to have a substantial magnitude of clinical benefit were of principal interest in this analysis. For the purposes of this report, each medicine-indication pair gap was categorised as one of the following:

- Gap - substantial clinical benefit (ie, ESMO-MCBS score A, B, 4 or 5)
- Gap – not substantial clinical benefit (ie, ESMO-MCBS score C, 3, 2, 1)
- Gap – no evaluable benefit (NEB)
- Gap – not scorable

Figure 1: ESMO-MCBS:H possible scores and definition of magnitude of clinical benefit



It is important to note that there is no single approach to measuring the likely magnitude of clinical benefit, and while the ESMO-MCBS:H is one validated and recognised tool, it has the following limitations.

- The ESMO-MCBS:H is reasonably prescriptive, meaning some of the nuances of the trials are not easily captured, or some of the clinical trials evaluating the medicines did not contain the information required to be scored.
- The ESMO-MCBS:H requires that the clinical trial that led to the medicine being licensed is assessed to determine the magnitude of clinical benefit. While the majority of these are trials are robust and of high quality, the benefit demonstrated in a clinical trial environment may not accurately reflect the clinical benefit that is realised in a real-world environment.
- The ESMO-MCBS:H assesses clinical benefit based on the average or median experience of patients in the clinical trials. While this is the most appropriate method for assessing the clinical benefit provided by medicines, it obscures the benefit individuals may experience. With any medicine some people will experience better outcomes than others.
- The scoring system and the assessed clinical trials do not include assessment of whether closing the gaps identified in this analysis would make a difference to equitable access to cancer treatment and to cancer outcomes.
- Sometimes the medicine that was used as a comparator in the clinical trial was different to the medicine that would be used for that treatment purpose in Aotearoa New Zealand. This means the magnitude of clinical benefit derived does not reflect the true magnitude of clinical benefit in Aotearoa New Zealand. While the ESMO-MCBS:H does not have a process for adjusting derived scores to manage this, the project team did make adjustments occasionally on a case-by-case basis as required.

As an additional check, where possible the scores derived by the project team were checked against the ESMO-MCBS:H scores derived during the tool's evaluation and validation process (Kiesewetter 2020).

What was the scope of our analysis?

The assessment of publicly funded blood cancer medicines in Australia and Aotearoa New Zealand was conducted based on medicine availability as of 1 January 2024.

Blood cancer medicines were defined as any medicine used to actively treat blood cancer. Medicines used exclusively to manage symptoms or side effects without any direct effect on the cancer, while critical to cancer care, were considered out of scope of this report. Further information on the scope of the analysis is noted in Table 2.

Table 2: Scope of analysis inclusions and exclusions for blood cancer medicines

	Australia	Aotearoa New Zealand
Included	• Blood cancer medicines listed on the Pharmaceutical Benefits Scheme (PBS) Schedule that were consistently available across Australia	• Blood cancer medicines funded via Pharmac's Pharmaceutical Schedule
Excluded	• Medicines publicly funded in Australia by other means, including public hospital inpatient settings or provided by an individual state or hospital • Medicines accessed privately through private financing, private health insurance or through pharmaceutical company compassionate supply	• Medicines publicly funded by other means, including Pharmac's exceptional circumstances process, paediatric cancer medicines or clinical trials • Medicines funded outside the publicly funded system, including through private financing, private health insurance or through pharmaceutical company compassionate supply

Our process

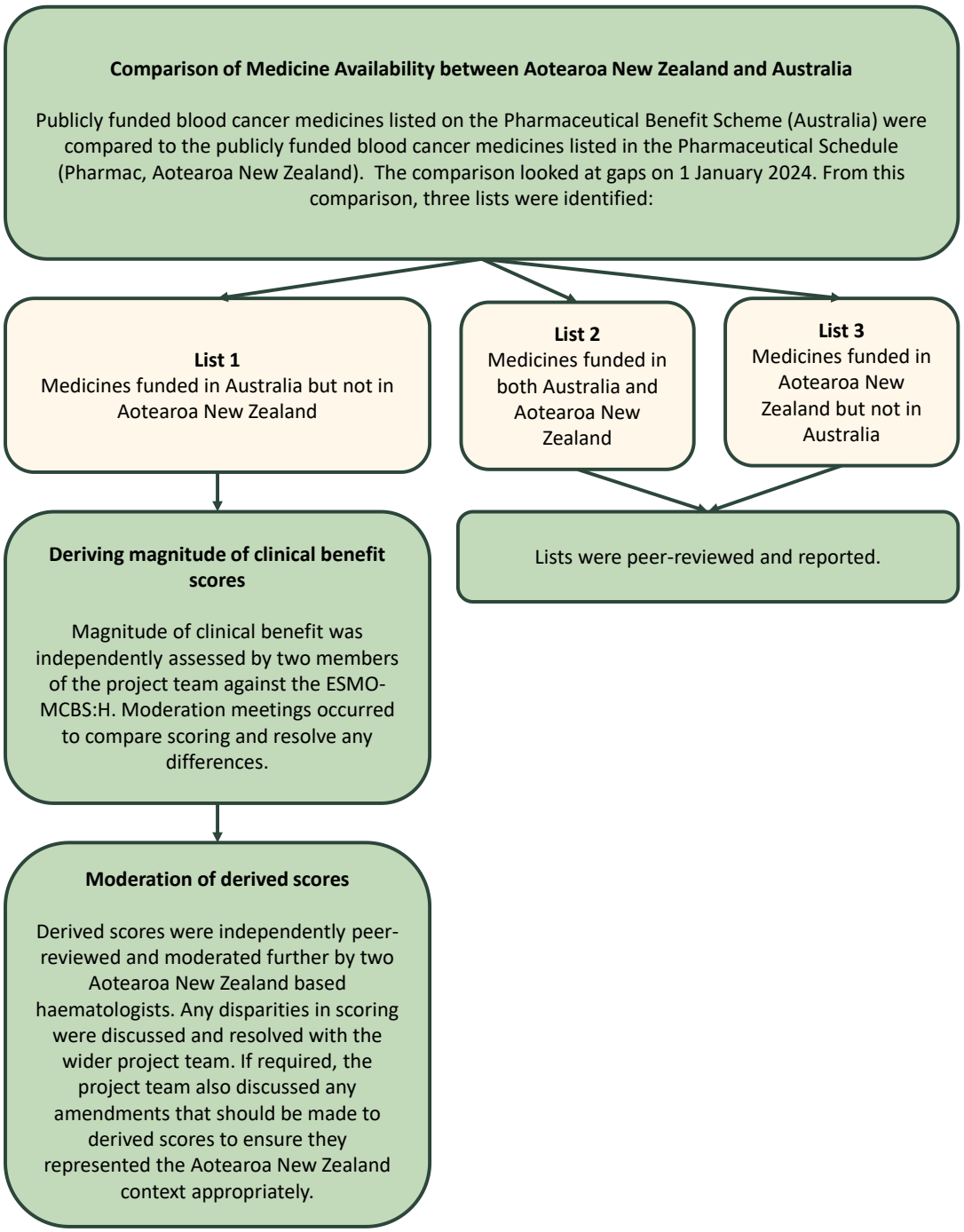
The general methodology of the analysis for this report was similar to the 2022 report. The main difference was that in the 2022 report the magnitude of clinical benefit scores for solid tumour medicines identified as medicine gaps were primarily taken from the scores previously derived and published by ESMO. Only a small number were scored by project staff, when a published ESMO-MCBS score was unavailable for a particular medicine. Published ESMO-MCBS:H scores were not available for blood cancer medicines when the analysis was undertaken for this 2024 report. As a result, the scoring of clinical benefit for blood cancer medicines identified as gaps was completed by the project team.

To ensure the score determination process was robust and reliable, a two-step review and moderation process was carried out. In the first step, two members of the project team conducted independent evaluations of each medicine's magnitude of clinical benefit and determined a score. The two members then met to discuss their findings and moderate any differences. Once moderation was complete, the scoring forms were sent to two haematologists who independently reviewed the scores and how they were derived. Again, where difference in opinion occurred, the entire project team met to discuss and moderate the information and come to a resolution. Where there was some uncertainty, the project team favoured the highest score possible for the medicine. The process of the analysis is detailed in Figure 2.

The magnitude of clinical benefit score allocation relied on the assessment of outcomes from the specific clinical trial that led to the medicine being licensed. Some clinical benefit scores were amended for accuracy in the context of Aotearoa New Zealand. This was necessary because, at times, there was a difference between the medicine that was used as a comparator in the clinical trial to the medicine that would be used for that treatment purpose in Aotearoa New Zealand. Without allowing for this context, the score allocated might not have reflected the potential benefit offered by the medicine should it be made publicly available in Aotearoa New Zealand. Again, the project team erred on

allocating the highest possible score for the medicine in this instance. Where several medicines with the same mode of action (such as multiple options within the same medicine class) and used for the same indication were available in Australia, these were represented as a single medicine gap with the highest ESMO-MCBS:H score applied.

Figure 2: Summary of analysis methodology



NGĀ HUA
RESULTS

Overall comparison of blood cancer medicine availability

In comparing the publicly funded blood cancer medicines that were available in Australia and Aotearoa New Zealand on 1 January 2024, we found that:

- 58 medicines were publicly available for the treatment of blood cancer in both Australia and Aotearoa New Zealand
- 13 medicines were publicly available for the treatment of blood cancer in Aotearoa New Zealand but not in Australia
- 24 medicines were publicly available for the treatment of blood cancer in Australia but not in Aotearoa New Zealand.

The 24 individual medicines funded in Australia but not in Aotearoa New Zealand made up 42 medicine-indication pairs and 37 regimen-indication pairs.

Figure 3: Summary of similarities and differences in blood cancer medicine availability in Australia and Aotearoa New Zealand

58 blood cancer medicines were publicly funded in both Aotearoa New Zealand and Australia.

13 blood cancer medicines were publicly funded in Aotearoa New Zealand but not Australia.

24 individual blood cancer medicines were publicly funded in Australia but not in Aotearoa New Zealand.

This correlated with **42** medicine-indication pairs and **37** regimen-indication pairs.

The 2022 report noted 28 medicine-indication pair gaps for blood cancers, which represented 26 medicine treatment regimens. Two of the 28 medicine-indication pairs have since been funded in New Zealand. These were brentuximab vedotin for relapsed or refractory anaplastic large cell lymphoma and for relapsed or refractory Hodgkin's lymphoma (funded on 1 December 2022). The remaining 26 blood cancer medicine-indication pairs were still considered gaps as of 1 January 2024.

The 2024 report found that the number of blood cancer medicine-indication pair gaps had increased to 42. Since the assessment of gaps on the 1 January 2024, 6 medicine-indication pairs have been funded by Pharmac. This means in October 2024, 36 medicine-indication gaps were identified between Australia and Aotearoa New Zealand for blood cancer medicines.

Blood cancer medicines funded in both jurisdictions

Fifty-eight blood cancer medicines were funded in both Australia and Aotearoa New Zealand. These medicines were either funded with the same restrictions in both countries or were funded without restriction for use (ie, open-listed) according to the licensed indications.

These 58 medicines were used for multiple different indications, including some which are used for solid tumour cancers as well as blood cancers. This means some of these medicines may have also been identified in the 2022 report where they are indicated for treatment of solid tumour cancers.

The full list of blood cancer medicines funded in both Australia and Aotearoa New Zealand can be found in Appendix 3.

Blood cancer medicines funded in Aotearoa New Zealand but not in Australia

Thirteen blood cancer medicines were funded in Aotearoa New Zealand but not in Australia. It is important to note that, due to differences in funding arrangements between Aotearoa New Zealand and Australia, some of these identified gaps may be available in Australia through public funding mechanisms that sit outside the PBS.

Since the gaps analysis was conducted on 1 January 2024, Pharmac have funded bendamustine for relapsed or refractory chronic lymphocytic leukaemia. Bendamustine for this indication will be available in Aotearoa New Zealand from the 1 November 2024. Bendamustine for this indication is not currently publicly funded in Australia so is a medicine funding advantage in favour of Aotearoa New Zealand

A list of the blood cancer medicines funded in Aotearoa New Zealand but not in Australia via the PBS is presented in Appendix 4.

Blood cancer medicines funded in Australia but not in Aotearoa New Zealand

On 1 January 2024 there were 24 individual blood cancer medicines that were available in Australia but not in Aotearoa New Zealand. This corresponded to 42 medicine-indication pairs and 37 regimen-indication pairs. That is, there are 37 blood cancer treatment regimens available in Australia but not in Aotearoa New Zealand, and 24 different blood cancer medicines for 42 different indications would need to be funded in Aotearoa New Zealand to close the gap.

Of the 42 medicine-indication pair gaps, 12 were found to have a substantial magnitude of clinical benefit (see Figure 4).

The gaps found spanned the spectrum of blood cancer types, with 20 gaps identified for the treatment of leukaemia, 11 for the treatment of lymphoma, seven for the treatment of myeloma and four for other blood cancers (see Table 3).

Figure 4: Summary of analysis of medicines available in Australia but not in Aotearoa New Zealand

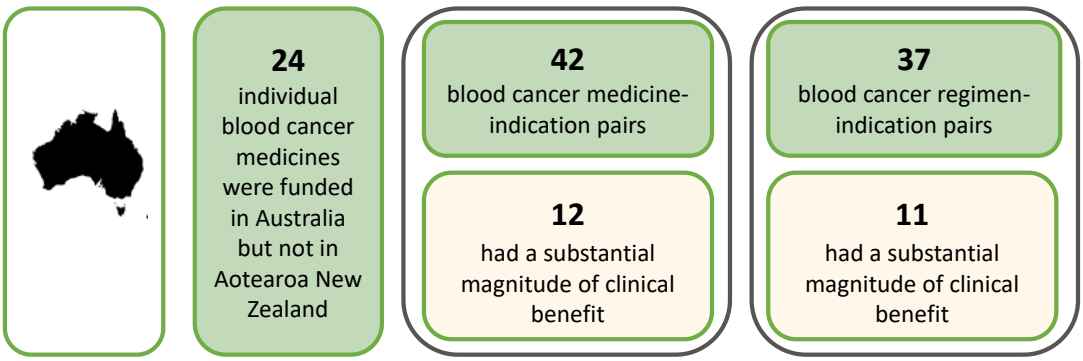


Table 3: Summary of medicine availability gaps by type of cancer and ESMO-MCBS:H score

Blood cancer type	Total	Substantial clinical benefit			Not substantial clinical benefit				
		Curative	Non-curative						
		A*	5*	4*	3	2	1	NEB†	Not scorable
Leukaemia									
Acute lymphoblastic leukaemia	4	1	1	1	–	1	–	–	–
Acute myeloid leukaemia	6	1	2	1	–	–	–	–	2
Chronic lymphoblastic leukaemia	7	–	–	1	5	–	1	–	–
Chronic myeloid leukaemia	3	–	–	1	1	–	–	–	1
Lymphoma									
Hodgkin's lymphoma	1	–	–		1	–	–	–	–
Non-Hodgkin's lymphoma	5	–	–	1	1	–	–	2	1
Lymphoma B-cell	1	–	–	–	1	–	–	–	–
Lymphoma T-cell	4	–	–	–	1	1	2	–	–
Myeloma									
Multiple myeloma	7	–	–	2	3	2	–	–	–
Other									
Other‡	4	–	–	–	1	1	–	–	2
Total									
Total	42	2	3	7	14	5	3	2	6

Note: Gaps shown are for medicine-indication pairs. Total gaps are less if regimen-indication pairs were considered. No gaps had an ESMO-MCBS:H score of B or C.

* Indicates an ESMO-MCBS:H score of substantial clinical benefit.

† NEB = no evaluable benefit.

‡ 'Other' includes systemic light chain amyloidosis, myelodysplastic syndrome and chronic myelomonocytic leukaemia.

Gaps associated with substantial clinical benefit

Of the 42 medicine-indication pair gaps found, 12 were considered to have a substantial magnitude of clinical benefit using the ESMO-MCBS:H.

