Submission to Pharmac's review of rule 8.1b of the Pharmaceutical Schedule

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Declaration of interest

Brain Tumour Support NZ works with clinicians, researchers, allied health professionals, academia, government and industry to achieve better outcomes for New Zealand brain tumour patients and their whānau. We are funded by grants, donations and fundraising events. Brain Tumour Support NZ does not receive any income from the pharmaceutical industry. This submission is in response to Pharmac's review of rule 8.1b of the Pharmaceutical Schedule and the funding of paediatric cancer treatments in New Zealand.

Childhood Brain Cancer in New Zealand

Brain cancer is the most common solid tumour cancer in children aged 0-14 years. In the five years 2015 – 2019, there were 179 children diagnosed with brain and central nervous system (CNS) tumours in New Zealand, an average of 36 children per year[1]. Brain tumours are responsible for the most deaths in New Zealand children of any cancer type (42% of all childhood cancers).[2]

A childhood brain tumour can be a devastating diagnosis that changes the lives of children and their families with major impacts on how a person feels, learns, and interacts with the world. Our brain is central to our identity - it controls what we do, think and feel. The brain is also the only vital organ with core functions that continue to develop right through to adulthood. For Māori, the head is also the most tapu/sacred part of the body.

Question 1

Is our understanding of the overall health outcomes being achieved for people with paediatric cancers correct? If not, please provide any further information or context.

The overall childhood cancer survival statistics listed in Tables 3, 4 and 5 of the Pharmac discussion paper *Funding of paediatric cancer treatments in New Zealand* reports a 5-year survival rate of 86% across all childhood cancers. However this statistic masks the relatively dire survival rate for CNS tumours which have a 5-year survival of just 73.5% and are responsible for 42% of all cancer deaths in children aged 0-14 years[3].

[1] *Childhood Cancer Incidence in Aotearoa, New Zealand 2015-2019*, National Child Cancer Network
[2] *Childhood cancer survival in Aotearoa, New Zealand 2010-2019*, National Child Cancer Network
[3] *Childhood cancer survival in Aotearoa, New Zealand 2010-2019*, National Child Cancer Network

The 5-year survival rate of 73.5% is averaged across all brain tumour types and misrepresents the real world situation for the aggressive sub-types of paediatric brain and CNS tumours because:

1. The overall survival rate includes benign CNS tumours which have a much better prognosis and longer survival time than malignant CNS tumours;
2. The overall survival rate masks the survival data for aggressive sub-types such as DIPG/DMG (diffuse intrinsic pontine glioma/diffuse midline glioma) which has a 5-year survival of 2% and median overall survival of 8-11 months[4].

Furthermore, survival statistics fail to tell the whole story. They do not accurately describe the harm, suffering and multiple stresses experienced by families dealing with a paediatric cancer diagnosis, especially those with a rare cancer such as brain tumours.

Although they account for 23% of all childhood cancer cases, the highest incidence of any solid tumour, brain tumours are still considered rare with an average of 36 diagnoses per year. The rare nature of paediatric brain tumours often results in delayed or mis-diagnosis, particularly if the patient presents at a smaller medical centre or hospital which may not see many (if any) brain tumour cases in any one year.

This problem is compounded by the fact that children with brain tumours can present with a wide range of symptoms, including: headaches; seizures; personality changes; behavioural problems; hearing and/or vision loss; problems with balance; nausea and vomiting; fatigue; and hemiparesis. Many of these symptoms are common in other diseases or health conditions and it is not uncommon for children to be mis-diagnosed with migraines, epilepsy, ADHD or other conditions.

A brain tumour is typically discovered by imaging, usually CT or MRI scan, and families can be denied immediate access to these diagnostic services due to capacity or resourcing constraints. Capacity constraints can also limit access to allied health services such as physical therapy, speech and language therapy and mental health services.

The lack of psychosocial support systems in the community is a constant area of concern in the childhood brain tumour community, particularly immediately after discharge from hospital. Leaving hospital with a rare condition and returning home to a local community where people have no experience of caring for a child with a brain tumour generates feelings of isolation or not belonging.

The multiple stresses surrounding obtaining a correct diagnosis, access to imaging, and access to allied health services, including psychosocial support and palliative care services, impact the quality of life of the patients and their whānau.

Financial toxicity is a term used to describe financial hardship experienced by families having to self-fund medical treatments. This is not uncommon in families with a childhood cancer diagnosis, as the changing family dynamic often necessitates one or more parent changing their work situation to care for the patient. It is yet another stress for families who are already dealing with a serious medical diagnosis.

