Medicines Australia | Better health through research and innovation

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Committee Secretary
Senate Standing Committees on Community Affairs
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Dear Committee Members,

Re. Submission from Medicines Australia on the Equitable access to diagnosis and treatment for individuals with rare and less common cancers, including neuroendocrine cancer

Medicines Australia welcomes the opportunity to provide a submission to this Senate Community Affairs References Committee Inquiry.

Medicines Australia represents the research based pharmaceutical industry responsible for the research and development of new innovative and specialised medicines that are used to treat patients living with a range of different cancers. As the representative body of these pharmaceutical companies, this submission will focus on the barriers to accessing appropriate treatments.

This submission builds on the recommendations of previous Parliamentary Inquiries, the National Strategic Action Plan for Rare Diseases, Australia's National Medicines Policy, and Medicines Australia's contributions to the Health Technology Assessment Policy and Methods Review currently in progress. This submission is also informed my Medicines Australia's Oncology Industry Taskforce and Rare Diseases Working Group.

The overarching recommendations in this submission are:

1. Reform Health Technology Assessment (HTA) processes and policies to allow Australians living with a rare cancer to have equitable, timely and sustainable access to medicines.
2. Acknowledge the need to invest in rare diseases beyond rare cancers.
3. Commit to funding the Clinical Trials National One Stop Shop and National Clinical Trials Front Door, to harmonise Australia's clinical trials sector and provide better access to cutting edge medical technologies.

If you have any questions about our submission, or if we can be of any further assistance, please contact Constantine Tablan, Policy Manager, at .

Yours sincerely,

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1 Introduction

1.1 Building on previous work

Patients with cancer do not have time to wait to get access to diagnosis and treatments. Furthermore, patients with rare and less common cancers face additional challenges due to the rarity of their conditions. Rare cancers can be difficult to diagnose and lack established treatment protocols, treatments may not be readily available or accessible, and research for treatments may be further away due to lack of awareness and research funding.

'*Rare cancers*' is a term which encompasses both rare and less common cancers. A rare cancer is defined as a type of cancer that has less than 6 incidences per year per 100,000 population, whilst a less common cancer is defined as one that has between 6 and 12 incidences per year per 100,000 population. (1) Although each type of rare and less common cancers are individually rare, collectively, they add up. While 30% of all cancers diagnosed are classified as rare or less common cancers, these are responsible for 42% of all cancer deaths. (2)

This Senate inquiry into *Equitable access to diagnosis and treatment for individuals with rare and less common cancers, including neuroendocrine cancer*, is timely as it coincides with the Health Technology Assessment (HTA) Policy and Methods Review (HTA Review). (3) The HTA Review is one of the main commitments under the 2022-27 Strategic Agreement between the Commonwealth and Medicines Australia. (4) It will ensure Australia's HTA system evolves to keep pace with advances health technologies, including finding efficient ways of assessing treatments and therapies that do not fit neatly into the system, such as many new treatments for rare cancers.

Addressing the barriers that prevent patients with rare and less common cancers from accessing appropriate treatment is not a new issue. These barriers were discussed in The Senate Inquiry into the *Availability of new, innovative and specialist cancer drugs in Australia* in 2014; (5) *The National Strategic Action Plan for Rare Diseases (The Action Plan),* published in 2020; (6) The Parliamentary Inquiry into *Approval processes for new drugs and novel medical technologies in Australia* in 2020, and the following report: *The New Frontier - Delivering better health for all Australians (The New Frontier Report)* (7). Recommendations from these reports and guidelines all called for system improvements to support better access to innovative treatments.

Medicines Australia's submission to this Senate inquiry builds on previous recommendations and findings. As the representative body of pharmaceutical companies who develop new medicines, this submission will focus on the barriers to accessing appropriate treatments. This submission will outline the barriers that prevent patients with rare and less common cancers from accessing appropriate treatment and explore potential solutions.