Of the 12 medicine-indication pair gaps with substantial clinical benefit:

- three of the medicine-indication pairs have been funded since our gaps analysis
- four of the gaps identified are currently ranked on Pharmac's OFI list, the prioritised list of medicines they would fund if a budget was available
- two are being assessed by Pharmac for funding
- three have not had an application for funding submitted to Pharmac.

Table 4 summarises the identified gaps of substantial clinical magnitude. Further detailed information on the gaps identified can be found in Appendix 7.

Gaps associated with substantial clinical benefit – curative setting[2]

Only two medicine-indication pairs – midostaurin for acute myeloid leukaemia and blinatumomab for precursor B-cell acute lymphoblastic leukaemia – were evaluated to have an ESMO-MCBS:H score of A, which indicates a substantial magnitude of clinical benefit in a curative setting. No identified medicine-indication pair gaps were found to have an ESMO-MCBS:H score of B, which also indicates substantial clinical benefit in a curative setting.

See Table 4 and Appendix 7 for more information.

Gaps associated with substantial clinical benefit – non-curative setting[3]

Ten of the 12 medicine-indication pair gaps identified as having a substantial magnitude of clinical benefit were in a non-curative setting. Seven were for leukaemia, two were for multiple myeloma and one was for lymphoma.

See Table 4 and Appendix 7 for more information.

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[2] An ESMO-MCBS score of A or B indicates a medicine-indication pair associated with substantial clinical benefit and used with curative intent. Curative intent treatments are used with the intent of curing the disease. The medicines are usually used in combination with surgery and/or radiation therapy – they are given with the intention of stopping a tumour that was treated from recurring.

[3] An ESMO-MCBS score of 5 or 4 indicates a medicine-indication pair associated with substantial clinical benefit in the non-curative setting. Non-curative intent treatments are not used with the intent of curing the disease; instead, they are used with the intention of increasing the duration and/or quality of a person's remaining life living with the cancer. Medicines used in this setting may be used alone or alongside palliative surgery or radiation therapy.

Table 4: Blood cancer medicines funded in Australia but not in Aotearoa New Zealand with a substantial clinical benefit ESMO-MCBS:H score

ESMO-MCBS:H score	Medicine name	Used in combination with	Cancer type	Indication per PBS	Formulation	Medicine funded in NZ for other indications	Current Pharmac status (Oct 2024)†	Noted as a gap in 2022
A Substantial clinical benefit – curative	Midostaurin	Anthracycline and cytarabine chemotherapy (both already funded in Aotearoa New Zealand)	Acute myeloid leukaemia (AML)	Newly diagnosed patients with an internal tandem duplication (ITD) or tyrosine kinase domain (TKD) FMS-like tyrosine kinase 3 (FLT3) mutation	Oral capsule	No	Funded from 1 July 2024	Yes
A Substantial clinical benefit – curative	Blinatumomab	Monotherapy	Precursor B-cell acute lymphoblastic leukaemia (pre-B-cell ALL)	Complete haematological remission with measurable residual disease (MRD)	Continuous intravenous infusion	No	Seeking clinical advice	Yes
5 Substantial clinical benefit – not curative	Azacitidine*	Venetoclax*	Acute myeloid leukaemia (AML)	Patients who are unfit for intensive chemotherapy	Subcutaneous injection or intravenous infusion	Yes	OFI list	No
5 Substantial clinical benefit – not curative	Blinatumomab	Monotherapy	Precursor B-cell acute lymphoblastic leukaemia (pre-B-cell ALL)	Patients with relapsed or refractory disease	Continuous intravenous infusion	No	No application	Yes
5 Substantial clinical benefit – not curative	Venetoclax*	Azacitidine*	Acute myeloid leukaemia (AML)	Patients who are unfit for intensive chemotherapy	Oral tablet	Yes	OFI list	No

ESMO-MCBS:H score	Medicine name	Used in combination with	Cancer type	Indication per PBS	Formulation	Medicine funded in NZ for other indications	Current Pharmac status (Oct 2024)[†]	Noted as a gap in 2022
4 Substantial clinical benefit – not curative	Acalabrutinib, ibrutinib or zanubrutinib[‡]	Monotherapy	Mantle cell lymphoma (MCL)	Relapsed or refractory to at least one prior therapy	Oral capsule/ tablet	Yes	Acalabrutinib – no application Ibrutinib – OFI list Zanubrutinib – OFI list	Yes
4 Substantial clinical benefit – not curative	Asciminib	Monotherapy	Chronic myeloid leukaemia (CML)	Philadelphia chromosome positive or with transcript BCR-ABL1 tyrosine kinase mutation positive without T315I mutation in chronic phase previously treated with two or more tyrosine kinase inhibitors	Oral tablet	No	Seeking clinical advice	No
4 Substantial clinical benefit – not curative	Gilteritinib	Monotherapy	Acute myeloid leukaemia (AML)	Relapsed or refractory with FLT3 ITD or TKD mutation	Oral tablet	No	No application	No
4 Substantial clinical benefit – not curative	Idelalisib	Rituximab for 8 doses followed by monotherapy (already funded in Aotearoa New Zealand)	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Relapsed or refractory to at least one prior therapy, CD20-positive	Oral tablet	No	No application	Yes
4 Substantial clinical benefit – not curative	Inotuzumab ozogamicin	Monotherapy	Precursor B-cell acute lymphoblastic leukaemia (pre-B-cell ALL)	Relapsed or refractory B-precursor cell, CD22-positive	Intravenous infusion	No	OFI list	Yes

ESMO-MCBS:H score	Medicine name	Used in combination with	Cancer type	Indication per PBS	Formulation	Medicine funded in NZ for other indications	Current Pharmac status (Oct 2024)†	Noted as a gap in 2022
4 Substantial clinical benefit – not curative	Lenalidomide	Dexamethasone with or without bortezomib	Multiple myeloma (MM)	Newly diagnosed	Oral capsule/ tablet	Yes	Funded from 1 August 2024	Yes
4 Substantial clinical benefit – not curative	Pomalidomide	Dexamethasone (already funded in Aotearoa New Zealand)	Multiple myeloma (MM)	Relapsed or refractory third-line treatment	Oral capsule	No	Funded from 1 August 2024	Yes

Note: a score of A or B indicates curative, a score of 5 or 4 indicates substantial clinical benefit but not curative.

* Represents a regimen-indication pair – where more than one medicine is taken as part of the same treatment, and both would need to be funded to close the gap.

† Status as of May 2024. The status of medicine applications at Pharmac is constantly being progressed and updated. Please refer to Pharmac's Application Tracker (connect.pharmac.govt.nz/apptracker) for up-to-date information on a medicine application.

‡ Medicines that are part of the Bruton's tyrosine kinase (BTK) inhibitors medicine class – only one medicine from the medicine classes would need to be funded to close the identified gap. The ESMO-MCBS:H score reflects the highest score of the medicines scored in the class. Differences in ESMO-MCBS:H score are likely due to differences in trial design, follow-up periods and available data.

Gaps associated with substantial clinical benefit – by cancer type: Leukaemia

Eight regimen-indication pair gaps of substantial clinical benefit were for the group of blood cancers called leukaemia (Table 5). Six of the identified gaps were determined to be providing benefit in a non-curative setting, and two of the identified gaps were determined to be providing benefit in a curative setting.

Table 5: Substantial clinical benefit gaps in leukaemia

Medicine name	Cancer type	Indication per PBS	ESMO-MCBS:H score	Current Pharmac status (October 2024)	Appendix table for further detail
Midostaurin	Acute myeloid leukaemia (AML)	Newly diagnosed patients with an internal tandem duplication (ITD) or tyrosine kinase domain (TKD) FMS-like tyrosine kinase 3 (FLT3) mutation	**A** (curative)	Funded from 1 July 2024	Table 22
Blinatumomab	Acute lymphoblastic leukaemia (ALL)	Complete haematological remission with measurable residual disease (MRD)	**A** (curative)	Seeking clinical advice	Table 17
Azacitidine with venetoclax	Acute myeloid leukaemia (AML)	Patients who are unfit for intensive chemotherapy	**5** (non-curative)	OFI list	Table 23
Blinatumomab	Acute lymphoblastic leukaemia (ALL)	Patients with relapsed or refractory disease, precursor B-cell	**5** (non-curative)	No application	Table 18
Asciminib	Chronic myeloid leukaemia (CML)	Philadelphia chromosome positive or with transcript BCR-ABL1 tyrosine kinase mutation positive without T315I mutation in chronic phase previously treated with two or more tyrosine kinase inhibitors	**4** (non-curative)	Seeking clinical advice	Table 16

Medicine name	Cancer type	Indication per PBS	ESMO-MCBS:H score	Current Pharmac status (October 2024)	Appendix table for further detail
Gilteritinib	Acute myeloid leukaemia (AML)	Relapsed or refractory with FLT3 ITD or TKD mutation	**4** (non-curative)	No application	Table 19
Idelalisib (with 8 cycles of rituximab)	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Relapsed or refractory to at least one prior therapy, CD20-positive	**4** (non-curative)	No application	Table 20
Inotuzumab ozogamicin	Acute lymphoblastic leukaemia (ALL)	Relapsed or refractory B-precursor cell, CD22-positive ALL	**4** (non-curative)	OFI list	Table 21

Incidence of leukaemia

Leukaemia (acute and chronic combined, all ages) is the seventh most commonly diagnosed cancer in Aotearoa New Zealand – with an average of 650 people diagnosed each year, including 75 Māori. When age-standardised, the rate of leukaemia is higher for Māori (9 per 100,000) compared with non-Māori (7 per 100,000). The rate of leukaemia is also higher among Pacific peoples (9 per 100,000) compared with the non-Māori, non-Pacific, non-Asian population (7 per 100,000) (Te Aho o Te Kahu 2021).

Leukaemia survival[4]

Approximately 60% of those diagnosed with leukaemia will survive to five years (60% Māori, 62% non-Māori) (Gurney, Stanley et al 2020). This can be compared to outcomes internationally, with estimates from Cancer Research UK showing five-year survival in the United Kingdom at 56% for this cancer, while in the United States five-year survival is around 60% (Cancer Research UK 2023; Ellington et al 2023). Based on data from 2007 to 2016, Māori with leukaemia are 64% more likely to die from their cancer than non-Māori with the same cancer (Gurney, Stanley et al 2020).

Leukaemia mortality

Over the last decade, there has been an average of approximately 310 deaths each year from leukaemia, including around 30 Māori (Te Aho o Te Kahu 2021). The age-standardised mortality rate for leukaemia is higher among Māori (3 per 100,000) compared with non-Māori (2 per 100,000). The leukaemia mortality rate is also higher for Pacific peoples (4 per 100,000) compared with the non-Māori, non-Pacific, non-Asian population (3 per 100,000) (Te Aho o Te Kahu 2021).

[4] Survival data from Gurney, Stanley et al (2020) used cause-specific survival analysis methods, while survival data from other sources used relative survival analysis methods. While both approaches can produce robust survival estimates and data should generally be comparable between the two, each has its own strengths and limitations (Sarfati et al 2010).

Gaps associated with substantial clinical benefit – by cancer type: Lymphoma

One regimen-indication pair gap of substantial clinical benefit was for the group of blood cancers called lymphoma (Table 6). The identified gap was determined to provide benefit in a non-curative setting.

Table 6: Substantial clinical benefit gap in lymphoma

Medicine name	Cancer type	Indication per PBS	ESMO-MCBS:H score	Current Pharmac status (October 2024)	Appendix table for further detail
Acalabrutinib, ibrutinib or zanubrutinib*	Mantle cell lymphoma (MCL)	Relapsed or be refractory to at least one prior therapy	**4** (non-curative)	Acalabrutinib – no application Ibrutinib – OFI list Zanubrutinib – OFI list	Table 24

* Medicines that are part of the Bruton's tyrosine kinase (BTK) inhibitors medicine class – only one medicine from the medicine classes would need to be funded to close the identified gap. The ESMO-MCBS:H score reflects the highest score of the medicines scored in the class. Differences in ESMO-MCBS:H score are likely due to differences in trial design, follow-up periods and available data.

Incidence of lymphoma

Lymphomas can be broadly categorised as Hodgkin's lymphoma or non-Hodgkin's lymphoma. The two cancers differ somewhat in terms of age at diagnosis: Hodgkin's lymphoma has a 'double peak' in incidence (one in childhood/young adulthood, one in older adults), while non-Hodgkin's lymphoma has a single peak in older age (Cancer Research UK 2024). Hodgkin's lymphoma is the rarer cancer, with around 104 people diagnosed each year, including 12 Māori (Te Aho o Te Kahu 2021).

On the other hand, non-Hodgkin's lymphoma is the sixth most common cancer diagnosed in Aotearoa New Zealand – with around 800 people diagnosed each year, including 70 Māori. When age-standardised, the rate of non-Hodgkin's lymphoma is similar between Māori and non-Māori (both around 5 per 100,000). The rate of non-Hodgkin's lymphoma is also similar between Pacific peoples (9 per 100,000) and the non-Māori, non-Pacific, non-Asian population (8 per 100,000) (Te Aho o Te Kahu 2021).

Lymphoma survival[5]

While measuring survival among those with Hodgkin's lymphoma is difficult, because of the rarity of this cancer, we would expect that around 80%–90% of Māori and non-Māori

[5] Survival data from Gurney, Stanley et al (2020) used cause-specific survival analysis methods, while survival data from other sources used relative survival analysis methods. While both approaches can produce robust survival estimates and data should generally be comparable between the two, each has its own strengths and limitations.

diagnosed with this cancer will survive to five years (Soeberg et al 2015). This survival is broadly comparable to that experienced in other countries, including England (Cancer Research UK 2023).

Around 60%–70% of those diagnosed with non-Hodgkin's lymphoma will survive to five years (61% Māori, 69% non-Māori) (Gurney, Stanley et al 2020). In terms of international comparison, estimates show five-year survival among those with non-Hodgkin's lymphoma at around 66% in England, 70% in the United States, and 75% in Australia (Cancer Australia 2022; Cancer Research UK 2023; Ellington et al 2023). Based on data from 2007 to 2016, Māori with non-Hodgkin's lymphoma are 97% more likely to die from their cancer than non-Māori with the same cancer (Gurney, Stanley et al 2020).

Lymphoma mortality

On average over the last decade, there have been around 19 deaths each year from Hodgkin's lymphoma, including 2 Māori. There have been around 290 deaths each year from non-Hodgkin's lymphoma, including 22 Māori (Gurney, Robson et al 2020; Te Aho o Te Kahu 2021). The rarity of Hodgkin's lymphoma prevents us from determining robust mortality rates for this cancer.

Mortality rates for non-Hodgkin's lymphoma are broadly similar between Māori and non-Māori (both 2 per 100,000). The age-standardised lymphoma mortality rate is higher for Pacific peoples (3 per 100,000) compared with the non-Māori, non-Pacific, non-Asian population (2 per 100,000) (Te Aho o Te Kahu 2021).

Gaps associated with substantial clinical benefit – by cancer type: Myeloma

Two regimen-indication pair gaps of substantial clinical benefit were for the group of blood cancers called myeloma (Table 7). All of the identified gaps were determined to provide benefit in a non-curative setting.

Table 7: Substantial clinical benefit gaps in myeloma

Medicine name	Cancer type	Indication per PBS	ESMO-MCBS:H score	Current Pharmac status (October 2024)	Appendix table for further detail
Lenalidomide (with bortezomib and dexamethasone)	Multiple myeloma (MM)	Newly diagnosed	**4** (non-curative)	Funded from 1 August 2024	Table 25
Pomalidomide (with dexamethasone)	Multiple myeloma (MM)	Relapsed or refractory third-line treatment	**4** (non-curative)	Funded from 1 August 2024	Table 26

Incidence of myeloma

Myeloma (also known as 'multiple myeloma' or 'plasma cell myeloma') is the sixteenth most commonly diagnosed cancer in Aotearoa New Zealand – with an average of 350 people diagnosed each year, including 40 Māori. When age-standardised, the rate of myeloma is higher for Māori (7 per 100,000) compared with non-Māori (5 per 100,000). The rate of myeloma is also higher among Pacific peoples (8 per 100,000) compared with the non-Māori, non-Pacific, non-Asian population (5 per 100,000) (Te Whatu Ora | Health New Zealand 2023).