[4] *Hoffman, L.M. et al. Clinical, radiological, and histo-genetic characteristics of long-term survivors of diffuse intrinsic pontine glioma: A collaborative report form the International and SIOP-E DIPG Registries. Neuro-Oncology 18, iii65-iii66 (2016)*

Any changes to rule 8.1b which restricts access to new medicines has the real potential to cause significant financial toxicity to families. These multiple stresses are not adequately represented in a mere survival statistic.

Question2
In what other clinical contexts is participation in clinical trials the 'standard of care'?

While New Zealand does not have its own clinical guidelines for brain and CNS tumours, either paediatric or adult, international guidelines such as the United States' National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Pediatric Central Nervous System Cancers lists participation in a clinical trial as the preferred first-line treatment option (the standard of care) in several tumour types.

Similarly, the equivalent guidelines for adult brain and CNS tumours list clinical trial participation as the standard of care in the adjuvant setting (post-surgery) for several tumour types.

Both the paediatric and adult guidelines state: "NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged."[5] [6]

Participation in clinical trials is especially important for those tumour sub-types with exceptionally poor prognosis, such as diffuse midline glioma (DMG), and for recurrent or progressive tumours where the patient has exhausted all other treatment options.

In general, Brain Tumour Support NZ believes that any disease with a poor prognosis and lack of effective treatments would benefit from 'participation in a clinical trial' as part of the standard of care.

Question 3
To what extent is access to paediatric cancer clinical trials dependent on access to medicines through rule 8.1b?

Paediatric cancers are rare. This makes drug development for these cancers difficult because:

1. Biotech and pharmaceutical companies are less incentivised to develop drugs for paediatric cancers as the commercial opportunity is limited;
2. Many trials consist of a combination of different drugs belonging to different pharmaceutical companies. These combination trials are difficult to set up as they require close co-operation between commercial competitors;
3. Clinical trials for paediatric cancers are difficult to recruit due to the small patient population, resulting in high drug development costs and lower profit margins for developers.

For these reasons, many paediatric cancer trials are 'investigator-led' trials, or trials conducted through co-operative trial networks, rather than pharma-sponsored trials. Without the financial support of the pharmaceutical companies that supply the treatments, trial investigators in New Zealand require access to experimental medicines through rule 8.1b.

[5] *Pediatric Central Nervous System Cancers, NCCN Clinical Practice Guidelines in Oncology, Version 1.2023 – July 12, 2022*
[6] *Central Nervous System cancers, NCCN Clinical Practice Guidelines in Oncology, Version 1.2022 – June 2, 2022*

Question 4

How sensitive is this system of care to changes to rule 8.1b?

Any changes to rule 8.1b which result in reduced access to new paediatric cancer medicines will threaten the viability of clinical trials which rely on this rule for access to new medicines.

Outside of clinical trials, restricted access to new medicines will prevent paediatric oncologists from prescribing novel, experimental treatments for a specific indication which:

1. Have shown efficacy in clinical trials but are yet to obtain final regulatory approval;
2. Have been approved by regulatory agencies (such as the United States' FDA or New Zealand's Medsafe) for other indications;
3. Have been approved by regulatory agencies (such as the US FDA, NZ's Medsafe, etc.) for the indication but are not funded by Pharmac.

Early intervention using new medicines is an important component of the system of care of paediatric brain tumour and other cancer patients. Paediatric oncologists can use rule 8.1b to offer new treatments for patients who would otherwise have exhausted all other standard treatment options.

If rule 8.1b was changed so that new medicines were required to go through the regular Pharmac funding process, we believe the current system of care would be adversely affected as access to these medicines would be restricted.

Question 5

To what extent are good health outcomes for children with cancer in New Zealand dependent on making paediatric cancer treatments available through rule 8.1b?

Rule 8.1b plays an important role in the treatment of paediatric cancer patients in Aotearoa New Zealand to the extent that health outcomes for many in this patient population are dependent on access to novel treatments. However health outcomes for children overall would be improved if the rule was extended to other paediatric diseases or conditions, including children with rare disorders.

Health outcomes for children with cancer will continue to be highly dependent on rule 8.1b because many cancer therapies are developed for adults and not specifically for the paediatric population. This is in part due to the difficulties in recruiting paediatric patients for statistically meaningful clinical trials compared with adults. Many new treatments may never be approved for children if regulatory approval is dependent on large-scale, randomised clinical trials, so the only mode of access is through funding pathways such as rule 8.1b.

Question 6

Is timely access to paediatric cancer treatments more important than timely access to other medicines or for other populations? If so, why?

Patient populations which face similar economic characteristics to paediatric cancer, such as children with rare diseases or disorders, are likely to face similar issues and challenges with respect to medicines access.