The overarching recommendations in this submission are to:

1. Reform Health Technology Assessment processes and policies to allow Australians living with a rare cancer to have equitable, timely and sustainable access to medicines.
2. Acknowledge the need to invest in rare diseases beyond rare cancers.
3. Commit to funding the Clinical Trials National One Stop Shop and National Clinical Trials Front Door, to harmonise Australia's clinical trials sector and provide better access to cutting edge medical technologies.

Despite a decade of reviews and calls to reform of the system, the current situation is that people diagnosed with rare and less common cancers do not have the same access to diagnosis, treatment, and care that those with more common cancers have. A decade of reviews brings us no closer to closing the survival gap between common and rare cancers with rare cancers collectively accounting for 42% of cancer deaths. A stark reminder of the inherent inequities in the system and the urgency required to address the imbalance.

Addressing these issues will require collaborative efforts among all stakeholders, building on the work that has already been done. Medicines Australia hopes this inquiry, along with the concurrent HTA Review, will lead to real policy changes that make meaningful differences to patients living with rare cancers.

1.2 About Medicines Australia

Medicines Australia leads the research-based medicines industry of Australia. Our members discover, develop and manufacture prescription pharmaceutical products, biotherapeutic products and vaccines that bring health, social and economic benefits to Australia. Our members invest in Australian medical research and take local discoveries and developments to the world.

1.3 About the Oncology Industry Taskforce (OIT)

Medicines Australia has a dedicated group, the Oncology Industry Taskforce (OIT) that was formed in 2012 to catalyse an informed public debate about accessing new medicines generally, and new cancer medicines in particular, and to work collaboratively with Government, clinicians, and patients to address the challenge of access to cancer medicines.

1.4 About the Rare Diseases Working Group (RDWG)

The vision for Medicines Australia's Rare Diseases Working Group (RDWG) is to create a sustainable, world-leading healthcare system that makes a meaningful difference to the lives of Australians living with a rare disease. This includes amplifying the importance of early screening and diagnosis; and fast, equitable access to innovative medicines.

2 Barriers to accessing appropriate treatment (Terms of Reference: b)

Recommendation 1: Reform Health Technology Assessment processes and policies to allow Australians living with a rare cancer to have equitable, timely and sustainable access to medicines.

2.1 The long wait for treatments

The purpose of HTA is to provide necessary information to understand the benefits and comparative value of health technologies and procedures. HTA assists and informs government funding decisions. The main bodies involved in the assessment of treatments for rare cancers include the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC). Some state hospitals also do HTAs.

At present, the average time from registration to reimbursement of innovative medicines across all diseases in Australia is 466 days, compared to 102 days in Japan, 136 days in Germany and 156 days in the UK. (8) For medicines that treat rare diseases including rare cancers, that wait is even longer being two to four years longer than other comparable countries. In some cases, Australian patients miss out entirely on treatments where other countries have established HTA processes tailored to evaluate treatments for rare diseases, including rare cancers. (9)

Even when effective treatments are available, the reimbursement pathway for rare cancer treatments can be difficult. In the rapidly evolving landscape of treatments for rare cancers, new therapies frequently incorporate innovative technologies with new mechanisms of action. Australia's HTA processes need to be fit for purpose to allow innovative health technologies to be provided to the patients who need them. (7)

The New Frontier Report found that Australian HTA processes utilise models that are designed primarily for more common diseases. (7) The lack of evidence for treatments, the challenges of demonstrating cost-effectiveness of those treatments, and the lack of clinical expertise of rare cancers, make the HTA evaluation of treatments for rare cancers through a non-rare lens difficult. It is therefore important that HTA processes accommodate for the limitations and challenges associated with rare cancers when reimbursement decisions are being made.

ACTION:

- **Adapt HTA processes so they accommodate the limitations and challenges associated with rare cancers when reimbursement decisions are being made**.

2.2 Limited clinical evidence

HTA Evaluators require substantial clinical evidence to support the efficacy and safety of treatments. Randomised Controlled Trials (RCTs) are often seen as the gold standard of clinical evidence used in HTA evaluations. However, the small patient populations of people living with rare cancers can make gathering clinical evidence difficult.