Myeloma survival[6]

Around 50%–55% of those diagnosed with myeloma will survive to five years (50% Māori, 55% non-Māori) (Gurney, Stanley et al 2020). In terms of international comparisons, data from Cancer Research UK (2023) shows five-year survival in England at 56% for this cancer, while in the United States five-year survival is around 61% (National Cancer Institute 2012). Based on data from 2007 to 2016, Māori with myeloma are 60% more likely to die from their cancer than non-Māori with the same cancer (Gurney, Stanley et al 2020).

Myeloma mortality

On average over the last decade, there have been around 170 deaths each year from myeloma, including around 16 Māori (Gurney, Robson et al 2020; Te Aho o Te Kahu 2021). Mortality rates for myeloma are higher among Māori (3 per 100,000) compared with non-Māori (2 per 100,000). The myeloma mortality rate is also higher for Pacific peoples (4 per 100,000) compared with the non-Māori, non-Pacific, non-Asian population (2 per 100,000) (Te Whatu Ora | Health New Zealand 2023).

Changes to identified gaps since this analysis

Some of the medicine gaps identified have been funded since the analysis date of 1 January 2024. Table 8 summarises the gaps that have been funded and their associated magnitude of clinical benefit according to the ESMO-MCBS:H.

[6] Survival data from Gurney, Stanley et al (2020) used cause-specific survival analysis methods, while survival data from other sources used relative survival analysis methods. While both approaches can produce robust survival estimates and data should generally be comparable between the two, each has its own strengths and limitations (Sarfati et al 2010).

Table 8: Medicine-indication pairs identified as gaps on 1 January 2024 that have since been funded by Pharmac

Medicine	Indication	Date funded in Aotearoa New Zealand	ESMO-MCBS:H score
Midostaurin*	Acute myeloid leukaemia with FLT3 mutation	1 July 2024	A (Substantial clinical benefit)
Lenalidomide	Newly diagnosed multiple myeloma	1 August 2024	4 (Substantial clinical benefit)
Lenalidomide	Myelodysplastic syndrome with del(15q), low risk or intermediate-1 and red blood cell transfusion dependent	1 August 2024	3
Pomalidomide	Relapsed or refractory multiple myeloma third line	1 August 2024	4 (Substantial clinical benefit)
Pomalidomide	Progressive disease after at least one prior therapy that is either lenalidomide monotherapy or contains lenalidomide and the patient has undergone or is ineligible for an autologous haematopoietic stem cell transplant	1 August 2024	2
Pembrolizumab**	Relapsed or refractory Hodgkin lymphoma	1 October 2024	3

* Pharmac's funding of Midostaurin covers use as induction and consolidation therapy. It does not cover use in a maintenance setting which is permitted in Australia.

** Medicine-indication pair funded from 2024 Government budget increase.

HE KŌRERO
DISCUSSION

Cancer medicines, provided alone or in combination with surgery and/or radiation therapy, are a critical part of blood cancer care. Medicines can give people the opportunity to be cured of blood cancer, increase their quality of life with blood cancer, or extend how long they live with blood cancer. People with blood cancer, their whānau, and their treatment team expect that the medicines they need will be available when they need them.

This report is a continuation of the 2022 report, which could not be completed for blood cancer medicines at that time. The same methodology was used to describe the difference in blood cancer medicine availability between Australia and Aotearoa New Zealand. The magnitude of clinical benefit of those gaps was also identified now that a validated tool has become available to do so.

Summary of main findings

This analysis quantitively assessed the differences in blood cancer medicine availability between Australia and Aotearoa New Zealand and found that there were 58 medicines available in both countries, 13 medicines available in Aotearoa New Zealand but not in Australia, and 24 medicines available in Australia but not in Aotearoa New Zealand across 42 medicine-indication pairs. The likely magnitude of clinical benefit that could be realised if these medicine gaps were addressed was then determined, identifying 12 medicines of substantial magnitude of clinical benefit.

With consideration to the fact that some treatment regimens require more than one medicine to be administered at the same time, the 42 medicine-indication pairs available in Australia but not in Aotearoa New Zealand equate to 37 regimen-indication pairs. Of the 37 identified regimen-indication pairs, 11 were determined to have a substantial magnitude of clinical benefit. Two of these were regimens used in a curative setting and 9 were in a non-curative setting. The medicine gaps of substantial magnitude of clinical benefit covered a variety of different blood cancer types.

Overall, this means for Aotearoa New Zealand to close the gaps for those medicines identified as having a substantial magnitude of clinical benefit that are funded in Australia but not in Aotearoa New Zealand, 24 individual medicines would need to be funded. These medicines are for 42 specific indications and would cover 37 blood cancer treatment regimens.

Since the analysis date of 1 January 2024, four individual blood cancer medicines for six different indications have been funded by Pharmac, closing the gaps identified to 36 medicine-indication pairs, 9 with a substantial magnitude of clinical benefit.

Strengths of this analysis

This report goes beyond counting medicines, to consideration of medicine gaps according to their specific uses and the magnitude of clinical benefit of the identified medicines. One cancer medicine can be used to treat multiple different types and stages of cancer, so it is important to consider the medicine-indication and regimen-indication pairs. In addition, not all gaps are equal in terms of the health benefit Aotearoa New Zealand may achieve if a medicine was funded. Consideration of the identified gaps in terms of their magnitude of clinical benefit therefore provides important context for understanding which gaps possibly offer more health benefit to Aotearoa New Zealand.

Considerations when interpreting the findings of this report – methodology

The methodology of this analysis should be considered when interpreting the results of this report.

The analysis only compares medicine availability in Aotearoa New Zealand with one other country.

While Australia is a country Aotearoa New Zealand is often compared with, and Australia has higher cancer medicine availability than Aotearoa New Zealand, it is important to remember that medicine availability in Australia is not reflective of an international 'gold standard'. There is variation in medicine availability between all countries, and there is no 'right' or 'correct' level of medicine access. There may be blood cancer medicines not yet available in Australia that could provide significant health benefit to New Zealanders if they were available in Aotearoa New Zealand.

Clinical benefit is examined at a population level.

The magnitude of clinical benefit scores in this report were derived from clinical trial evidence, which represent analysis at a group level. This means that there may be individuals who experience a different outcome when receiving a medicine. This analysis focuses on the outcomes of the treated group as an average.

The ESMO-MCBS:H is only one of a few different ways to quantify and compare clinical benefit.

This report used the ESMO-MCBS:H to estimate clinical benefit. While this is an internationally validated tool that is often used internationally, there are other methods available to determine clinical benefit that might have generated different findings.

The ESMO-MCBS:H has limitations.

Using the ESMO-MCBS:H itself has the following limitations.

- The ESMO-MCBS:H is very prescriptive in nature and is focused on assessment of evidence for increased survival or improved quality of life associated with the use of a medicine. It is also very prescriptive about what cannot be considered in the assessment of a medicine's magnitude of clinical benefit. This is both a strength and a limitation of the tool. It is a strength as it allows for consistent comparison of the magnitude of clinical benefit of medicines. However, some aspects of clinical trial

quality are not considered by the ESMO-MCBS:H, and it does not allow for evidence of clinical benefit outside a clinical trial to be considered. Some scoring might be different when longer-term clinical data becomes available. The ESMO-MCBS:H also does not consider clinical trial information that was not part of the medicine becoming licensed. This might include valuable evidence that could alter clinical practice. Some medicines were unable to be scored because the information available in the trials did not meet the requirements of the ESMO-MCBS:H.

- The ESMO-MCBS:H does not include consideration of equity.
- The ESMO-MCBS:H is limited to consideration of clinical trial evidence. Māori and other populations experiencing health disparities are under-represented in clinical trials.
- While we have done our best to ensure the scores represent the context of medicines that are available in Aotearoa New Zealand, there are some instances where the prescribed nature of the ESMO-MCBS:H made this difficult. For example, the control arm of some clinical trials did not represent the current funding situation in Aotearoa New Zealand, and some medicines do not meet the ESMO-MCBS threshold for what is considered treatment with curative intent but in Aotearoa New Zealand they would be considered a curative treatment.
- The scores were derived in a robust process with as much quality control as possible. However, it is possible that the scores derived in this report will differ from those published by ESMO when it was evaluating the ESMO-MCBS:H tool (Kiesewetter 2020). Some of these differences will be due to changes made to reflect the context in Aotearoa New Zealand, while others will be due to different interpretations of the clinical evidence.
- Decisions about the funding of medicines are complex, and Pharmac takes into consideration a wide range of factors to determine which medicines are included in the OFI list. The medicine gaps noted in this report count the numbers of medicines funded in Australia but not in Aotearoa New Zealand. They do not measure the health benefits across all New Zealanders that aren't achieved because those medicines are not available in Aotearoa New Zealand (ie, the number of people with blood cancer affected, multiplied by how many healthy life years each person on average loses by not having the Australian-funded medicine).

Considerations when interpreting the findings of this report – context

There are important contextual aspects that should be considered when interpreting the results of this report.

Improving cancer outcomes requires a variety of actions that extend beyond increased funding for cancer medicines.

While cancer medicines are a key part of blood cancer treatment, ensuring New Zealanders have fewer cancers, better survival and more equitable cancer outcomes going forward will require coordinated action across the entire cancer continuum (ie, from prevention to early diagnosis through to palliative care).

Decisions about how much money should be invested in health, in cancer, and in cancer medicines specifically is extremely complex. It is important to keep in mind that there is

no ‘right’ or ‘correct’ amount of money to spend in these areas, and this is an issue every country has difficulty with. It is important that all action and investment in cancer treatment is balanced and coordinated to ensure that the limited resources in the wider cancer system achieve the best health outcomes possible for New Zealanders.

The impact of medicine availability on equity was out of scope.

For medicines to provide benefit they need to be accessible as well as available. Some members of the population already experience inequity in accessing cancer services and treatment opportunities. This is likely to contribute to the known inequities in cancer health outcomes. This report does not include assessment of whether closing the gaps identified in this analysis would make a difference to equitable access to cancer treatment and to cancer outcomes.

Medicine funding needs implementation support.

Providing New Zealanders with cancer treatment requires a coordinated team of health professionals and a series of health services and technologies. For funded medicine to be able to provide their intended benefit, people need to be able to access them, and for that to happen, the health system needs a variety of trained health professionals (haematologists, oncologists, pharmacists, imaging specialists, nurses, allied health professionals, and administrators), facilities (infusion sites, laboratories, imaging processing facilities, and pharmacies) and equipment. Funding of new medicines that provide treatment options for people who might not have had them otherwise, or that prolong the course of treatment through extending survival, means that more of all the associated services are needed. It is important that appropriate infrastructure, including the health workforce, is considered when new medicine funding decisions are made. This is to ensure new medicines can be administered effectively, efficiently and equitably.

Decisions on which medicines should be available requires consideration of factors in addition to clinical benefit.

Decisions about which medicines are publicly funded in Aotearoa New Zealand are made by Pharmac. Pharmac is an independent Crown entity tasked with publicly funding medicines that secure the best health outcomes that can reasonably be achieved within the fixed pharmaceutical budget it is allocated.

Pharmac uses a framework called the Factors for Consideration to evaluate the benefit of a proposed new medicine and how this compares to other proposed new medicines. The Factors for Consideration include:

- the health need of the patient population
- the health/clinical benefits of the new medicine compared to what is already available
- the cost implication of funding this new medicine, including potential savings
- how suitable the new medicine is compared to what patients receive now.

Using the Factors for Consideration, Pharmac creates a list of medicines in priority order that it would fund if/when budget is available. This is the OFI list. Additional budget to fund new medicines primarily arises due to:

- savings Pharmac achieves in payment for medicines it already funds
- additional budget provided by the Government.

As of June 2024, there are 140 medicines on the OFI list that Pharmac would fund if it had available budget. Fifty-seven are for the treatment of cancer generally, with 17 specifically for blood cancers.

Te Tiriti o Waitangi responsibilities and cancer medicines

This work recognises that Māori are a legitimate and critical part of decision-making and acknowledges Māori interests in decision-making about cancer medicine availability, including how cancer medicines are made accessible to Māori.

In health, the principle of equity refers to the absence of systemic differences in health that are not only avoidable but also unfair and unjust (Ministry of Health 2019b). Māori are 20% more likely to develop cancer than non-Māori and twice as likely to die from cancer, with poorer survival for nearly all the most common cancers (Gurney, Stanley et al 2020). These inequities are even more stark for specific cancers, such as lung cancer. They also occur along every step of the cancer continuum; for example, Māori have higher exposure to cancer risk factors, poorer access to and through the health system, and consequently poorer outcomes (Gurney, Stanley et al 2020; Tin Tin et al 2018; Walsh and Grey 2019). Available and accessible cancer medicines are one of many tools needed to address these inequities and includes the consideration that Māori may require different access, approaches and resources to achieve equitable cancer outcomes.

Equity considerations for cancer medicines

The equity considerations of relevance to cancer medicines are varied and complex. In terms of the availability of cancer medicines, funding decisions must consider existing inequities in incidence, survival and mortality for the relevant cancer. Where such inequities are known for Māori and Pacific peoples, they have been included in the 'Ngā Hua | Results' section. There are likely to be similar inequities experienced by other population groups – for example, people living in deprived areas (Te Aho o Te Kahu 2021) or people living with mental illness (Cunningham et al 2015; Davis et al 2020). The degree to which these unacceptable differences in outcomes are impacted by improved access to cancer medicines, and the relative priority of cancer medicines compared with other treatment options, differs across cancer types.

Additionally, there are other inequities that relate to eligibility for the medicine, such as inequities in stage at diagnosis or differences in the prevalence of a particular molecular subtype. Differences in factors such as stage at diagnosis may also have a meaningful influence on which medicine gaps would have a greater impact on inequities if funded. For example, if a medicine were used in early-stage disease, but we know that the majority of Māori are diagnosed later in the disease course for that particular cancer type, there is the potential to inadvertently exacerbate inequities in outcomes for Māori. Conversely, not having the medicine available at that early stage specifically for Māori

who do have an earlier diagnosis will also have a negative implication for Māori health outcomes. These matters are complex and require thorough consideration when funding applications are being assessed and decisions are being made.

Delays in the availability of new effective cancer medicines in Aotearoa New Zealand exacerbate inequities in outcomes. Only those who can afford to pay personally for new, non-funded medicines (or have private insurance) may be able to receive them. Conversely, although other countries may have more medicines available, higher patient co-payments may limit patients' access to these medicines (Babar et al 2019). In Australia, it was observed that a 24% increase in co-payments for subsidised medicines in 2005 adversely affected dispensing of prescriptions, especially among those on lower incomes (Babar and Vitry 2014; Hynd et al 2008).

HE KUPU WHAKAKAPI
CONCLUSION

Cancer medicines, provided alone or in combination with surgery and/or radiation therapy, are a critical part of cancer care. Medicines can give people the opportunity to be cured of cancer, increase their quality of life with cancer, or extend how long they live with cancer. People with cancer, their whānau, and their treatment team expect that the medicines they need will be available when they need them.

This report is a continuation of the 2022 report (Te Aho o Te Kahu 2022), which could not be completed for blood cancer medicines at that time. The same methodology was used to describe the difference in blood cancer medicine availability between Australia and Aotearoa New Zealand. The magnitude of clinical benefit of those gaps was also identified now that a validated tool has become available to do so.

Along with the findings of the 2022 report, this 2024 report provides important context and detail to better understand the reality of cancer medicine availability in Aotearoa New Zealand, as compared to Australia. The results of this analysis show that there are differences in the number of blood cancer medicines available in Australia to those available in Aotearoa New Zealand and that some of those are likely to have a substantial clinical benefit, primarily in a non-curative setting.

The information presented in the 2022 and 2024 reports is designed to provide useful insights to people with cancer and their whānau, the health sector, Pharmac, the New Zealand Government, non-governmental organisations, and the general public about the scale and magnitude of clinical benefit of medicine gaps in Aotearoa New Zealand.

While optimising the availability of cancer medicines and their role in improving health outcomes for people with cancer are particularly important, medicine availability cannot be considered in isolation. Coordinated and prioritised action across the entire cancer care continuum is required to ensure outcomes for New Zealanders with cancer improve to the greatest extent possible. The wider cancer health system, which works to prevent cancer and provide access to diagnosis and treatment across the cancer continuum, must be functioning well.