Many of these diseases carry high risk of morbidity and/or mortality so timely access to effective medicines is crucial to alleviate suffering and extend survival.

The potential gains made by early intervention with medicines for paediatric cancer and other rare childhood disorders are larger than many other patient populations, given the relatively young age of the patients and the expectation that treatment will result in extended survival with good quality of life.

Question 7
Is our understanding of how rule 8.1 operates in practice correct? What else should we know?

Timely access to modern medicines has the potential to improve health outcomes early in the disease trajectory and avoid costly hospital stays and medical interventions, such as surgery, further downstream. Conversely, restricted access to effective medicines has the opposite effect of requiring ongoing costly medical interventions throughout the course of the disease.

The wider economic costs of not treating the disease early include loss of productive work or school hours, resulting in an increase demand for social welfare payments and services. There is also a social cost, which contributes to demand for mental health services, and is characterised by increased levels of stress, anxiety and depression among those affected.

From the perspective of Brain Tumour Support NZ and the brain cancer community that we serve, there is a lack of effective treatments for high-grade (malignant) paediatric brain tumours so it is not so much how rule 8.1b is operating now but how it will affect access to new treatments in the future. There are several experimental treatments for paediatric brain tumours which are now in clinical trials after showing promising signs of efficacy in pre-clinical studies, and it is likely that paediatric oncologists will want the option of accessing these treatments under rule 8.1b.

Any changes to rule 8.1b which restricts access to paediatric cancer medicines by forcing new medicines to go through the regular Pharmac funding process has the potential to seriously impact health outcomes for childhood cancer patients.

In general, the drug development process is not conducive to producing new medicines to treat paediatric brain tumours and other paediatric cancers. The requirement of regulatory authorities or drug funding agencies to require “gold-standard evidence” based on large, randomised clinical trials would be a major hurdle for new paediatric cancer treatments to overcome. Some of the reasons for this include:

1. The clinical trials usually require a control arm where a significant number of patients are randomised to receive either standard of care and/or placebo;
2. To reach statistical significance the trials require large number of participants which is very difficult when it comes to paediatric cancers, due to the small and diverse patient population;
3. Many clinical trials exclude children, therefore the final marketing approval does not include children and doctors are required to prescribe the treatment “off-label”;
4. The economics and logistics of these trials mean they are very costly to run, which is a negative incentive for the drug developers, usually biotech or pharmaceutical companies;

5. The small patient population, high drug development costs and limited patent lifespan combine to produce a high list price when the drug is finally approved;
6. A high list price is a disincentive for centralised drug funding agencies, such as Pharmac, to reimburse the drug.

Given these headwinds, many potentially effective new paediatric cancer medicines may struggle to progress successfully through the drug development process into late stage clinical trials.

If rule 8.1b were to change so that new medicines were required to undergo the normal Pharmac funding pathway, it is likely that access to these medicines will be greatly restricted.

As it stands, we believe that paediatric oncologists are currently being overly conservative in their use of rule 8.1b. Many seem to be requiring a high standard of clinical evidence before they will consider access to a new medicine under the rule, which means families are still having to self-fund new medicines or travel overseas for treatment. Awareness of rule 8.1b among patients and families appears to be low and it is not commonly discussed in consultations with the paediatric oncologist.

Question 8
How much increase in the use of rule 8.1b do you think will happen as a result of the growing range of new paediatric cancer treatments?

Without an increase in the Combined Pharmaceuticals Budget (CPB), resulting in a larger number of medicines funded by Pharmac, the use of rule 8.1b would be expected to rise as paediatric oncologists would have no other way of accessing the treatments their patients need. However the financial costs of funding treatments under rule 8.1b will be greatly offset by lower medical costs, economic costs and social costs.

Question 9
Do you see the costs of paediatric cancer treatments accessed through rule 8.1b increasing significantly in the foreseeable future?

Major advances in the understanding of the biology of paediatric cancers are continuing at pace. The discovery of new therapeutic targets opens the opportunity to develop new medicines and treatments. Often these new medicines will have an expensive list price, due to the high costs of drug development and fixed patent lifespan limiting the commercial opportunity for the developers. However paediatric cancers are rare and the small numbers of patients requiring the medicines will mean that the total impact on the CPB should be limited.

Rather than fear the costs of new treatments, Brain Tumour Support NZ believes that Pharmac should consider the revolutionary health benefits that many of these treatments can provide. A value-based funding approach, rather than a cost-based approach, should be employed to assess these benefits.

Question 10

How could we assess what value paediatric cancer treatments provide against other medicines that could be funded with the same money?