Due to the smaller patient numbers, there is less clinical evidence available due to the limitations of conducting large-scale RCTs for rare cancers. Comparisons across data sets are also made more problematic as rare cancers encompass a wide range of diseases, each with its own unique biological characteristics and treatment options. (10) This can severely limit the depth of the evaluation of a rare cancer therapy. There needs to be a more pragmatic approach to HTA evaluations that utilise all available evidence used to treat rare cancers.

The NICE Real-World Evidence Framework highlighted how different evidence standards could be applied to orphan drugs, and the need for greater acceptance of real-world evidence. That is, evidence that is generated through non-randomised studies, single-arm studies, registry data or other methods of evidence generation. (11) HTA reform that includes greater acceptance of real-world evidence in evaluations could help overcome the HTA evaluation challenges of rare cancer treatments relating to the lack of clinical data.

ACTION:

- **Accept real-world evidence in evaluations for rare cancer treatments to address the limited availability of clinical data.**

2.3 The challenge of demonstrating cost-effectiveness

Traditional cost-effectiveness metrics of Incremental Cost-Effectiveness Ratios (ICERs) used in HTA might not capture the full value of a treatment for rare cancers. Rare cancer treatments, including targeted therapies and new personalised medicine approaches, can be expensive due to their specialised nature. Evaluators may be hesitant to cover treatments with high costs, especially when the evidence of their benefit is limited.

In the rapidly evolving area of precision medicine, the use of diagnostic information extends well beyond determining eligibility for a single therapy. However, a significant challenge in proving the cost-effectiveness of personalised and precision medicine arises from the necessity to factor in the expenses of screening tests (like genomic testing) alongside the specific therapy, (12) especially if the tests aren't covered by the Medicare Benefits Schedule (MBS). Including the screening test costs in the evaluation can dilute the apparent incremental benefit of the new therapy within the conventional cost-effectiveness framework, due to the increased attributed costs linked to the therapy.

The New Frontier Report found many stakeholders recommended economic evaluations having a broader consideration of value including the magnitude of clinical benefit, rarity, severity, equity, burden of disease, innovation or scientific advance, budget impact, societal benefits, and indirect costs. (7) Although broader aspects are considered by HTA decision makers on a case-by-case basis, more transparency on the factors considered by the PBAC is required, and how this information should be presented in HTA applications.

Patient engagement is also critical to understanding the full impact of the treatment and the meaningfulness of the clinical benefits. Therefore, consumer hearings should be offered to patient groups for all proposed treatments for rare cancers. Respondents from patient groups in *The New Frontier Report* highlighted that “it is critical that HTA processes formally embed, capture and promote the voice of people living with rare disease and their families and carers” to “provide much needed narrative and context to the data presented.” (7)

HTA reform that incorporates a more flexible and tailored approach to cost-effectiveness analysis rather than more traditional metrics is necessary for rare cancers. This will involve having a broader consideration of value, collaborating with patient advocacy groups to measure patient level impacts, and leveraging real-world evidence, to account for the specific challenges of the assessment of rare cancer treatments.

ACTION:

- **Provide more transparency on the factors considered by the PBAC, and how this information should be presented in HTA applications.**

- **Ensure patients with rare cancers are provided a hearing with PBAC so they can speak to the real-life impacts and benefits of treatments.**

2.4 Lack of clinical experts

HTA decisions for rare cancer therapies rely heavily on input from clinical experts who possess specialised knowledge of these rare conditions. However, rare cancers are typically managed by a small number of specialised health care professionals. Beyond this group, there may be limited understanding of the cancer management and treatment outcomes. (13)

Further, the lack of clinical experts makes it more likely that the few who do have experience with rare cancers may have participated in company-sponsored clinical trials. This adds a layer of complexity to HTA processes as there are strict conflict of interest principles to clinicians providing input into the evaluation. (13)

Relaxing the accepted conflict of interest principles in HTA processes is recommended for rare cancers. It would allow for better input from clinical experts prior to HTA evaluation and could facilitate early agreement on therapy, comparator, and patient relevant outcomes. Early and more structured engagement with clinical experts for rare cancer therapies would better inform issues such as the applicability of the evidence, or eligibility criteria, during consideration of value.