Te Aho o Te Kahu remains committed to working with all relevant stakeholders to strengthen services across the cancer care continuum and deliver on the goal of fewer cancers, better survival, and equity for all.

NGĀ ĀPITIHANGA
APPENDICES

Appendix 1: Key sources of information

This appendix lists the key sources of information used in this analysis.

Information type	Source(s)	Link(s) (if applicable)
Medicines funded in Aotearoa New Zealand	Pharmac's Pharmaceutical Schedule	schedule.pharmac.govt.nz/ScheduleOnline.php schedule.pharmac.govt.nz/HMLOnline.php
Medicines funded in Australia	PBS Schedule	www.pbs.gov.au/browse/body-system
Indications for medicines funded without restriction	TGA product information	www.ebs.tga.gov.au
	eviQ	www.eviq.org.au
	Medsafe Data Sheets	www.medsafe.govt.nz/Medicines/infoSearch.asp
ESMO-MCBS:H scores	ESMO	www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-haematological-malignancies/esmo-mcbs-h-evaluation-forms
Pharmac status	Pharmac application tracker	connect.pharmac.govt.nz/apptracker/s
Clinical relevance of gaps	Clinical advice	
	ACT-NOW SACT regimen library	nzf.org.nz/regimens
	eviQ	www.eviq.org.au
Patient and health sector considerations	ACT-NOW SACT regimen library	nzf.org.nz/regimens
	eviQ	www.eviq.org.au
	Medsafe Data Sheets	www.medsafe.govt.nz/Medicines/infoSearch.asp

Appendix 2: Definitions

Adjuvant therapy: Therapy given after the main treatment option; for example, chemotherapy administered after surgery.

Available medicines: Refers to publicly funded medicines. For Aotearoa New Zealand, this means medicines funded by Pharmac (see definition of 'Pharmac' below).

Blood cancers: Cancers of blood cells. Also known as haematological cancers or haematological malignancies. Examples include leukaemias, lymphomas and multiple myeloma.

Chemotherapy: A type of cancer treatment that uses medicines to destroy or slow the growth of cancer cells. It may be given alone or with other cancer treatments, such as surgery or radiotherapy. Chemotherapy can be given in a variety of ways, including taken by mouth, given via infusion or an injection.

Consolidation treatment: Treatment that is given together with, or after, the main treatment option, with the aim of enhancing the response to treatment.

Curative intent treatment: Treatment given with the goal of achieving complete remission and preventing the recurrence of cancer.

Disease-free survival: A surrogate (or proxy) endpoint often used in clinical trials of cancer medicines. Definitions may differ from study to study, but generally this term is used to mean the length of time that a patient lives without any signs or symptoms of the cancer after the main curative treatment for their cancer has ended. Disease-free survival results are often described using the median (see definition of 'Median' below). Also known as relapse-free survival (see definition of 'Relapse-free survival' below).

ESMO: European Society for Medical Oncology; an international professional organisation for medical oncology.

ESMO-MCBS: European Society for Medical Oncology – Magnitude of Clinical Benefit Scale; a tool used to assess the magnitude of benefit of medicines for solid tumours, based on information from clinical trials.

ESMO-MCBS:H: European Society for Medical Oncology – Magnitude of Clinical Benefit Scale for Haematological Malignancies; a tool used to assess the magnitude of benefit of medicines for blood tumours, based on information from clinical trials.

First-line therapy: The first method chosen to treat a particular illness or condition. For example, the first line of therapy in metastatic breast cancer may not be the first treatment the patient has received for breast cancer, but it is the first treatment they have received in the metastatic setting (see also definition of 'Line (of treatment)' below).

Immunotherapy: A type of cancer treatment that uses medicines or other substances to activate a person's immune system to identify and target cancer cells. There are different types of immunotherapies, including checkpoint inhibitors and monoclonal antibodies.

Incidence: The number of new cases of a condition in a population over a specified period of time.

Indication: The reason for using a particular medicine or treatment. For example, headache is one indication for paracetamol.

Induction treatment: Treatment administered at the beginning of treatment, typically before surgery.

Line (of treatment): The term 'line' or 'lines' of treatment is used to refer to the order in which therapies are used to manage a person's cancer. For example, chemotherapy may be used first; if the cancer progresses, a different chemotherapy or immunotherapy may be used, which would be a second-line treatment.

Maintenance treatment: Treatment that is given together with, or after, the main treatment option, with the intent of lengthening the duration of, or maintaining the response to, treatment.

Median: The mid-point of a range. In clinical trials of cancer medicines, the median is often used to describe the point in time at which half the people in a study population reached a specified endpoint. For example, a median overall survival timepoint is the point in time when half the people receiving a given treatment are still alive.

Medicine-indication pair: A medicine linked to a specific indication. For example, paracetamol for headache is one medicine-indication pair; paracetamol for fever is another medicine-indication pair.

Medsafe: The New Zealand Medicines and Medical Devices Safety Authority (Medsafe) is responsible for the regulatory approval of therapeutic products for use in Aotearoa New Zealand, based on an assessment of the efficacy and safety of those products. Medsafe approval does not guarantee public funding.

Neoadjuvant therapy: Therapy given before the main treatment option; for example, chemotherapy administered before surgery.

Non-curative intent treatment: Treatment that is given with the intent of prolonging life and/or improving quality of life but where a cure of the underlying cancer is unlikely to be achieved.

Objective response rate: The percentage of people on a particular treatment who have a complete (ie, all signs of cancer in the body disappear) or partial response (ie, decrease in the size of the tumours) to treatment in a given time period.

OFI list: Options for Investment list; the list of medicines in priority order that Pharmac would fund if/when budget is available.

Overall survival: An outcome measure often used in clinical trials of cancer medicines. Definitions may differ from study to study, but in general, this is a measure of how long people live after a cancer diagnosis or from the start of treatment. Overall survival results are often described using the median (see definition of 'Median' above).

PBAC: Pharmaceutical Benefits Advisory Committee; an independent statutory body in Australia responsible for recommending new medicines for funding via the PBS (see definition of 'PBS' below).

PBS: Pharmaceutical Benefits Scheme; a scheme that provides universal access to funded medicines for people living in Australia (in broad terms, Australia's equivalent to Pharmac for Aotearoa New Zealand).

Pharmac: Te Pātaka Whaioranga | Pharmaceutical Management Agency; the New Zealand government organisation responsible for approving medicines for public funding in Aotearoa New Zealand based on a number of factors, including unmet need, effectiveness, value for money, budget impact and suitability for use.

Prevalence: The number of people with a disease or condition in a population at a given point in time.

Progression-free survival: A surrogate (or proxy) endpoint often used in clinical trials of cancer medicines. Definitions may differ from study to study, but in general, this is the

time from allocation of treatment to either cancer progression or death from any cause. Progression-free survival results are often described using the median (see definition of 'Median' above).

Quality of life: The degree to which a person feels healthy, comfortable and able to participate in or enjoy life events. This can mean different things to different people and can be heavily influenced by things such as a person's culture and value systems. In clinical trials of cancer medicines, changes in quality of life may be reported using a variety of methods.

Radiotherapy: A type of cancer treatment that uses high-dose radiation to destroy or damage cancer cells. It can be used to cure cancer (curative radiotherapy), with other treatments to make treatment more effective (neoadjuvant or adjuvant radiotherapy), or to relieve symptoms (palliative radiotherapy). Also called radiation therapy.

Regimen-indication pair: Medicines that must be used in combination for a specific indication, for example, fludarabine, cyclophosphamide and rituximab are used in combination for chronic lymphocytic leukaemia. This would be one regimen-indication pair.

Regulatory agency: A government organisation responsible for approving a medicine for use, based on a balance of benefit and risk. For example, Medsafe is the regulatory agency in Aotearoa New Zealand.

Relapse-free survival: A surrogate (or proxy) endpoint sometimes used in clinical trials of cancer medicines. Definitions may differ from study to study, but in general, this term is used to mean the length of time that a patient survives without any signs or symptoms of cancer, after the main curative treatment for their cancer has ended. Also known as disease-free survival (see definition of 'Disease-free survival' above).

Schedule: In medicines funding, a list of medicines that are available, under specific conditions and at specific prices. For example, in Aotearoa New Zealand, the list of medicines available via public funding is Pharmac's Pharmaceutical Schedule. The comparable list in Australia is the PBS Schedule.

Second-line treatment: The second therapy given in a particular treatment setting, after the first-line treatment was shown to be ineffective or has stopped working.

Solid tumours: Cancers that occur in cells or parts of the body outside of the blood system (ie, cancers that are not blood cancers). Examples include lung, breast, bowel and skin cancer.

Targeted therapy/treatment: A type of cancer treatment that targets specific molecules displayed on cancer cells without affecting normal cells.

TGA: Therapeutic Goods Administration; the agency responsible for the regulatory approval of medicines in Australia. The Australian equivalent of Medsafe.

Appendix 3: Blood cancer medicines publicly funded in both Aotearoa New Zealand and Australia

This appendix provides results from the comparison of publicly funded blood cancer medicines in Aotearoa New Zealand through Pharmac with those publicly funded in Australia through the Australian PBS Schedule, specifically for medicines funded in both jurisdictions (Table 9).

Table 9: Blood cancer medicines funded in both Aotearoa New Zealand and Australia

		Australia		Aotearoa New Zealand	
Medicine	**Indication***	Funded **without** restriction	Funded **with** restriction	Funded **without** restriction	Funded **with** restriction
Arsenic trioxide	Acute promyelocytic leukaemia		✓	✓	
Azacitidine	Acute myeloid leukaemia		✓		✓
Azacitidine	Chronic myelomonocytic leukaemia		✓		✓
Azacitidine	Myelodysplastic syndrome		✓		✓
Bendamustine	Follicular lymphoma		✓		✓
Bendamustine	Indolent non-Hodgkin's lymphoma		✓		✓
Bendamustine	Mantle cell lymphoma		✓		✓
Bleomycin	Lymphoma		✓	✓	
Bortezomib	Multiple myeloma		✓		✓
Brentuximab vedotin	Anaplastic large cell lymphoma		✓		✓
Brentuximab vedotin	Hodgkin's lymphoma		✓		✓
Busulfan	No restriction on cancer type	✓		✓	
Carboplatin	No restriction on cancer type	✓		✓	
Chlorambucil	No restriction on cancer type	✓		✓	
Cisplatin	No restriction on cancer type	✓		✓	
Cladribine	Hairy cell leukaemia		✓	✓	
Cyclophosphamide	No restriction on cancer type	✓		✓	
Cytarabine	No restriction on cancer type	✓		✓	
Dasatinib	Acute lymphocytic leukaemia		✓		✓
Dasatinib	Chronic myeloid leukaemia		✓		✓
Doxorubicin	No restriction on cancer type	✓		✓	

		Australia		Aotearoa New Zealand	
Medicine	**Indication***	Funded **without** restriction	Funded **with** restriction	Funded **without** restriction	Funded **with** restriction
Epirubicin	No restriction on cancer type	✓		✓	
Etoposide	No restriction on cancer type	✓		✓	
Fludarabine	No restriction on cancer type	✓		✓	
Gemcitabine	No restriction on cancer type	✓		✓	
Gemtuzumab ozogamicin	Acute myeloid leukaemia		✓		✓
Hydroxycarbamide (hydroxyurea)	No restriction on cancer type	✓		✓	
Ibrutinib	Chronic lymphocytic leukaemia or small lymphocytic leukaemia		✓		✓
Idarubicin	Acute myeloid leukaemia		✓	✓	
Ifosfamide	No restriction on cancer type	✓		✓	
Imatinib	Acute lymphocytic leukaemia		✓	✓	
Imatinib	Chronic eosinophilic leukaemia or hypereosinophilic syndrome		✓	✓	
Imatinib	Chronic myeloid leukaemia		✓	✓	
Imatinib	Myelodysplastic syndrome		✓	✓	
Imatinib	Myeloproliferative neoplasm		✓	✓	
Imatinib	Systemic mastocytosis (aggressive)		✓	✓	
Lenalidomide	Multiple myeloma		✓		✓
Melphalan	No restriction on cancer type	✓		✓	
Mercaptopurine	No restriction on cancer type	✓		✓	
Methotrexate	No restriction on cancer type		✓	✓	
Nilotinib	Chronic myeloid leukaemia		✓		✓
Obinutuzumab	Chronic lymphocytic leukaemia		✓		✓
Obinutuzumab	Follicular lymphoma		✓		✓
Oxaliplatin	No restriction on cancer type	✓		✓	
Peginterferon alfa-2a	Myeloproliferative neoplasm	✓			✓
Peginterferon alfa-2a	T-cell lymphoma – cutaneous	✓			✓
Rituximab	Acute lymphocytic leukaemia B-cell precursor	✓			✓
Rituximab	Aggressive non-Hodgkin's lymphoma	✓			✓

Medicine	Indication*	Australia		Aotearoa New Zealand	
		Funded **without** restriction	Funded **with** restriction	Funded **without** restriction	Funded **with** restriction
Rituximab	Chronic lymphocytic leukaemia or small lymphocytic leukaemia	✓			✓
Rituximab	Hairy cell leukaemia	✓			✓
Rituximab	Indolent low-grade lymphomas	✓			✓
Ruxolitinib	Myelofibrosis		✓		✓
Thalidomide	Multiple myeloma		✓		✓
Tioguanine [Thioquanine]	No restriction on cancer type	✓		✓	
Venetoclax	Chronic lymphocytic leukaemia		✓		✓
Vinblastine	No restriction on cancer type	✓		✓	
Vincristine	No restriction on cancer type	✓		✓	
Vinorelbine	No restriction on cancer type	✓		✓	

Note: There may be some duplication with the previously published medicine availability analysis (Te Aho o Te Kahu 2022) as some medicines are used in the treatment of both solid tumour cancers and blood cancers.

* The medicines listed in this table cover a broad range of specific indications or therapeutic uses that are outlined in the funding or registration restrictions – please refer to the PBS, TGA, Pharmac and Medsafe for more information.

Appendix 4: Blood cancer medicines publicly funded in Aotearoa New Zealand but not in Australia

This appendix provides results from the comparison of blood cancer medicines that are publicly funded in Aotearoa New Zealand through Pharmac with those publicly funded in Australia through the Australian PBS Schedule, specifically for medicines funded in Aotearoa New Zealand but not in Australia (Table 10).

Table 10: Medicines funded in Aotearoa New Zealand but not in Australia*

Medicine	Indication per Pharmac's schedule†
Bendamustine	Chronic lymphocytic leukaemia†
Bendamustine	Hodgkin's lymphoma†
Bendamustine	Follicular lymphoma†
Bendamustine	Indolent non-Hodgkin's lymphoma†
Bendamustine	Mantle cell lymphoma (MCL)†
Carmustine	Listed with no restrictions on funding
Cladribine	Chronic lymphocytic leukaemia†
Imatinib	Acute lymphocytic leukaemia†
Melphalan	Not listed on PBS Schedule
Obinutuzumab	Marginal zone lymphoma†
Pegaspargase	Not listed on PBS Schedule
Thalidomide	Systemic light chain (AL) amyloidosis†
Venetoclax	Chronic lymphocytic leukaemia†

* In contrast to Aotearoa New Zealand, medicines used by inpatients in public hospitals in Australia are not funded via the PBS. Instead, individual states have different public funding arrangements in place – either at a state-wide level or at different health district or individual hospital levels. Therefore, some of these medicines may be publicly funded by mechanisms other than the PBS.

† Treatment/indication pair not funded via the PBS.

Appendix 5: Blood cancer medicines publicly funded in Australia but not in Aotearoa New Zealand determined to not have a substantial magnitude of clinical benefit according to the ESMO-MCBS:H, had no evaluable benefit or were not scorable.

This appendix provides results from the comparison of cancer medicines publicly funded in Aotearoa New Zealand with those included in the Australian PBS Schedule, specifically for medicines funded in Australia but not in Aotearoa New Zealand.

