9 October 2020
Committee Secretariat
PO Box 6021
Parliament House
CANBERRA
Canberra ACT 2600
Health.Reps@aph.gov.au

Dear Committee Secretariat,

Re: House of Representatives Standing Committee on Health, Aged Care and Sport inquiry into approval processes for new drugs and novel medical technologies in Australia

Thank you for the opportunity to make a submission to the *Inquiry into approval processes for new drugs and novel medical technologies in Australia*.

Multiple myeloma (MM), a cancer of plasma cells (a type of white blood cell), is the second most common form of blood cancer, and despite the significant advances made in cancer treatment over the past decade ***is one of the few cancers that still remains incurable***.

The global incidence of MM increased by 126% between 1990 and 2016, with Australasia demonstrating the highest age-standardised incidence rate (ASIR 5.8 per 100,000 population) and second highest age-standardised death rate (ASDR 2.8 per 100,000) in the world. Data from the 2019 Australian Institute of Health and Welfare 'Cancer in Australia' report demonstrates that the ASIR and ASDR for MM in Australia continue to rise, and while representing only 1-2% of cancers ***MM is in the top ten cancer diagnoses in terms of frequency of requirement for hospitalisation.*** This is largely due to the fact that MM is a highly complex and heterogenous disease that involves multiple organs and can cause pathological bone fractures, kidney failure and severe immunosuppression necessitating access to complex supportive care including orthopaedic surgery, radiotherapy, dialysis and anti-infective prophylaxis – the latter including both antimicrobials and high-cost immunoglobulin (antibody) replacement therapy.

Currently, the therapeutic approach for MM in Australia is based on the use of 2 classes of anti-MM drugs – immunomodulators and proteasome inhibitors – either individually or in combination. ***No new class of anti-MM therapeutic agent had been approved and reimbursed in Australia for 13 years, in contrast to many first-world nations,*** where in the last 5 years, one or all of, a range of new and highly active anti-MM therapeutics with alternative mechanisms of action (elotuzumab, daratumumab, isatuximab, panobinostat, ixazomib, selinexor and belantamab) have been made available to MM patients.

The ***Myeloma and Related Diseases Registry (MRDR), a clinical quality registry,*** was established in 2012 as an online platform for a multi-centre collaboration, collecting prospective data on patients with MM.

The MRDR was developed to monitor and explore variations in practices, processes and outcomes and to provide benchmark outcomes nationally and internationally for MM and related plasma cell disorders. ***A recent analysis of MRDR data, on now more than 4000 newly diagnosed patients, has demonstrated a number of critical shortcomings in MM diagnostics and treatment in Australia.*** First, only 50% of patients undergo chromosome (genetic) testing so as to attribute disease 'risk' and hence provide prognostic insight and guidance to patients, their families and clinicians when making treatment decisions. Importantly, a survey subsequently undertaken by the Haematology Society of Australia and New Zealand (HSANZ) has confirmed a lack of uniformity in chromosome testing around Australia and that in the majority of instances the results of testing are not available at the time of initiating treatment. Second, >80% of newly diagnosed patients are treated in the same way (therapies based around the use of the proteasome inhibitor bortezomib) despite significant variation in disease biology and prognosis. Third, 23% of newly diagnosed Australian MM patients will relapse within 12 months of starting treatment and then largely fail to respond to second line salvage treatment. The median survival from diagnosis for these 'early progressors' is only 16 months.

The real-world picture emerging from the MRDR is now enabling us to understand more clearly the key areas of unmet need in the management of MM in Australia, namely the paucity of treatment choices available to Australian MM patients and the lack of access to accurate and validated genetic testing at diagnosis. Treatment choices for MM in Australia are continuing to fall behind those available in other jurisdictions.

This situation is highlighted by the ***ongoing lack of access to the monoclonal antibody datatumumab.*** Daratumumab has been available overseas for the treatment of MM for more than 5 years with multiple clinical trials having demonstrated its highly significant impact on MM patient outcomes. After multiple submissions to the PBAC, daratumumab has finally been given a positive recommendation for reimbursement, but only in a restricted group of MM patients, and if and when it will actually be listed on the PBS is unclear. The difficulty in providing access to daratumumab (or indeed any of the newer therapeutics mentioned above) reflects a ***drug reimbursement model that was adopted prior to the advent of more costly anti-cancer therapeutics and the concept of multiagent or combinatorial treatments. Without a significant revision of this model the treatment of MM and other cancers in Australia will increasingly lag behind accepted 'standards of care' utilised elsewhere.***

This situation is exacerbated by the ***absence of an accessible and accurate platform for genetic testing in MM that would empower both patients and clinicians to make informed treatment choices.*** Genetic testing for MM utilising a highly accurate and extensively validated assay, the MMProfiler™, from SkylineDx has been approved for use in both Europe and the US. MMProfiler™ is a gene expression platform utilising a standard Affymetrix platform, has a turn-around time of <72 hours and can accurately define truly 'high-risk' MM patients who have a median survival of <24 months and who gain no survival benefit from high-cost drugs such as the immunomodulator lenalidomide, a drug currently reimbursed and used extensively for the treatment of both newly diagnosed and relapsed MM in Australia. The assay has been established at The Alfred Hospital and successfully utilised in several multi-centre clinical trials over the past 3 years. Importantly, the MMProfiler™ when combined with readily available clinical data can define the approximately 30% of MM patients with an excellent prognosis, with median survivals approaching 10 years. One could therefore anticipate that ***the availability of the prognostic information afforded by such genetic testing would enable highly informed and critical treatment decisions,*** both in terms of seeking alternative therapies, for example, younger high-risk patients accessing newer drugs via clinical trials, elderly high-risk patient perhaps selecting to pursue palliative treatment approaches, or

conversely good-risk patients electing to de-escalate therapy and thus avoiding unnecessary toxicities and the adverse effects on quality of life.

The ***real-world data provided by the MRDR demonstrates that MM management in Australia is at a critical juncture where we need to decide whether to embrace a broader range of anti-MM therapeutics and contemporary genetic testing that will enable more rational, personalised and effective treatment strategies for this complex and incurable malignancy***. For this to happen there will need to be fundamental changes to the evaluation and approval processes for both new drugs and novel medical technologies that acknowledges the ever increasing complexity involved in optimising cancer diagnosis and management.

On behalf of the patients and families dealing with this terrible disease, the healthcare professionals managing MM across Australia, and the research community participating in the Myeloma and Related Diseases Registry, we thank you for your consideration of the points raised here as you conduct this review. We would be happy to provide additional information on any aspect of this submission.

Yours sincerely

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Professor Andrew Spencer

Principal Specialist & Head of Service,
Malignant Haematology & Stem Cell Transplantation,
Alfred Health.

Principal Investigator,
Myeloma & Related Disorders Registry,
School of Public Health & Preventive Medicine,
Monash University.

Professor of Haematology
Monash University.

[redacted]

Professor Erica Wood

School of Public Health & Preventive Medicine
Monash University.