Reforming the HTA process to value the collaborative efforts between healthcare professionals, specialist networks, and patient advocacy groups can help bridge this gap. This can ensure that assessments are informed by knowledgeable individuals who understand the intricacies of rare cancers, and evaluators can be made aware of patient-level impacts of rare cancer therapies.

ACTION:

- **Allow the collaborative voice of healthcare professionals, specialist networks, and patient advocacy groups to provide advice on the value of a medicine for a rare disease in the absence of a clinical expert.**

2.5 The HTA Review

Bold and pragmatic reform of HTA processes is needed so patients living with rare cancers can access medicines as soon as possible after regulatory approval. Looking at the shortcomings of our current HTA system, and comparing it to our international counterparts to guide Australia's HTA Review, may help to accommodate the unique challenges of rare cancers and promises several benefits.

Currently, PBAC assessments can take 33-35 weeks from submission of a major application to full publication of summary documents. (8) This can be even longer for treatments for rare diseases, including rare cancers. (9) This is far below international standards and increases the waiting time for patients. The evaluation of treatments for rare conditions is only 17 weeks in England. (9) The need for HTA reform is consistent with the findings from *The New Frontier Report* and the Senate inquiry into the *Availability of new, innovative and specialist cancer drugs in Australia.* New evaluation and funding pathways for rare

cancer therapies are needed to ensure time to patient access is improved and aligned with TGA pathways such as Project Orbis and priority review. (14)

Several countries have successfully reformed their HTA processes to address the evaluation of treatments for rare cancers, offering valuable lessons for Australia. A review across international examples showed that there is no one model of funding that addresses the complexity of HTA review. Adaptive evaluation and funding pathways, excluding cost-effectiveness analysis in HTA evaluations, collaborative partnerships among stakeholders, and higher or more flexible thresholds for funding, have been effective methods for improving patient access to rare cancer treatments in Japan, (15) the UK, (16) and France. (17)

Improving the HTA process in Australia, has an additional effect of encouraging multinational clinical trials to be conducted in Australia and advance local clinician experience with innovative medicines. Clinical trials are often designed with the ultimate aim of registering a drug for a specific indication (7). If the HTA process can provide greater certainty about reimbursement, companies may be more likely to conduct clinical trials in Australia, allowing greater opportunities for patients to access to treatments, as well as a stronger evidence base for HTA evaluations.

Reforming the HTA processes and policies is a crucial step towards providing Australians living with rare cancers equitable, timely, and sustainable access to life-saving therapies. Patients must be at the centre of the process, so reimbursement decisions consider the impact and benefits of medicines from their perspective. Embracing international best practices that tailor assessment criteria can lead to a more accurate and rapid evaluation that is fit for purpose, ensuring patients with rare cancers receive timely access to treatments. Consequently, Australia can become a more attractive destination to conduct clinical trials, providing additional access to treatments. HTA reforms ultimately will ensure people living with rare cancers in Australia are not left behind in the pursuit of improved healthcare outcomes.

ACTION:

- **Implement reform of HTA processes rapidly following the conclusion of the HTA Review, especially reforms that will deliver equitable access to metastatic and rare cancer patients regardless of their type or stage of disease, location, or ethnicity**.

3 Any other related matters (Terms of Reference: e)

Recommendation 2: Acknowledge the need to invest in rare diseases beyond rare cancers.

3.1 Rare diseases beyond cancer

Treating rare non-cancer diseases can be even more challenging than treating rare cancers due to several factors that are inherent to the nature of these diseases. These conditions encompass a diverse array of genetic, metabolic, autoimmune, and neurological disorders, each characterised by complex underlying mechanisms and distinct clinical presentations. (18) This complexity, coupled with limited treatment options, present unique difficulties that often surpass the challenges posed by rare cancer treatments.

(19) These highlight the need for appropriate investment in rare diseases and not be simply categorised with rare cancers.