Table 11 summarises the blood cancer medicines publicly available in Australia but not in Aotearoa New Zealand that were determined not to have a substantial magnitude of clinical benefit according to the ESMO-MCBS:H, had no evaluable benefit or were not scorable.

Table 11: Summary of blood cancer medicines publicly available in Australia but not in Aotearoa New Zealand that were determined to not have a substantial magnitude of clinical benefit according to the ESMO-MCBS:H (Curative: C; Non-curative: 3, 2, 1, or no evaluable benefit (NEB)) or were not scoreable

ESMO-MCBS:H score	Medicine name	Used in combination with	Cancer type	Indication per PBS	Formulation	Medicine funded in NZ for other indications	Current Pharmac status (October 2024)*	Noted as a gap in 2022
3	Acalabrutinib, ibrutinib or zanubrutinib†	Monotherapy	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Relapsed or refractory, second line, prior therapy, TP53 wildtype.	Oral capsule/ tablet	No	Acalabrutinib – Under-assessment Ibrutinib – Under assessment Zanubrutinib – Under assessment	Yes
3	Acalabrutinib‡	Obinutuzumab‡	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Untreated patients or those who have developed an intolerance resulting in withdrawal from another first-line agent	Oral capsule/ tablet	No	No application	No
3	Carfilzomib	Dexamethasone with or without lenalidomide	Multiple myeloma (MM)	Progressive disease after at least one prior therapy (once or twice weekly)	Intravenous infusion	No	OFI list	Yes
3	Daratumumab§	Bortezomib and dexamethasone	Multiple myeloma (MM)	Progressive disease after only one prior therapy	Intravenous infusion/ subcutaneous injection	No	OFI list	Yes
3	Elotuzumab‡	Dexamethasone and lenalidomide¶	Multiple myeloma (MM)	Progressive disease after at least one prior therapy	Intravenous infusion	No	No application	No

3	Idelalisib	Monotherapy	Follicular B-cell non-Hodgkin's lymphoma	Refractory to rituximab and an alkylating agent within 6 months after completion of the treatment	Oral tablet	No	No application	Yes
3	Lenalidomide	Monotherapy	Myelodysplastic syndrome	Low risk or intermediate-1 with del(5q), and red blood cell transfusion dependent	Oral capsule/ tablet	Yes	Funded from 1 August 2024	Yes
3	Obinutuzumab‡	Acalabrutinib‡	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Untreated patients or those who have developed an intolerance resulting in withdrawal from another first-line agent	Intravenous infusion	Yes	No application	No
3	Obinutuzumab‡	Venetoclax‡	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Previously untreated disease	Intravenous infusion	Yes	Under assessment	Yes
3	Pembrolizumab	Monotherapy	Hodgkin's lymphoma	Relapsed or refractory Hodgkin's lymphoma after autologous haematopoietic stem cell transplant, and if transplant ineligible, has relapsed after 2 prior treatments	Intravenous infusion	Yes	Funded from 1 October 2024	Yes
3	Pembrolizumab	Monotherapy	Primary mediastinal B-cell lymphoma	Relapsed or refractory after autologous stem cell transplant, or after 2 prior treatments and if transplant ineligible has relapsed after 1 prior treatment. Patient must have been treated with rituximab	Intravenous infusion	Yes	No application	Yes

3	Ponatinib	Monotherapy	Chronic myeloid leukaemia (CML)	At least two prior tyrosine kinase inhibitors have failed or have not been tolerated with a severity necessitating permanent treatment withdrawal	Oral tablet	No	No application	Yes
3	Pralatrexate	Not specified	Peripheral T-cell lymphoma	Relapsed or chemotherapy-refractory after appropriate prior first-line curative intent chemotherapy	Intravenous bolus	No	No application	Yes
3	Venetoclax‡	Obinutuzumab‡	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Previously untreated disease	Oral tablet	Yes	Under assessment	Yes
2	Brentuximab vedotin	Cyclophosphamide, doxorubicin and prednisone	Peripheral T-cell lymphoma, non-cutaneous	First-line treatment with curative intent, CD30-positive	Intravenous infusion	Yes	Under assessment for anaplastic large cell lymphoma only	Yes
2	Daratumumab	Cyclophosphamide, bortezomib and dexamethasone	Systemic light chain (AL) amyloidosis	Newly diagnosed	Intravenous infusion/ subcutaneous injection	No	OFI list	No
2	Pomalidomide	Dexamethasone and bortezomib	Multiple myeloma (MM)	Progressive disease after at least one prior therapy (that is either lenalidomide monotherapy or contains lenalidomide) and patient has undergone or is ineligible for an autologous haematopoietic stem cell transplant	Oral capsule	No	Funded from 1 August 2024	No

2	Ponatinib	Monotherapy	Acute lymphoblastic leukaemia (ALL)	Second line treatment for patients with T315I, Philadelphia chromosome positive or BCR-ABL mutation	Oral tablet	No	No application	Yes
2	Selinexor	Triplet with dexamethasone and bortezomib. Doublet with dexamethasone	Multiple myeloma (MM)	Progressive disease after at least one prior therapy	Oral tablet	No	No application	No
1	Brentuximab vedotin	Monotherapy	T-cell lymphoma, cutaneous	Relapsed or refractory to prior treatment, CD30-positive	Intravenous infusion	Yes	No application	Yes
1	Vorinostat	Monotherapy	T-cell lymphoma, cutaneous	Relapsed or chemotherapy-refractory and ineligible for autologous haematopoietic stem cell transplant	Oral capsule	No	No application	Yes
1	Acalabrutinib or zanubrutinib†	Monotherapy	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Previously untreated or intolerant to another first-line drug treatment	Oral capsule	No	Acalabrutinib – no application Zanubrutinib – no application for whole group. Application for 17p deletion or TP53 mutation disease, first line specifically – OFI list	No
NEB	Bendamustine‡	Obinutuzumab‡ or rituximab	Follicular lymphoma stage II bulky or stage III/IV	Induction, previously untreated, CD20-positive	Intravenous infusion	Yes	No application	Yes

NEB	Obinutuzumab	Bendamustine‡	Follicular lymphoma stage II bulky or stage III/IV	Induction, previously untreated, CD20-positive	Intravenous infusion	Yes	Application declined	Yes
Not scorable	Asciminib	Monotherapy	Chronic myeloid leukaemia (CML)	Philadelphia chromosome positive or with transcript BCR-ABL1 tyrosine kinase chronic myeloid leukaemia in chronic phase with the T315I mutation	Oral tablet	No	No application	No
Not scorable	Azacitidine	Monotherapy	Acute myeloid leukaemia (AML)	Intermediate or poor risk at diagnosis. Treatment follows intensive induction chemotherapy, with complete remission, in patients who have not undergone or are not proceeding to allogeneic haematopoietic stem cell transplant	Oral tablet	Yes	No application	No
Not scorable	Decitabine with cedazuridine	Not specified	Acute myeloid leukaemia (AML)	With 20%–30% marrow blasts and multi-lineage dysplasia	Oral tablet	No	No application	No
Not scorable	Decitabine with cedazuridine	Not specified	Chronic myelomonocytic leukaemia (CMML)	With 10%–29% marrow blasts without myeloproliferative disorder	Oral tablet	No	No application	No
Not scorable	Decitabine with cedazuridine	Not specified	Myelodysplastic syndrome	Intermediate-2 or high risk 20% marrow blasts	Oral tablet	No	No application	No
Not scorable	Zanubrutinib	Monotherapy	Waldenstrom macroglobulinaemia	Relapsed or be refractory to at least one prior chemo-immunotherapy or be unsuitable for treatment with chemo-immunotherapy	Oral capsule	No	Under assessment	No

Definitions: 'Monotherapy' means the medicines are taken by themselves; 'NEB' means no evaluable benefit; 'Not scoreable' primarily indicates clinical trials with outcomes that cannot be assessed using the ESMO-MCBS:H.

* Status as of May 2024. The status of medicine applications at Pharmac is constantly being progressed and updated. Please refer to Pharmac's Application Tracker for up-to-date information on a medicine application (**connect.pharmac.govt.nz/apptracker/s**).

† Medicines that are part of the Bruton's tyrosine kinase (BTK) inhibitors medicine class – only one medicine from the medicine classes would need to be funded to close the identified gap. The ESMO-MCBS:H score reflects the highest score of the medicines scored in the class. Differences in ESMO-MCBS:H score are likely due to differences in trial design, follow-up periods and available data.

‡ Represents a regimen-indication pair – where more than one medicine is taken as part of the same treatment, and both would need to be funded to close the gap.

§ The ESMO-MCBS:H score for daratumumab reflects the intention to treat the population of the CASTOR trial (Hungria et al 2021), which included patients using daratumumab second line treatment or later. The analysis that examined the benefit of taking daratumumab as a second-line treatment (ie, the population funded in Australia) was unable to be scored by the ESMO-MCBS:H as it was a post-hoc analysis (ie, an analysis that was not planned to be conducted at the beginning of the trial).

¶ Lenalidomide is funded in Aotearoa New Zealand with a Special Authority restricting use to people with relapsed or refractory multiple myeloma with progressive disease as a third-line treatment, with second-line use permitted in the presence of dosing limiting neuropathy to first-line agents. Clinical advice received indicated that only a small number of patients will not be covered by the current access criteria.

Appendix 6: Blood cancer medicines publicly funded in Australia but not in Aotearoa New Zealand – gap categorisation

This appendix provides additional information about the rationale for the ESMO-MCBS:H score for each of the blood cancer medicines identified as being available in Australia but not in Aotearoa New Zealand. The ESMO-MCBS:H evaluation form used to determine the ESMO-MCBS:H score for each identified gap is also detailed.

- Table 12 outlines the gap categorisation for gaps identified as having an ESMO:MCBS-H score of substantial clinical benefit.
- Table 13 outlines the gap categorisation for gaps identified as having an ESMO:MCBS-H score of non-substantial clinical benefit.
- Table 14 outlines the gap categorisation for gaps identified as having an ESMO:MCBS-H score of no evaluable benefit.
- Table 15 outlines the rationale for the gaps identified that could not be scored.

Table 12: Medicines funded in Australia but not in Aotearoa New Zealand – gap categorisation: substantial clinical benefit

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
Blinatumomab	Monotherapy	Precursor B-cell acute lymphoblastic leukaemia (pre-B-cell ALL)	Complete haematological remission with measurable residual disease (MRD)	BLAST (Bargou et al 2018; Gökbuget et al 2018)	**A Curative** (1b)	• Derived ESMO-MCBS:H score is based on a single-arm study. • The primary endpoint was rate of complete MRD response. Recurrent/Disease-free survival was measured as a secondary endpoint and showed improvement. • Disease-free survival was 54% at 18 months, exceeding the pre-specified endpoint.
Midostaurin	Induction and consolidation with standard anthracycline and cytarabine chemotherapy	Acute myeloid leukaemia (AML)	Newly diagnosed patients with an internal tandem duplication (ITD) or tyrosine kinase domain (TKD) FMS-like tyrosine kinase 3 (FLT3) mutation	RATIFY (Stone et al 2017)	**A Curative** (1a)	• Derived ESMO-MCBS:H score is based on a comparator (chemotherapy) that is available in Aotearoa New Zealand. • The primary endpoint was overall survival. The median overall survival was 75 months with midostaurin vs 26 months with chemotherapy.
Asciminib	Monotherapy	Chronic myeloid leukaemia (CML)	Philadelphia chromosome positive or with transcript BCR-ABL tyrosine kinase without T315I mutation in chronic phase previously treated with two or more tyrosine kinase inhibitors	ASCEMBL (Hochhaus et al 2023; Réa et al 2023)	**4** (2c)	• Derived ESMO-MCBS:H score is based on a comparator (bosutinib) that is not available in Aotearoa New Zealand. However, other medicines in the same class (ie, dasatinib) are.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
						• The primary objective was major molecular response rate (MMR) at 24 weeks. At 24-weeks the MMR was 26% vs 13% in the comparator. • Quality of life was an exploratory endpoint only. Fewer grade 3–4 toxicities that affect wellbeing of patients were demonstrated.
Azacitidine*	Venetoclax*	Acute myeloid leukaemia (AML)	Patients who are unfit for intensive chemotherapy	VIALE-A (DiNardo et al 2020; Pratz et al 2024)	**5** (2a)	• Derived ESMO-MCBS:H score is based on azacitidine monotherapy, which is not available for most AML patients in Aotearoa New Zealand. Clinical advice was that the gap in Aotearoa New Zealand would therefore be materially larger, so the derived score was upgraded from a 4 to a 5. • The primary trial endpoint was overall survival. After a median of 20.5 months follow-up, overall survival was 15 months in the azacitidine with venetoclax group vs 9.6 in the control arm. • Quality of life was measured as a secondary endpoint but no difference in the two groups was reported. • Both azacitidine and venetoclax would need to be funded for this indication to close this gap.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
Blinatumomab	Monotherapy	Precursor B-cell acute lymphoblastic leukaemia (pre-B-cell ALL)	Patients with relapsed or refractory disease	TOWER (Kantarjian et al 2017; Topp et al 2018)	**5** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (chemotherapy) that is available in Aotearoa New Zealand. • The primary endpoint was overall survival. The median overall survival was 8 months with blinatumomab vs 4 months in the chemotherapy group. • The derived score was upgraded due to evidence of improved quality of life. • Clinical advice indicated this treatment would likely be considered curative (as a path to allograft) in an Aotearoa New Zealand context despite it not reaching the threshold for curative therapies with the ESMO-MCBS:H.
Gilteritinib	Monotherapy	Acute myeloid leukaemia (AML)	Relapsed or refractory with FLT3 ITD or TKD mutation	ADMIRAL (Perl et al 2022; Perl et al 2023; Perl et al 2019)	**4** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (salvage chemotherapy) that is available in Aotearoa New Zealand. • The primary endpoint was overall survival. The median overall survival was 9 months with gilteritinib vs 6 months in the salvage chemotherapy group. • Quality of life was explored as an exploratory endpoint only.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
Acalabrutinib, Ibrutinib or Zanubrutinib	Monotherapy	Mantle cell lymphoma	Relapsed or refractory to at least one prior therapy	Ibrutinib RAY (Dreyling et al 2016; Rule et al 2018)	**4** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (temsirolimus) that is not publicly funded in Aotearoa New Zealand. • Clinical advice received on review of the study was that the likely comparator in Aotearoa New Zealand (salvage chemotherapy) was unlikely to be inferior to temsirolimus in terms of efficacy, so the derived score was not changed. • Primary end point was progression-free survival with a median progression-free survival with ibrutinib of 16 months vs 6 months in the control group. • Quality of life was measured and showed improvement.
				Acalabrutinib ACE-LY-004 (Wang et al 2018; Wang et al 2019)	**3** (3)	• Derived ESMO-MCBS:H score is based on a single-arm study. • Primary end point was overall response. After a median follow-up of 26 months the overall response rate was 81%, with 43% having a complete response. • Quality of life was not measured as a primary or secondary endpoint.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
				Zanubrutinib BGB-3111–206 and BGB-3111-AU-003 (Song et al 2020; Song et al 2022; Tam et al 2021)	**3** (3)	• Derived ESMO-MCBS:H score is based on single-arm study. • Primary end point was overall response rate. The overall response rate was 84%. • Quality of life did not appear to be measured.
Idelalisib	Rituximab for 8 doses followed by monotherapy	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Relapsed or refractory to at least one prior therapy, CD20-positive	NCT01539512 (Furman et al 2014; Ghia, Coutre et al 2020)	**4** (2b)	• Derived ESMO-MCBS:H score is based on a placebo comparator, so reflects the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival with median progression-free survival not reached with idelalisib vs 5.5 weeks in the control group. At 24 weeks, progression-free survival was 93% with idelalisib vs 46% in the comparator. • Quality of life was measured and showed improvement.
Inotuzumab ozogamicin	Monotherapy	Precursor B-cell acute lymphoblastic leukaemia (pre-B-cell ALL)	Relapsed or refractory CD22-positive	INO-VATE (Kantarjian et al 2019; Kantarjian, DeAngelo, et al 2016; Kantarjian, Su, et al 2016)	**4** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (salvage chemotherapy) that is available in Aotearoa New Zealand.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
						• The primary endpoint was overall survival. The median overall survival was 7.7 months with inotuzumab ozogamicin vs 6 months with standard of care. • Quality of life was measured as a secondary endpoint, but no statistically significant benefit in overall quality of life measures were demonstrated.
Lenalidomide	Bortezomib and dexamethasone for 8 cycles then with dexamethasone from cycle 9	Multiple myeloma (MM)	Newly diagnosed	SWOG-SO77 (Durie et al 2017; Durie et al 2020)	**4** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (lenalidomide with dexamethasone). Lenalidomide is not currently available in Aotearoa New Zealand for this indication. • The primary endpoint was progression-free survival, but overall survival was a secondary endpoint and showed statistically significant improvement. • After a median follow-up period of 84 months, the median overall survival was not reached for lenalidomide, bortezomib and dexamethasone vs 69 months with lenalidomide with dexamethasone. • Quality of life did not appear to be measured.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
Pomalidomide	Dexamethasone	Multiple myeloma (MM)	Relapsed or refractory third-line treatment	MM-003 (Miguel et al 2013)	**4** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (dexamethasone) that is available in Aotearoa New Zealand for this indication. • The primary trial endpoint was progression-free survival, but overall survival as a secondary endpoint showed statistically significant improvement. • Overall survival was 12 months with pomalidomide vs 8 months with dexamethasone. • Quality of life did not appear to be measured.
Venetoclax*	Azacitidine*	Acute myeloid leukaemia (AML)	Patients who are unfit for intensive chemotherapy	VIALE-A (DiNardo et al 2020; Pratz et al 2024)	**5** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (azacitidine monotherapy) that is not available in Aotearoa New Zealand for this indication. Clinical advice was that the gap in Aotearoa New Zealand would therefore be materially larger, so the derived score was upgraded from a 4 to a 5. • The primary trial endpoint was overall survival. After a median of 20.5 months follow-up, overall survival was 15 months in the azacitidine with venetoclax group vs 9.6 in the control arm.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: substantial clinical benefit
						• Quality of life was measured as a secondary endpoint, but no differences in the two groups were reported. • Both azacitidine and venetoclax would need to be funded for this indication to close this gap.