Paediatric cancer treatments are designed to be 'curative' as opposed to 'palliative'. Given the relatively young age of the patient, early intervention with new medicines can avoid a significant number of 'life years lost' due to premature death of the patient (in the absence of treatment). Delays in accessing new medicines can have the converse effect of many years of costly medical interventions in managing the patient's disease.

The effects of paediatric cancer are wide ranging and typically impact not only the child but their immediate family, the wider whānau and community. Brain Tumour Support NZ firmly believes that any assessment of value of a paediatric cancer treatment should weigh up the direct cost of the medicine against the medical, economic and social costs incurred if the medicine is not funded.

Question 11

What should Pharmac take into account when considering equity issues with respect to rule 8.1b of the Pharmaceutical Schedule?

There is inequity in the current drug funding policy surrounding rule 8.1b because medicines for children with diseases or disorders other than cancer are not covered by the rule. Brain Tumour Support NZ believes that the health of all children in Aotearoa should be prioritised and that extension of rule 8.1b to other paediatric diseases and disorders will help achieve this.

Any changes to rule 8.1b which result in reduced access to new medicines have the potential to increase inequities in the health system, as it exacerbates the situation of 'haves and have-nots' in regard to affordability of medicines. Families who are not in a position to self-fund their treatment, which may include Māori, Pacifica or groups with lower socio-economic status, will be disadvantaged. The current rule 8.1b eliminates this inequity for paediatric cancer patients.

The paramount objective to take into account is to achieve the best health outcomes for *all* New Zealand children facing serious illness. Therefore the key priority should be to expand rule 8.1b to lift all groups currently facing inequities in medicines access to the level of paediatric cancer patients enjoy under this rule.

Question 12

Do you consider rule 8.1b to be inequitable from the perspective of other children or those with rare disorders? Why?

Children with rare disorders are currently at a disadvantage to paediatric cancer patients in terms of access to new medicines because rule 8.1b only applies to paediatric cancer medicines. Brain Tumour Support NZ would like to see this inequity removed by expanding the provisions of rule 8.1b to include diseases/disorders other than cancer.

Question 13

To what extent do the current policy settings, including rule 8.1b, contribute to the health outcomes achieved for tamariki Māori and Pacific children with cancer?

The current policy, including rule 8.1b, removes a vital layer of inequity in that the financial barrier of access to many medicines is removed. Without rule 8.1b, access to some expensive medicines would be restricted to those that can afford them. Families in the lower socio-economic sector, which include Māori and Pacifica families, will face a major barrier to access.

Question 14

Do you consider rule 8.1b to be inequitable from the perspective of adolescent and young adults with cancer? Why?

Yes, adolescent and young adults (AYA) with cancer face many of the same challenges and issues as children with cancer, including the rare nature of their disease and the lack of effective treatments. We believe that AYA cancer patients deserve early access to modern medicines in the same way that paediatric cancer patients do.

Question 15

How might we address equity and fairness concerns related to paediatric cancer medicines through rule 8.1b and access to medicines for other groups?

Children and adolescents are one of the most vulnerable groups in our society and Brain Tumour Support NZ firmly believes that the health of all children should be prioritised, not just for humanistic but economic reasons. Paediatric cancers are life-limiting diseases and it makes economic sense to invest in medicines at an early stage so that:

1. Potential years of life lost due to premature death of the patient are minimised;
2. The patient's quality of life is improved and maintained;
3. A lifetime of costly medical interventions and hospital visits is avoided;
4. Mental and social well-being of the patient and their whānau is restored;
5. Wider social and economic costs of ill health are eliminated.

Many other rare paediatric diseases or disorders either life-limiting or cause serious morbidity leading to poor quality of life. The effects of these diseases/disorders on the patient and whānau are similar to those of paediatric cancers.

Question 16

Is there anything else we need to know to inform the review? If so, please add your information or thoughts here.

When cancer strikes someone so young, the potential number of years of life lost is much higher than in adults, when cancer typically strikes at a more advanced age. We now know that many types of paediatric brain tumours differ from adult brain tumours at the molecular level, meaning tumours with similar

histology have different molecular profiles. Often the paediatric tumours have a better prognosis if the correct targeted treatments can be employed.

Early access to modern, targeted medicines has the potential to extend overall survival and preserve high quality of life for many paediatric brain tumour patients over the course of their lifetime. The cost of funding this early access can be offset against the cost of non-pharmaceutical medical interventions, and the associated economic and social costs, incurred throughout the disease trajectory by both the patient and their wider whānau.

The economic and humanistic argument which supports the principles behind rule 8.1b can be equally applied to other childhood diseases. Therefore Brain Tumour Support NZ supports the expansion of rule 8.1b to include all children with serious illnesses, including those with rare disorders.

Brain Tumour Support NZ
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