One of the primary hurdles in addressing rare non-cancer diseases stems from their heterogeneity. (20) Unlike rare cancers that may share common genetic mutations or pathways, non-cancer diseases display a variety of causative factors and biological pathways. (21) This complexity hinders the development of one-size-fits-all treatment approaches, necessitating targeted and individualised strategies. (20)

The limited understanding of mechanisms underlying many rare non-cancer diseases further exacerbates the treatment challenge. In some rare cancers, specific mutations are more straightforwardly linked to disease progression. (21) However, the multifaceted interactions of genes, proteins, and cellular processes in non-cancer diseases can make identifying effective interventions a daunting task. (19)

Scarcity of treatment options for rare diseases compounds the challenges. For certain cancer types, there have been breakthroughs in targeted therapies and immunomodulation. (22) Unfortunately, many non-cancer rare diseases lack clear modalities for drug targets and pathways to developing intervention. This scarcity underscores the need for intensive research efforts, often hampered by limited funding due to the lower public profile of rare non-cancer diseases. (9)

Like rare cancers, the small patient populations of rare non-cancer diseases pose obstacles to conducting meaningful clinical trials and accumulating substantial data. This limitation, coupled with ethical considerations in trials involving vulnerable populations, contributes to delays in developing and obtaining regulatory approval for potential treatments. (7)

The HTA pathways for rare non-cancer diseases can be even more complex than those for rare cancers. HTA pathways for rare diseases have evolved over time, resulting in multiple inconsistent evaluation and funding pathways. For example, 'life-saving' ultra-rare disease treatments must first be rejected by the PBAC before they can be considered for funding under the Life Saving Drugs Program (LSDP), adding an additional 12-month delay to reimbursement. *The New Frontier Report* recommends the pathway for the LSDP be streamlined to accelerate access to patients with rare diseases. (7)

Definitions of rare diseases are narrower than those for rare cancers, and differ across agencies and programs, which can lead to inconsistencies across rare disease policies. The TGA eligibility for orphan drugs is a disease with fewer than 5 in 10,000 individuals. (23) A more restrictive definition of fewer than 1 in 50,000 people (sometimes called 'ultra-orphan') is applied for eligibility for funding via the LSDP. (24) Consistent definitions for rare disease populations will help streamline HTA evaluations and funding of rare disease therapies.

The very small populations of people living with rare diseases makes it difficult in the current system to move beyond simplistic conceptualisations of cost-effectiveness. Cost-effectiveness on the LSDP is seen in its requirement that costs be framed against an increase in life expectancy. Therefore, if a treatment is not recognised as 'life-saving' it will not meet the criteria for the LSDP. This mean people living with rare diseases only get access to new therapies that are 'life-saving', which is a different benchmark for treatments of other conditions. (9)

Though rare cancers and rare non-cancer diseases share many similarities, the distinctly different and multifaceted challenges of rare non-cancer diseases should not be simply classified within the same encompassing category. By acknowledging these distinctions, approaches to treatment, research, and

investment can be more appropriately channelled to offer a brighter outlook for individuals living with rare non-cancer conditions and their families.

Recommendation 3: Commit to funding the Clinical Trials National One Stop Shop and National Clinical Trials Front Door, to harmonise Australia's clinical trials sector and provide better access to cutting edge medical technologies.

3.2 A fragmented clinical trial system

For many patients living with a rare cancer, clinical trials are essential for improving outcomes, and for some, are the only means of accessing treatments. However, there are disparities in access to clinical trials in Australia, which can be exacerbated for those living with a rare cancer. There are several factors that cause these inequities, which could be improved if the current federated clinical trials system were harmonised to a national system.

The current landscape of clinical trials in Australia is marked by fragmentation due to a federated system. There is variability in trial protocols and regulatory processes between each jurisdiction. (25) Rare cancer trials suffer from disparities in access to cutting-edge treatments due to these inconsistencies, leaving patients and researchers struggling to navigate a complex and inefficient system.

The key benefit of harmonising clinical trials is the standardisation of trial protocols and procedures. Nationally consistent and harmonised operating environments for the approval and management of clinical trials, would encourage multinational innovator companies to bring their trials to Australia. More trials in Australia means more opportunities for patients with rare cancers to access new treatments.