* Represents a regimen-indication pair – where more than one medicine is taken as part of the same treatment, and both would need to be funded to close the gap.

Table 13: Medicines funded in Australia but not in Aotearoa New Zealand – gap categorisation: no substantial clinical benefit

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Acalabrutinib, ibrutinib or zanubrutinib	Monotherapy	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Relapsed or refractory to at least one prior therapy	ASCEND (Ghia, Pluta et al 2020, Ghia et al 2022)	**3** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (idelalisib with rituximab/ bendamustine with rituximab). Only rituximab is funded in Aotearoa New Zealand for this patient group. Clinical advice was that the lack of a funded comparator in Aotearoa New Zealand being represented in the clinical trial was unlikely to materially impact the classified gap, so no change in the derived score was made. • Primary end point was progression-free survival – median progression-free survival for acalabrutinib not met after 47 months. 42-month progression-free survival rate was 62% (acalabrutinib) vs 19% in the comparator. • Global quality of life was an exploratory endpoint only.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
				Ibrutinib RESONATE (Byrd et al 2014; Munir et al 2019)	**2** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (ofatumumab) that is not publicly funded for blood cancer in Aotearoa New Zealand or Australia. Clinical advice received was that the likely comparator in Aotearoa New Zealand (chlorambucil with obinutuzumab, venetoclax or fludarabine-cyclophosphamide-rituximab (FCR)) was unlikely inferior to ofatumumab in terms of efficacy, so the derived score was not changed. • Primary end point was progression-free survival. Median progression-free survival with ibrutinib was 44 months vs 8 months in the control group. • Quality of life was measured as an exploratory endpoint only.
				Zanubrutinib ALPINE (Brown et al 2023; Tam et al 2023)	**1** (2c)	• Derived ESMO-MCBS:H score is based on a comparator (ibrutinib) that is publicly funded in Aotearoa New Zealand but not for this indication.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Primary end point was overall response, which was achieved in 84% with zanubrutinib vs 74% with ibrutinib. • Quality of life was measured as a secondary endpoint, but no statistically significant difference in global quality of life measures was evident.
Acalabrutinib*	Obinutuzumab	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Untreated patients or those who have developed an intolerance resulting in withdrawal from another first-line agent	ELEVATE-TN (Sharman et al 2020; Sharman et al 2023)	**3** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (obinutuzumab with chlorambucil) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival – median progression-free survival for acalabrutinib not met after 28 months and 23 months in the comparator arm. Estimated 24-month progression-free survival rate was 93% (acalabrutinib) vs 47% in the comparator. • Quality of life measured as exploratory endpoint only.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Both acalabrutinib and obinutuzumab would need to be funded for this indication to close this gap.
Carfilzomib	Dexamethasone with or without lenalidomide*	Multiple myeloma (MM)	Progressive disease after at least one prior therapy (one or twice weekly) in combination with dexamethasone	Carfilzomib with dexamethasone ENDEAVOUR (Dimopoulos et al 2017; Dimopoulos et al 2016; Ludwig et al 2019)	**3** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (bortezomib and dexamethasone) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • The primary end point was progression-free survival, but overall survival as a secondary endpoint showed statistically significant improvement. • Median overall survival was 48 months for carfilzomib vs 40 months with the comparator. • Quality of life measured as exploratory endpoint only.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
				Carfilzomib with dexamethasone and lenalidomide ASPIRE (Siegel et al 2018; Stewart et al 2016; Stewart et al 2015)	**3** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (lenalidomide with dexamethasone). Lenalidomide is not publicly funded in Aotearoa New Zealand for all patients with this indication. There is a small number of patients who will not be able to access lenalidomide second line currently in Aotearoa New Zealand. Clinical advice was that this was not material. • Primary end point was progression-free survival; however, overall survival as a secondary endpoint showed statistically significant differences. • Median survival was 48 months with carfilzomib, lenalidomide and dexamethasone vs 40 months with lenalidomide and dexamethasone. • Quality of life did not appear to be measured. • Both lenalidomide and carfilzomib need to be funded to close this gap.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Daratumumab	Bortezomib and dexamethasone	Multiple myeloma (MM)	Treatment of relapsed/refractory disease	CASTOR (Hungria et al 2021; Palumbo et al 2016)	**3** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (bortezomib and dexamethasone) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • The primary end point was progression-free survival, but overall survival as a secondary endpoint showed statistically significant improvement. • Median overall survival was 50 months for daratumumab vs 39 months with the comparator. • Available evidence for quality of life was measured for the intervention trial arm only. • The main trial evidence was for daratumumab used in the treatment of relapsed multiple myeloma second line treatment or later. Data for second line only was conducted as a post-hoc sub-group analysis. Post-hoc sub-group analyses are unable to be scored using the ESMO-MCBS:H.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Elotuzumab*	Dexamethasone and lenalidomide*	Multiple myeloma (MM)	Treatment of relapsed/refractory disease	ELQOUENT-2 (Dimopoulos et al 2020; Lonial et al 2015)	**3** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (lenalidomide with dexamethasone) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • The primary end point was progression-free survival and overall response rate; however, the secondary endpoint of overall survival showed statistically significant improvement. • Median overall survival was 48 months for elotuzumab with lenalidomide and dexamethasone vs 40 months with the comparator. • Quality of life was measured as an exploratory endpoint. • Both lenalidomide and elotuzumab need to be funded to close this gap.
Idelalisib	Monotherapy	Follicular B-cell non-Hodgkin's lymphoma	Refractory second line	Delta (Gopal et al 2014)	**3** (3)	• Derived ESMO-MCBS:H score is based on a single-arm study. • The primary end point was overall response rate.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• The overall response rate was 57%, and median progression-free survival was 11 months. • Quality of life was measured as a secondary endpoint, but results do not appear to have been published.
Lenalidomide	Not specified	Other	Myelodysplastic syndrome with del(15q)	MDS-004 (Fenaux et al 2011)	**3** (2c)	• Derived ESMO-MCBS:H score is based on a placebo compactor so reflects the gap between Australia and Aotearoa New Zealand. • The primary end point was red blood cell transfusion independence for ≥ 26 weeks. • Red blood cell transfusion independence for ≥ 26 weeks was achieved by 56% of patients with lenalidomide 10mg, 42.6% of patients with lenalidomide 5mg vs 5.9% with placebo • Quality of life was measured and showed improvement and fewer grade 3-4 toxicities that effect patient well-being were demonstrated.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Obinutuzumab	Acalabrutinib*	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Untreated patients or those who have developed an intolerance resulting in withdrawal from another first-line agent	ELEVATE-TN (Sharman et al 2020; Sharman et al 2023)	**3** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (obinutuzumab with chlorambucil) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival. Median progression-free survival for acalabrutinib was not met after 28 months vs 23 months in the comparator arm. Estimated 24-month progression-free survival rate was 93% (acalabrutinib) vs 47% in the comparator. • Quality of life measured as exploratory endpoint only. • Both acalabrutinib and obinutuzumab would need to be funded for this indication to close this gap.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Obinutuzumab*	Venetoclax*	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Previously untreated disease in combination with venetoclax	CLL14 (Al-Sawaf et al 2020; Fischer et al 2019)	**3** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (obinutuzumab with chlorambucil) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival – median progression-free survival for obinutuzumab with venetoclax was not met after 40 months vs 36 months in the comparator arm. Estimated 3-year survival was 82% vs 50% in the comparator. • Quality of life measured as exploratory endpoint only. • Both obinutuzumab and venetoclax would need to be funded for this indication to close this gap.
Pembrolizumab	Monotherapy	Hodgkin's lymphoma	Relapsed or refractory	KEYNOTE 204 (Kuruvilla et al 2021)	**3** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (brentuximab) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Primary end points were progression-free survival and overall survival (not analysed in interim analysis). • After a median of 26 months, median progression-free survival for pembrolizumab was 13 months vs 8 months for the comparator. • Quality of life measured as exploratory endpoint only.
Pembrolizumab	Monotherapy	Primary mediastinal B-cell lymphoma	Relapsed or refractory	KEYNOTE 170 (Armand et al 2019; Zinzani et al 2023)	**3** (3)	• Derived ESMO-MCBS:H score is based on single-arm study. • Primary end point was overall response rate. • Overall response rate was noted to be 42%. • Quality of life did not appear to be measured.
Ponatinib	Monotherapy	Chronic myeloid leukaemia (CML)	For patients when at least two prior tyrosine kinase inhibitors have failed or have not been tolerated to a severity necessitating permanent treatment withdrawal	PACE (Cortes et al 2013; Cortes et al 2018)	**3** (3)	• Derived ESMO-MCBS:H score is based on single-arm study. • Primary end point was major cytogenetic response within the first 12 months and major haematologic response at any time in the first 6 months. • This score reflects the aggregate of CML patients in blast, accelerated and chronic phases.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Major haematological response was achieved by 61% of accelerated phase CML patients and 31% of blast phase CML patients – 60% of chronic phase CML patients achieved major cytogenetic response. • Quality of life did not appear to be measured.
Pralatrexate	Not specified	Peripheral T-cell lymphoma	Relapsed or chemotherapy-refractory	PROPEL (O'Connor et al 2011)	**3** (3)	• Derived ESMO-MCBS:H score is based on single-arm study. • Primary end point was overall response rate. The overall response rate was 29%. • Quality of life did not appear to be measured.
Venetoclax*	Obinutuzumab*	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Previously untreated disease in combination with obinutuzumab	CLL14 (Al-Sawaf et al 2020; Fischer et al 2019)	**3** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (obinutuzumab with chlorambucil) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Primary end point was progression-free survival – median progression-free survival for obinutuzumab with venetoclax was not met after 40 months and was 36 months in the comparator arm. • Estimated 3-year survival was 82% vs 50% in the comparator. • Quality of life measured as exploratory endpoint only. • Both obinutuzumab and venetoclax would need to be funded for this indication to close this gap.
Brentuximab vedotin	Cyclophosphamide, doxorubicin and prednisone	Peripheral T-cell lymphoma, non-cutaneous type	First-line treatment with curative intent, CD30-positive	ECHELON-2 (Horwitz et al 2019; Horwitz et al 2022)	**2** (2a)	• Derived ESMO-MCBS:H score is based on a comparator (CHOP chemotherapy) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival; however, overall survival as a secondary endpoint showed statistically significant differences.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Median survival was not reached in either trial arm. Estimated 5-year survival was 70% for brentuximab vs 61% in the comparator. • Quality of life did not appear to be measured.
Daratumumab	Cyclophosphamide, bortezomib and dexamethasone	Systemic light chain (AL) amyloidosis	Newly diagnosed systemic light chain amyloidosis	ANDROMEDA (Kastritis et al 2021; Palladini et al 2020; Sanchorawala et al 2022)	**2** (2c)	• Derived ESMO-MCBS:H score is based on a comparator (bortezomib, cyclophosphamide, dexamethasone) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was haematologic complete response – 53% of patients in daratumumab trial arm achieved complete haematologic response vs 18% in the comparator arm. • Quality of life was measured but did not show a global statistically significant improvement.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Pomalidomide	Dexamethasone and bortezomib	Multiple myeloma (MM)	Second line triple combination therapy	OPTIMISMM (Dimopoulos et al 2021; Richardson et al 2019; Richardson et al 2022)	**2** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (bortezomib with dexamethasone) that is publicly funded in Aotearoa New Zealand for this indication, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival. Median progression-free survival was 11 months with pomalidomide with bortezomib and dexamethasone vs 7 months with the comparator. • Quality of life was measured as an exploratory endpoint only.
Ponatinib	Monotherapy	Acute lymphoblastic leukaemia (ALL)	Second line for patients with T315I, Philadelphia chromosome positive or BCR-ABL mutation	PACE (Cortes et al 2013; Cortes et al 2018)	**2** (3)	• Derived ESMO-MCBS:H score is based on single-arm study. • Primary end point was major cytogenetic response within the first 12 months and major haematologic response at any time in the first 6 months. • Major haematological response was achieved by 41% of patients. • Quality of life did not appear to be measured.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Selinexor	Triplet with dexamethasone and bortezomib or doublet with dexamethasone	Multiple myeloma (MM)	Relapsed and/or refractory	BOSTON (Grosicki et al 2020)	**2** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (bortezomib with dexamethasone) that is publicly funded in Aotearoa New Zealand for this indication, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival. Median progression-free survival was 14 months with selinexor vs 10 months with the comparator. • Quality of life was measured as a secondary endpoint, but no statistically significant improvement in global quality of life was reported.
Brentuximab vedotin	Monotherapy	T-cell lymphoma, cutaneous	Relapsed or refractory, CD30-positive	ALCANZA (Dummer et al 2020; Horwitz et al 2021; Prince et al 2017)	**1** (2c)	• Derived ESMO-MCBS:H score is based on a comparator (methotrexate or bexarotene). Methotrexate is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
						• Primary end point was overall response rate – 56% of patients achieved an overall response with brentuximab with bendamustine and rituximab vs 13% with the comparator. • Quality of life was measured as secondary endpoint, but no statistically significant difference in global quality of life was evident.
Vorinostat	Monotherapy	T-cell lymphoma, cutaneous	Relapsed or chemotherapy-refractory and ineligible for stem cell transplant	NCT00091559 (Duvic et al 2007; Olsen et al 2007)	**1** (3)	• Derived ESMO-MCBS:H score is based on a single-arm study. • Primary end point was objective response rate, which was achieved by 30% of patients. • Quality of life did not appear to be measured.

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
Acalabrutinib or Zanubrutinib	Monotherapy	Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)	Previously untreated or intolerant to another first-line drug treatment	Zanubrutinib SEQUOIA (Ghia et al 2023; Tam et al 2022)	**1** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (bendamustine and rituximab) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival. Median progression-free survival was not yet reached in either group. At 24 months, estimated progression-free survival was 86% with zanubrutinib vs 70% with the comparator. The study was stopped early due to preliminary progression-free survival results. • Quality of life was measured as a secondary endpoint, but no statistically significant difference in global quality of life measures was evident. •

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no substantial clinical benefit
				Acalabrutinib ELEVATE-TN (Sharman et al 2020; Sharman et al 2023)	Not scoreable	• Available trial evidence does not include parameters that permit the application of the ESMO-MCBS:H. Progression-free survival for aclarubicin as a monotherapy was a secondary trial endpoint.