A nationally consistent clinical trial environment will better facilitate the establishment of more clinical trial sites across Australia, helping to close the gap of a geographic inequity, which limits access for rural and remote patients. (7) More multinational trials will also bolster our health and medical staff by providing world-class training in new treatments, helping address the lack of clinical experts.

Further, more clinical trials available for patients to participate in will facilitate better data collection. More data on clinical trials for rare cancers will provide a stronger evidence base for HTA processes and improve the chances for positive reimbursement decisions. The interconnectedness of HTA and clinical trials highlights the value of considering access to treatments from a wholistic perspective, and why commitment from the Government to invest in harmonisation is important for people living with rare cancers.

3.3 The National One Stop Shop

For over two decades, Medicines Australia has been advocating for the streamlining and harmonisation of clinical trials in Australia. Successive Governments have recognised the opportunity to strengthen Australia's attractiveness as a destination for clinical trials. Clinical trials are important avenues for people with rare cancers to access treatments, and investment in harmonisation can bring more trials to Australia.

The National One Stop Shop (NOSS) is an initiative, proposed to the Federal Government, with an aim to harmonise clinical trial systems in Australia. It will transform the ability of patients to access clinical trials and therapeutic interventions, and make it easier for industry, sponsors, and researchers, to find, invest and conduct research in Australia. The concept for the National One Stop Shop builds on international evidence that nationalised platforms are critical to building a stronger, more competitive health-research sector, and ultimately, provide better outcomes for Australian patients. (25)

This platform would be supported by a National Front Door, which would "provide a public interface so the community and their carers can easily identify trial and research options." (25)

The Australian Commission on Safety and Quality in Health Care (The Commission) has conducted extensive consultations with a wide range of stakeholders including industry, health care providers, as well as State and Federal Government entities. The Consultation Report on the NOSS found strong support from the breadth of stakeholders involved in the consultations. Respondents believe the NOSS will deliver one platform for all aspects of trial, increasing the efficiency of conducting trials.

Despite the positive support from stakeholders, and the Federal Government acknowledging the NOSS as "a major step towards developing a platform that supports patients", (26) there have been no funding commitments for the development of the NOSS. The NOSS and National Clinical Trials Front Door are important opportunities that will need appropriate and sustainable investment if they are to deliver on their promise to significantly progress harmonisation of the clinical trial sector. Committing to invest in these initiatives is a commitment to provide greater access to innovative treatments to Australians living with rare cancers.

4 Conclusion

This submission highlights the urgency of addressing the critical challenges faced by individuals with rare and less common cancers in accessing timely and equitable diagnosis and treatment. It calls for comprehensive reforms in the Health Technology Assessment processes, emphasising the need to recognise the unique nature of rare diseases and cancers, leverage observational data, and establish streamlined pathways for funding.

This submission stresses the importance of addressing barriers such as the lack of evidence due to limited clinical trials, challenges in demonstrating cost-effectiveness, and the need for patient engagement and expert input. Furthermore, it highlights the need to extend similar considerations to rare non-cancer diseases, acknowledging their distinct complexities.

Medicines Australia advocates for the sustainable funding of the Clinical Trials National One Stop Shop and National Clinical Trials Front Door initiatives. The submission emphasises the benefit of harmonisation in the clinical trials sector to enhance patient access, clinician training, researcher opportunities, and data collection.

Addressing the barriers that prevent patients with rare and less common cancers from accessing appropriate treatments will require the collaboration of Government, the innovative medical industry, healthcare and research personnel, and patient groups, as well as building on recommendations from previous Parliamentary Inquiries and the HTA Review. Moreover, recognising the interconnectedness of

these sectors and solutions will be critical to the success and sustainability of providing equitable access to treatments.

The recommendations made in this submission echo those that have been made in Parliamentary Inquiries, guidelines, reports, and reviews, over the past decade, and the HTA Policy and Methods Review will also have important recommendations to make. If we are to make meaningful changes to the lives of people living with rare and less common cancers all of these recommendations will need to be acted on in the spirit of equitable access, which is the first pillar of Australia's National Medicines Policy. (27)

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