* Represents a regimen-indication pair – where more than one medicine is taken as part of the same treatment, and both would need to be funded to close the gap.

Table 14: Medicines funded in Australia but not in Aotearoa New Zealand – gap categorisation: no evaluable benefit

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score (ESMO-MCBS:H evaluation form)	Rationale for gap categorisation: no evaluable benefit
Zanubrutinib	Monotherapy	Waldenstrom macroglobulinaemia	Relapsed or refractory to at least one prior chemo-immunotherapy or be unsuitable for treatment with chemo-immunotherapy	ASPEN (Dimopoulos et al 2023; Tam et al 2020)	**NEB** (2c)	• Derived ESMO-MCBS:H score is based on a study that showed no statistically significant difference between zanubrutinib and the comparator ibrutinib in terms of the primary endpoint of number of patients achieving complete or very good partial response. • Non-statistically significant differences in primary endpoints cannot be scored using the ESMO-MCBS:H.
Bendamustine*	Obinutuzumab* or rituximab	Indolent non-Hodgkin's lymphoma stage II bulky or stage III/IV	Induction, previously untreated, CD20-positive	GALLIUM (Marcus et al 2017; Townsend et al 2023)	**NEB** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (rituximab-based chemotherapy) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival. Seven-year progression-free survival rate was 63.4% vs 55.7% in the comparator. • Quality of life was measured as a secondary endpoint, but no published results were found.

						• Both bendamustine and obinutuzumab would need to be funded for this indication and treatment combination to close the gap. The current funding restrictions for bendamustine in Aotearoa New Zealand do not permit use with obinutuzumab.
Obinutuzumab	Bendamustine*	Follicular lymphoma stage II bulky or stage III/IV	Induction, previously untreated, CD20-positive	GALLIUM (Marcus et al 2017; Townsend et al 2023)	**NEB** (2b)	• Derived ESMO-MCBS:H score is based on a comparator (rituximab-based chemotherapy) that is publicly funded in Aotearoa New Zealand, so the derived score is reflective of the gap between Australia and Aotearoa New Zealand. • Primary end point was progression-free survival. Seven-year progression-free survival rate was 63.4% vs 55.7% in the comparator. • Quality of life was measured as secondary endpoint but no published results were found. • Both bendamustine and obinutuzumab would need to be funded for this indication and treatment combination to close the gap. The current funding restrictions for bendamustine in Aotearoa New Zealand do not permit use with obinutuzumab.

Note: NEB = no evaluable benefit.

* Represents a regimen-indication pair – where more than one medicine is taken as part of the same treatment, and both would need to be funded to close the gap.

Table 15: Medicines funded in Australia but not in Aotearoa New Zealand – gap categorisation: not scorable

Medicine name	Used in combination with	Cancer type	Specific indication	Key pivotal trial used for scoring	ESMO-MCBS:H score	Rationale for gap categorisation: not scorable
Asciminib	Monotherapy	Chronic myeloid leukaemia (CML)	Philadelphia chromosome positive or with transcript BCR-ABL1 tyrosine kinase chronic myeloid leukaemia in chronic phase with the T315I mutation	NCT02081378 (Hochhaus et al 2023; Réa et al 2023)	Not scoreable	Available trial evidence does not include parameters that permit the application of the ESMO-MCBS:H. Primary evidence is a dose escalation trial.
Azacitidine (tablets)	Monotherapy	Acute myeloid leukaemia (AML)	Treatment following intensive induction chemotherapy	QUAZAR AML-001 (Wei et al 2020)	Not scoreable	Available trial evidence does not include parameters that permit the application of the ESMO-MCBS:H. No hazard ratios were presented and no 10% survival at 3 years reported.
Decitabine with cedazuridine (tablets)	Not specified	Acute myeloid leukaemia (AML)	With 20%–30% marrow blasts and multi-lineage dysplasia	ASCERTAIN (Garcia-Manero et al 2024)	Not scoreable	Available trial evidence does not include parameters that permit the application of the ESMO-MCBS:H. This trial was not scorable as although the clinical trial notes inclusions of AML patients, the results presented do not include AML patients. Published results for CML and MDS do not present end points that are scoreable.
Decitabine with cedazuridine (tablets)	Not specified	Chronic myelomonocytic leukaemia (CMML)	With 10%–29% marrow blasts without myeloproliferative disorder	ASCERTAIN (Garcia-Manero et al 2024)	Not scoreable	Available trial evidence does not include parameters that permit the application of the ESMO-MCBS:H. The primary endpoint was total decitabine exposure over 5 days.
Decitabine with cedazuridine (tablets)	Not specified	Myelodysplastic syndrome	Intermediate-2 or high risk 20% marrow blasts	ASCERTAIN (Garcia-Manero et al 2024)	Not scoreable	Available trial evidence does not include parameters that permit the application of the ESMO-MCBS:H. The primary endpoint was total decitabine exposure over 5 days.

Appendix 7: Description of each gap with associated substantial clinical benefit

This appendix provides a detailed description of each identified gap associated with substantial clinical benefit, organised by type of cancer. The table for each medicine-indication pair gap includes:

- the medicine class
- intent of treatment (whether curative or non-curative)
- where the gap is in the pipeline of Pharmac's assessment
- the associated ESMO-MCBS:H score for the gap
- how filling the gap would change current clinical practices
- how the medicine would be given
- additional considerations for patients, whānau and the health system.

Leukaemia

Table 16: Asciminib third line for chronic myeloid leukaemia

Indication description	Chronic myeloid leukaemia (without T315I mutation*)
Medicine	Asciminib
Description of medicine class	A novel, first-in-class specifically targeting the ABL myristoyl pocket (STAMP) inhibitor that potently inhibits the kinase activity of BCR-ABL1 via allosteric binding.
Intent of treatment	Long treatment-free remission.
Pharmac status (October 2024)	• Application received March 2024 • Currently seeking clinical advice • connect.pharmac.govt.nz/apptracker/s/application-public/a10OZ000000szzN/p002030
ESMO-MCBS:H score and summary of data informing the score	4 Compared to bosutinib: • Gain of 12.2% in the molecular response rate. • Quality-of-life improvement did not contribute to the score. • Fewer grade 3 or 4 toxicities contributed to the score.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Chronic myeloid leukaemia is currently treated with ATP-competitive tyrosine kinase inhibitors (TKIs), including imatinib, nilotinib and dasatinib. Asciminib targets a different domain of the BCR-ABL1 oncoprotein, offering another line of treatment if a patient develops resistance to, or intolerance to, the ATP-competitive TKIs.
How this medicine would be given	Asciminib is taken as an oral tablet 80 mg once daily or 40 mg twice daily (Q12H) continuously. This dose applies only to patients without the T315I mutation as per ASCEMBL trial.
Patient and whānau considerations	• Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant of asciminib. • Other medications may be needed to control side effects and to prevent infection.
Health system resource considerations	• Increased demand for laboratory services to monitor for treatment-related toxicities and disease response. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required.

* ASCEMBL trial excluded patients with bosutinib resistant BCR-ABL1 mutations of T315I or V299L

Table 17: Blinatumomab for acute lymphoblastic leukaemia – measurable residual disease (MRD) positive

Indication description	B-cell precursor acute lymphoblastic leukaemia (ALL) in first or later haematologic complete remission and with persistent or recurrent MRD $\geq 10^{-3}$ after a minimum of 3 blocks of intensive chemotherapy – bridge to allogeneic haematopoietic stem cell transplant (HSCT)
Medicine	Blinatumomab
Description of medicine class	Blinatumomab is a bispecific T-cell engager (BiTE®) molecule that binds specifically to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T-cells.
Intent of treatment	Curative.
Pharmac status (October 2024)	• Application received February 2024 • Currently seeking clinical advice • connect.pharmac.govt.nz/apptracker/s/application-public/a10OZ000000e52b/p002022
ESMO-MCBS:H score and summary of data informing the score	A^{PT} • Multicentre open-label, single-arm phase 2 study conducted at 46 centres in Europe and Russia. • Kaplan-Meier estimate for relapse-free survival at 18 months was 54% (95% CI, 33%–70%), exceeding the pre-specified boundary of 28% and thereby meeting the key secondary end point. • Acute transient toxicity of concern was not noted. • Persistent post-transplant toxicities are to be expected; hence, A^{PT}. (PT = persistent toxicity.)
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Typically, in Aotearoa New Zealand, only one cycle of blinatumomab is administered as a bridge to allogeneic HSCT. Only funded via NPPA.
How this medicine would be given	• This medicine is given by continuous intravenous infusion for 28 days. • Central venous access device (CVAD) is required to administer this treatment. • Each cycle is administered once every 6 weeks for 28 days. • Patients receive blinatumomab by continuous intravenous infusion for up to 4 cycles. First cycle as induction with up to three cycles as consolidation. Patients may proceed to allogeneic HSCT after cycle 1. • Australian PBS funding is for up to four cycles in a lifetime.
Patient and whānau considerations	• Patients will receive a continuous IV infusion for 28 days. • CVAD is required to administer this treatment. • Patients may be required to stay in a hospital or clinic for up to 9 days of the first cycle and the first 2 days of the second cycle of blinatumomab. • Patients who are MRD positive treated with blinatumomab may proceed to allogeneic HSCT.

Health system resource considerations	• CVAD is required to administer this treatment. • Stability of blinatumomab – reconstituted IV bag or cassettes 96 hours at room temperature and 10 days refrigerated. • Bags/cassettes need to be changed every 96 hours over 28 days. • Risk of cytokine release syndrome and hypersensitivity reactions, especially in cycle 1. Pre-medication required, monitoring and management of reactions if they occur. • Patients may be required to stay in a hospital or clinic for up to 9 days of the first cycle and the first 2 days of the second cycle of blinatumomab. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Allogeneic HSCT for suitable patients. • Increased demand for laboratory services to monitor for disease response.

* PT = persistent toxicity.

Table 18: Blinatumomab for acute lymphoblastic leukaemia relapsed or refractory – induction and consolidation

Indication description	Ph-negative CD19-positive B-cell precursor acute lymphoblastic leukaemia relapsed or refractory – induction and consolidation
Medicine	Blinatumomab
Description of medicine class	Blinatumomab is a bispecific T-cell engager (BiTE®) molecule that binds specifically to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T-cells.
Intent of treatment	To achieve a complete response and remission that may allow suitable patients to proceed to allogeneic haematopoietic stem cell transplant (HSCT). To improve overall survival.
Pharmac status (October 2024)	No application received for this indication.
ESMO-MCBS:H score and summary of data informing the score	5 Compared with standard-of-care chemotherapy: • Gain in median overall survival of 3.7 months. • Toxicity results did not contribute to the score. • Benefit in quality of life was observed.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Standard salvage chemotherapy may be used for relapsed refractory acute lymphoblastic leukaemia. The duration of remission, if achieved at all, is typically short. If a sufficiently long remission is induced a few patients may be able to proceed to allogeneic HSCT.
How this medicine would be given	• This medicine is given by continuous intravenous infusion. • Central venous access device (CVAD) is required to administer this treatment. • Each cycle is administered once every 6 weeks for 28 days. • Given as up to two cycles of induction therapy followed by up to three cycles of consolidation therapy if in morphologic remission (≤5% bone marrow blasts).
Patient and whānau considerations	• Patients will receive a continuous IV infusion for 28 days. • CVAD is required to administer this treatment. • Patients may be required to stay in a hospital or clinic for up to 9 days of the first cycle and the first 2 days of the second cycle of blinatumomab. • Patients who are treated with blinatumomab may proceed to allogeneic HSCT.
Health system resource considerations	• CVAD is required to administer this treatment. • Stability – reconstituted IV bag or cassettes 96 hours at room temperature and 10 days refrigerated. • Bags/cassettes need to be changed every 96 hours over 28 days. • Risk of cytokine release syndrome and hypersensitivity reactions, especially in cycle 1. Pre-medication required, monitoring and management of reactions if they occur. • Patients may be required to stay in a hospital or clinic for up to 9 days of the first cycle and the first 2 days of the second cycle of blinatumomab.

	• Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Allogeneic HSCT for suitable patients. • Increased demand for laboratory services to monitor for disease response.

Table 19: Gilteritinib for FLT3-positive acute myeloid leukaemia

Indication description	Acute myeloid leukaemia (AML) with FMS-like tyrosine kinase 3 (FLT3) gene relapsed or refractory
Medicine	Gilteritinib
Description of medicine class	Gilteritinib is a small-molecule, multi-targeted tyrosine kinase inhibitor including FLT3.
Intent of treatment	• Non-curative. • PBS funding initial treatment of relapsed disease, and if responding can proceed to allogeneic haematopoietic stem cell transplant (HSCT). • PBS funding is available for continuing treatment with gilteritinib for those who have not undergone or are not undergoing an allogeneic HSCT.
Pharmac status (October 2024)	No funding applications.
ESMO-MCBS:H score and summary of data informing the score	4 Compared with chemotherapy: • Gain in median overall survival of 3.7 months. • Toxicity results did not contribute to the score. • Health-related quality of life was an exploratory endpoint only, so no upgrade to a score of 5 was possible.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	• Relapsed or refractory FLT3-positive AML would be treated with salvage chemotherapy, and these patients may not respond. • Gilteritinib as a single-agent oral treatment improves overall survival compared with salvage chemotherapy. • Gilteritinib-induced remission may allow for some patients (eg, 25% in ADMIRAL study) to undergo a potentially curative allogeneic HSCT.
How this medicine would be given	• Gilteritinib dose 120 mg (3 × 40 mg) orally once daily day 1 to 28 Q4W, continuously. • Response may be delayed. Assess treatment response at 4 weeks and increase dose if not in complete remission. Assess for full clinical response after 6 months. • In ADMIRAL clinical trial 25% went on to receive an allogeneic HSCT if they were in remission and had a suitable donor.
Patient and whānau considerations	• A bone marrow sample is needed to screen for the FLT3 mutations. • This treatment would be an alternative to salvage chemotherapy, potentially offering improved survival and remission for AML with FLT3 mutation. • This treatment may be a bridge to allogeneic HSCT. • Gilteritinib needs to be taken orally once daily continuously, allowing treatment at home. • Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects and to prevent infection.

Health system resource considerations	• Increased demand for laboratory services to screen for FLT3-positive mutations in relapsed and refractory AML. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Increased demand for laboratory services to monitor for disease response.

Table 20: Idelalisib with rituximab for chronic lymphocytic leukaemia

Indication description	Idelalisib with rituximab second line plus for relapsed or refractory chronic lymphocytic leukaemia (CLL)
Medicine	Idelalisib
Description of medicine class	Idelalisib is a selective inhibitor of adenosine-5'-triphosphate (ATP) binding to PI3K-delta kinase, resulting in inhibition of the P13K signalling pathway in malignant B-cells.
Intent of treatment	Non-curative.
Pharmac status (October 2024)	No applications with Pharmac.
ESMO-MCBS:H score and summary of data informing the score	4 Compared with placebo: • Gain of >5.5 months median progression-free survival. • Toxicity results did not contribute to the score. • Improvement in health-related quality of life allows an upgrade to score from 3 to 4.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Standard chemotherapy treatments include purine analogues and alkylating agents, often combined with monoclonal antibodies. These treatments may have unacceptable side effects in older patients and those with coexisting illnesses. Idelalisib combined with rituximab is an alternative treatment option to treat relapsed and refectory CLL patients who can't receive chemotherapy due to cumulative myelotoxicity, poor renal function and/or comorbidities.
How this medicine would be given	Rituximab 375 mg/m^2 intravenous cycle 1, then 500 mg/m^2 cycles 2 to 4 Q2W, then 500 mg/m^2 IV cycles 5 to 8 Q4W. Idelalisib 150 mg orally twice daily continuously.
Patient and whānau considerations	• Rituximab is administered by slow IV infusion cycle 1 and may need to be as an inpatient if high risk of cytokine release syndrome. Further cycles can be administered in a chemotherapy outpatient clinic. • Idelalisib tablets allow treatment at home. • Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects and to prevent infections.
Health system resource considerations	• Rituximab is administered by slow IV infusion cycle 1 and may need to be as an inpatient if high risk of cytokine release syndrome. Further cycles can be administered in a chemotherapy outpatient clinic. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Increased demand for laboratory services to monitor for disease response.

Table 21: Inotuzumab ozogamicin for CD22-positive B-cell acute lymphoblastic leukaemia relapsed or refractory – induction and consolidation

Indication description	CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL) relapsed or refractory – induction and consolidation
Medicine	Inotuzumab ozogamicin
Description of medicine class	Inotuzumab ozogamicin is a CD22-directed antibody-drug conjugate (ADC).
Intent of treatment	To achieve a complete response and remission that may proceed to allogeneic haematopoietic stem cell transplant (HSCT) for suitable patients. To improve overall survival.
Pharmac status (October 2024)	• Funding application received for this indication (see connect.pharmac.govt.nz/apptracker/s/application-public/a102P00000BQ7JF/p001762). • Application received June 2021. – Proposes 3 × cycles as a bridge to HSCT. • Options compared March 2023. – The relative ranking of the pharmaceutical application has been completed. • Named Patient Pharmaceutical Assessment (NPPA) applications received and approved.
ESMO-MCBS:H score and summary of data informing the score	4 Compared with standard-of-care chemotherapy: • 2-year overall survival rate was 23% (95% CI, 16%–30%) vs 10% (5%–16%). • Toxicity results did not contribute to the score. • No upgrade for quality of life.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Current standard first-line salvage treatment for relapsed or refractory B-cell ALL is reintroduction of intensive chemotherapy treatment as part of an overall plan for long-term disease control to allow for an allografting procedure if eligible. Intensive chemotherapy regimens require extended hospital stays for patients, which are associated with adverse events, including haematotoxicity, infection, hepatotoxicity, nephrotoxicity, mucositis and neurotoxicity, which can limit further treatment and dose intensity, which may compromise patient outcomes. Inotuzumab ozogamicin would be an alternative second-line treatment for relapse after intensive combination chemotherapy for initial treatment of ALL or as third line after one prior line of salvage treatment. The goal would be to improve overall survival and, for some patients, provide a bridge to allogeneic HSCT.
How this medicine would be given	• Central venous access device (CVAD) is required to administer this treatment. • This medicine is given by intravenous infusion. • Cycle 1 is administered days 1, 8, and 15 for 28-day cycle. • Cycles 2 to 6 administered days 1, 8, and 15 every 21 days. • INO-VATE ALL trial patients received a median of 3 cycles = 9 administrations. • Pre-medications required to prevent infusion-related reactions. • Observe patient for 1 hour post-infusion.

Patient and whānau considerations	• Weekly administration with pre-medication. • CVAD is required to administer this treatment. • Patients may be required to stay in a hospital for some administrations. • Patients who are treated with inotuzumab ozogamicin may proceed to allogeneic HSCT.
Health system resource considerations	• Stability – 8 hours after compounding. • Mostly given Q1W for up to 18 administrations (equivalent to 6 cycles). INO-VATE ALL trial patients received a median of 3 cycles = 9 administrations. • Risk of hypersensitivity reactions, especially in cycle 1. Pre-medication required and post-infusion monitoring. • Patients may need some inpatient care, but it is less than for standard salvage chemotherapy. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Allogeneic HSCT for suitable patients. • Risk of sinusoidal obstruction syndrome increased in allogeneic HSCT patients. • Increased demand for laboratory services to monitor for disease response.

Table 22: Midostaurin for FLT3-positive acute myeloid leukaemia

Indication description	Acute myeloid leukaemia (AML) with FMS-like tyrosine kinase 3 gene (FLT3) newly diagnosed induction, consolidation and maintenance
Medicine	Midostaurin
Description of medicine class	Midostaurin inhibits multiple receptor tyrosine kinases, including FMS-like tyrosine kinase-3 (FLT-3) and stem cell factor receptor (c-Kit).
Intent of treatment	Curative.
Pharmac status (October 2024)	• Application received April 2019. • Funded from 1 July 2024 • connect.pharmac.govt.nz/apptracker/s/application-public/a102P000008ptwH/p000276).
ESMO-MCBS:H score and summary of data informing the score	A^{PT} Compared with placebo: • Gain in median overall survival of 49.1 months. • Toxicity results did not contribute to the score. • Persistent toxicity (PT) is applicable in the patients who received an allogeneic haematopoietic stem cell transplant (HSCT).
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	• Gemtuzumab ozogamicin is currently used with intensive chemotherapy induction and consolidation for de novo AML with favourable or intermediate cytogenetic risk. • There is greater survival benefit for midostaurin than that of gemtuzumab ozogamicin. • Midostaurin would provide a treatment benefit for the group of patients with AML with favourable or intermediate cytogenetic risk who have FLT3 mutation positive disease.
How this medicine would be given	• Midostaurin dose is 50 mg orally twice daily. – Induction on days 8 to 21 Q3W for 1 or 2 cycles. – Consolidation on days 8 to 21 Q4W for up to 4 cycles. – Maintenance on days 1 to 28 Q4W for maintenance for 12 cycles in patients not undergoing or have not undergone an allogeneic HSCT.
Patient and whānau considerations	• A bone marrow sample is needed to screen for the FLT3 mutations. • Induction and consolidation: Midostaurin needs to be taken orally twice daily days 8 to 21 Q3W or Q4W combined with intensive chemotherapy as an inpatient. • Maintenance: Midostaurin needs to be taken orally twice daily continuously, allowing treatment at home. • Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects and to prevent infection. • Patients who are treated with midostaurin may proceed to allogeneic HSCT.

Health system resource considerations	• Increased demand for laboratory services to screen for FLT3-positive mutation in de novo AML. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Allogeneic HSCT for suitable patients. • Increased demand for laboratory services to monitor for disease response.

Table 23: Azacitidine with venetoclax for acute myeloid leukaemia

Indication description	Acute myeloid leukaemia (AML) – untreated patients who are ineligible for intensive chemotherapy
Medicine	Azacitidine and venetoclax
Description of medicine class	Azacitidine is a histone deacetylase inhibitor. Venetoclax is a selective small-molecule BCL2 inhibitor.
Intent of treatment	Non-curative.
Pharmac status (October 2024)	Azacitidine, as of 1 January 2024, is funded as follows: • The patient has AML with 20%–30% blasts and multi-lineage dysplasia, according to World Health Organization (WHO) classification. • The patient has performance status (WHO/Eastern Cooperative Oncology Group (ECOG)) grade 0–2. • The patient has an estimated life expectancy of at least 3 months. Azacitidine is not funded for blasts >30%. Application to Pharmac as follows: • Application received February 2021. • Options compared June 2021. – The relative ranking of the pharmaceutical application was completed April 2022 (see **connect.pharmac.govt.nz/apptracker/s/application-public/a102P00000B0gUX/p001654**). Venetoclax is not funded for treatment of AML. Application to Pharmac as follows: • Application received November 2020. • Options compared October 2021. – The relative ranking of the pharmaceutical application was completed April 2022 (see **connect.pharmac.govt.nz/apptracker/s/application-public/a102P00000AmyhI/p001627).**
ESMO-MCBS:H score and summary of data informing the score	4 Compared with azacitidine with placebo: • Gain in median overall survival was 5.1 months. • Toxicity results did not contribute to the score. • No differences were observed between the two treatment groups with respect to quality-of-life measures.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	• Azacitidine is administered as monotherapy to patients who cannot tolerate intensive chemotherapy. • Azacitidine in combination with venetoclax (unfunded) is administered to patients who cannot tolerate intensive chemotherapy.
How this medicine would be given	• Azacitidine is administered by subcutaneous injection(s), maximum 100 mg per injection site. • Azacitidine is given by subcutaneous injection once daily days 1 to 7 Q4W. Venetoclax is taken once daily orally continuously. • Initially, venetoclax dose is up-titrated over 28 days monitoring carefully for development of tumour lysis syndrome. Inpatient admission may be required for dose titration.

Patient and whānau considerations	• Inpatient stay may be required for venetoclax dose titration. • Close laboratory monitoring for development of tumour lysis syndrome during dose titration phase. • Seven days of azacitidine administration Q4W may require daily visits to chemotherapy clinic for administration. • Some patients may be trained to self-administer azacitidine daily for 7 days Q4W at home. They can only collect a 2-day supply at a time. • Self-administering patients must have a refrigerator to store azacitidine syringes at 2–8°C. • Individual doses of azacitidine >100 mg will be administered as two subcutaneous injections at two sites. • Regular blood tests are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects, prevent tumour syndrome and to prevent infections.
Health system resource considerations	• Complete blood counts should be performed as needed to monitor response and toxicity, but at a minimum, prior to each dosing cycle. • Inpatient stay may be required for venetoclax dose titration. • Close laboratory monitoring for development of tumour lysis syndrome during dose titration phase. • Seven days of azacitidine administration Q4W. • Training of patients who self-administer. • Azacitidine subcutaneous syringes have a 48-hour expiry and need storage at 2–8°C creating complex logistics with supply. • Increased demand for other laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Increased demand for laboratory services to monitor for disease response.

Lymphoma

Table 24: Acalabrutinib, Ibrutinib and zanubrutinib for mantle cell lymphoma – relapsed refractory

Indication description	Mantle cell lymphoma (MCL) relapsed refractory – second line plus
Medicine	Acalabrutinib, Ibrutinib and zanubrutinib
Description of medicine class	Bruton's tyrosine kinase inhibitor.
Intent of treatment	Non-curative.
Pharmac status (October 2024)	Acalabrutinib • No application Ibrutinib • Application received August 2015. • Options compared June 2021. • See connect.pharmac.govt.nz/apptracker/s/application-public/a102P000008puXu/p001189). Zanubruitnib • Application received May 2023 • Options compared June 2024. • See connect.pharmac.govt.nz/apptracker/s/application-public/a102P00000BaaQE/p001913
ESMO-MCBS:H score and summary of data informing the score	4 Ibrutinib (RAY trial) Compared to temsirolimus:* • Gain of 8.4 months median progression-free survival. • Toxicity results did not contribute to the score. • Improved global health-related quality of life.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	MCL generally has rapid progression, a high rate of relapse after initial treatment, and a median survival time of approximately 3 years. There is limited evidence about the efficacy of treatment for MCL, and MCL patients who relapse or are refractory following treatment have limited effective treatment options in the current Aotearoa New Zealand setting.
How this medicine would be given	Orally once daily continuously.
Patient and whānau considerations	• Tablets allow treatment at home. • Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects, and to prevent infections.

Health system resource considerations	• Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Increased demand for laboratory services and imaging (eg, PET scan) to monitor for disease response.

* Temsirolimus is not available in Aotearoa New Zealand. Temsirolimus is probably not significantly clinically superior to investigator's choice chemotherapy with a progression-free survival gain of only 1.9 months. Quality of life not measured and no fewer toxicities (Hess 2009).

Multiple myeloma

Table 25: Lenalidomide with bortezomib and dexamethasone for multiple myeloma

Indication description	Lenalidomide with bortezomib and dexamethasone for untreated multiple myeloma (not intended for immediate autologous haematopoietic stem cell transplant) induction followed by maintenance
Medicine	Lenalidomide
Description of medicine class	Lenalidomide is an immunomodulatory agent that exhibits multifaceted, anti-myeloma activity by enhancing immune function, disrupting aberrant stromal cell support as well as having direct anti-myeloma cell effects.
Intent of treatment	Non-curative.
Pharmac status (October 2024)	Multiple myeloma, autologous haematopoietic stem cell transplant ineligible, first line. • Application received May 2016. • Funded from 1 August 2024. • connect.pharmac.govt.nz/apptracker/s/application-public/a102P000008pua9/p001248).
ESMO-MCBS:H score and summary of data informing the score	4 • Gain in median overall survival of >15 months. • Toxicity results did not contribute to the score. • Health-related quality of life was not different and did not contribute to the score. NB: In the SWOG S0777 trial 69% of patients were earmarked as having an intent to have a transplant.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Transplant-ineligible patients are treated with up to 9 cycles of a bortezomib-based regimen (cyclophosphamide, bortezomib and dexamethasone (CyBorD); bortezomib, thalidomide and dexamethasone (BTD); or bortezomib, melphalan and prednisone (BMP)) or thalidomide-based regimens (cyclophosphamide, thalidomide and dexamethasone (CTD) or melphalan, prednisone and thalidomide (MPT)). Most patients would be treated with CyBorD; however, there may be a group of patients who are treated with one of the thalidomide-based regimens.
How this medicine would be given	• Induction consists of 8 cycles: lenalidomide 25 mg orally once daily days 1 to 14 with bortezomib subcutaneous days 1, 4, 8 and 11* and dexamethasone orally days 1 and 2; 8 and 9; 15 and 16; and 22 and 23 Q4W. • Maintenance: lenalidomide 25 mg orally once daily days 1 to 21 with weekly dexamethasone Q4W continuously.
Patient and whānau considerations	• Lenalidomide is taken orally on days 1 to 14 or 21 of a 28-day cycle allowing for treatment at home. • All patients must fulfil the requirements of the pregnancy prevention risk management programme to ensure pregnant women are not exposed to lenalidomide. • Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects and to prevent infection.

Health system resource considerations	• An access programme application is required by clinicians for approval to prescribe lenalidomide for individual patients for every prescription. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Increased demand for laboratory services to monitor for disease response.

* Aotearoa New Zealand practice is to administer bortezomib 1.3 mg/m^2 subcutaneous once a week.

Table 26: Pomalidomide and dexamethasone for relapsed or refractory multiple myeloma

Indication description	Pomalidomide and low-dose dexamethasone third line plus for relapsed or refractory multiple myeloma
Medicine	Pomalidomide
Description of medicine class	Pomalidomide is an immunomodulatory agent that exhibits multifaceted, anti-myeloma activity by enhancing immune function, disrupting aberrant stromal cell support as well as having direct anti-myeloma cell effects.
Intent of treatment	Non-curative.
Pharmac status (October 2024)	Multiple myeloma, relapsed or refractory, third line with dexamethasone. • Application received November 2015. • Funded from 1 August 2024. • connect.pharmac.govt.nz/apptracker/s/application-public/a102P00000BIsCh/p001701).
ESMO-MCBS:H score and summary of data informing the score	4 Compared to high-dose dexamethasone: • Gain in median overall survival of 4.6 months. • Toxicity results did not contribute to the score. • Health-related quality of life did not contribute to the score. MM-003 (NIMBUS) study patients were a heavily pre-treated and disease-refractory population with about 95% of participants having received more than two prior lines of treatment (median 5 previous treatments). More than 90% of patients were refractory to lenalidomide, and about 80% of patients were refractory to bortezomib.
Current clinical practice in Aotearoa New Zealand and how this would change if the gap were filled	Pomalidomide represents an additional line of treatment that may be reserved for use as a third or later line. These patients would likely benefit most as they have few other options available. Pomalidomide appears to be effective regardless of prior therapy. Use of this agent would be preferred for patients with multiply relapsed disease (who have progressed on other lines of treatment).
How this medicine would be given	Pomalidomide 4 mg orally once a day on days 1 to 21 with low-dose dexamethasone 40 mg orally once a week on days 1, 8, 15 and 22 Q4W.
Patient and whānau considerations	• Pomalidomide capsules and tablets allow treatment at home. • All patients must fulfil the requirements of the pregnancy prevention risk management programme to ensure pregnant women are not exposed to pomalidomide. • Regular blood tests and other monitoring are required to monitor for toxicity and response to treatment. • Dose modifications or delays may be needed if patient is intolerant to treatment. • Other medications may be needed to control side effects and to prevent infection.

Health system resource considerations	• An access programme application is required by clinicians for approval to prescribe pomalidomide for individual patients for every prescription. • Increased demand for laboratory services to monitor for treatment-related toxicities. • Potential for increased demand for supportive care and toxicity management (including health care professionals' time and adjustment of pharmaceuticals). • Additional follow-up appointments required. • Increased demand for laboratory services to monitor for disease response.

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