PHARMAC

Pharmaceutical Management Agency

BRIEFING

PHARMAC's progress on funding medicines for rare disorders

Date: **26 November 2018 (updated 17 December 2018)**

To: **Hon Dr David Clark (Minister of Health)**

Copies to: Manager Governance and Crown Entities
PHARMAC Board
Director General of Health
Lead DHB Chief Executive, Pharmaceuticals

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Purpose

In PHARMAC's 2018/19 Letter of Expectations, the Minister of Health requested PHARMAC report back in November 2018, on our work to ensure fair consideration of funding medicines for people with rare disorders. This briefing provides an update on the work we have continued to progress following the completion of our rare disorders medicines pilot in 2016.

Executive Summary

- People living with rare disorders in New Zealand face a myriad of challenges in accessing suitable health care, including access to effective pharmaceutical treatment. Medicines for rare disorders are often very highly priced despite relatively poor efficacy, and high launch prices are a matter of global debate. Jurisdictions around the world are grappling with similar challenges to New Zealand, as indicated by significant shifts in policy settings internationally.

- To tackle this global issue and improve access to effective treatments for rare disorders PHARMAC commenced a contestable funding pilot in 2014 to see if we could introduce competitive tension between products that wouldn't usually compete with one another. An external evaluation of the pilot drew favourable conclusions.

- Following on from this, over the past 12 months PHARMAC has initiated a comprehensive work programme to improve our processes and develop our knowledge base for rare disorders medicines. This has included introducing new policy settings for funding applications for medicines for rare disorders, establishing a Rare Disorders Subcommittee, and preparing a report for external publication about our work over the past few years relating to funding medicines for rare disorders.

- PHARMAC's commercial activity has included a call for funding applications for medicines for rare disorders which elicited 13 applications for 10 different medicines. These were considered by our Rare Disorders Subcommittee in early November 2018.

- PHARMAC has also continued to fund medicines for rare disorders through our usual processes, including the Pharmaceutical Schedule listing process and via the Exceptional Circumstances framework.

- PHARMAC continues to engage closely with key stakeholders including consumer groups, treating clinicians, patients and their carers. Our relationships with these groups have become stronger through the dedicated work we've undertaken over the past few years. We recognise, however, that it is likely some groups may be dissatisfied with the final outcome of the recent call for applications if their specific desired medicine is not funded.

Background

PHARMAC recognises the challenges that exist for people living with rare disorders in New Zealand. We know that there are many barriers in the health system as a result of the small number of people with rare disorders, and that these are exacerbated by the population size of New Zealand and our geographical isolation. People with rare disorders face difficulties with diagnosis, accessing specialist care, and navigating the health system and support services. Access to effective pharmaceutical treatments to treat their underlying disease is one element of the broader challenges facing people living with rare disorders.

Medicines for rare disorders are often very highly priced despite relatively poor efficacy, with high launch prices that have become a matter of global debate. Because there is no competition for branded products that are on patent or for which there are no alternative medicines available, suppliers can command premium prices. This has been exacerbated by changes to policy settings in the United States where the FDA has lowered the bar for entry into this market and provided significant incentives, encouraging more suppliers to enter into the market and drive up the market price of new and existing medicines for rare disorders.

Public funders come under pressure to pay the high price or, occasionally, exercise the option to decline to fund any access. Due to the premium prices that can be obtained from selling products with market exclusivity, research expenditure on medicines for rare disorders has increased relative to medicines for common conditions. The size of the New Zealand market can be an added barrier for pharmaceutical suppliers, given the cost of registration with Medsafe, and the potentially very small patient population.

Another challenge for medicines for rare disorders is the small number of patients make it difficult to conduct clinical trials that will attain high levels of clinical evidence. Evidence is often limited to observational studies, and real-world data and clinical benefits of treatment can be difficult to determine or quantify.

Jurisdictions around the world are grappling with similar challenges as New Zealand, as demonstrated by significant shifts in policy settings around the world over the past 12 months. Countries such as Australia and Scotland are adapting the same definition of 'rare' as New Zealand (see below), and Australia is looking to implement similar features to PHARMAC to manage expenditure on medicines for rare disorders.

In recent years, PHARMAC has sought to test how we can influence the pharmaceutical market to make clinically effective medicines for rare disorders more affordable for the public health system. The pilot Request for Proposals (RFP) process that commenced in 2014 demonstrated that competition can be introduced into this market, and the outcome of this process was 10 new rare disorders medicines being approved for listing on the Pharmaceutical Schedule. An external evaluation of the pilot, and our own assessment of learnings, has led us to introduce a set of permanent policy settings for rare disorders medicines, as part of a package of work focused on rare disorders medicines over the past 9-12 months.

This briefing summarises our progress in three areas: policy, commercial activity, and stakeholder engagement.

Policy activity

Permanent policy settings introduced

PHARMAC has introduced new permanent policy settings which apply to funding applications for medicines for rare disorders. These are represented by three principles, outlined in the table on the following page. When a treatment meets all three principles, this enables a different entry into our usual Pharmaceutical Schedule funding process.

Unlike our normal process, suppliers are not required to have gained Medsafe approval for the medicine before it can be considered for funding. Medsafe approval can cost suppliers a significant amount of money and time. For suppliers of medicines for rare disorders this is often not considered to be commercially viable, particularly where there is only a very small potential patient population (therefore low total usage/revenue) and uncertainty of public funding. This separate entry into the Pharmaceutical Schedule funding process therefore helps reduce the current market challenges for these medicines in New Zealand.

These principles apply at any time for medicines for rare disorders, and do not require PHARMAC to make a call for funding applications or run a specific competitive funding process. This gives suppliers of these pharmaceuticals the flexibility to submit an application at any time and enables PHARMAC to consider which process would be best to elicit the best health outcomes from within our current budget.

Additionally, PHARMAC's processes allow for clinicians and patient groups to submit funding applications, and also the ability to generate applications ourselves where we consider evidence or information to be sufficient for an application to be produced.

Principle	**Explanation**
1. The medicine has been approved by Medsafe, or an approved international regulatory authority, for the identified indication.	PHARMAC generally requires Medsafe approval before a medicine is considered for funding on the Pharmaceutical Schedule. Recognising this can be a significant barrier for suppliers of pharmaceuticals for very small population groups in New Zealand, this principle loosens our standard requirement so PHARMAC will consider funding applications for medicines that have approval granted by an approved international regulatory authority. Medsafe approval is still required prior to listing on the Pharmaceutical Schedule.
2. The disorder is a clinically defined disorder affecting an identifiable and measurable patient population with a prevalence of less than 1:50,000 in New Zealand.	This principle defines the patient population who may be living with the rare disorder in New Zealand. This definition equates to approximately 90 people in the New Zealand population. We have retained this definition from the 2014 pilot, which was consulted on during the development of that process. This definition of rare aligns with Australia, and also England and Scotland's definition of 'ultra-rare.'
3. The medicine is only registered for the treatment of the rare disorder, or if it is registered for other disorders (or is part of phase three clinical trials for other disorders), the cumulative prevalence across all indications still meets principle 2.	This principle defines the treatment as 'rare', and therefore ensures that only those suppliers of treatments that are disadvantaged as a result of their very small patient population, are given consideration through this alternative entry. Where the treatment may be appropriate for multiple indications, is it likely the patient population potentially benefiting from the treatment will not meet principle 2. In these circumstances, the standard entry into the Pharmaceutical Schedule is more appropriate.

If the above principles have been met, PHARMAC will assess funding applications as per our standard pharmaceutical funding process, which includes assessment against the Factors for Consideration (FFC), and comparative ranking against all other possible funding options. The FFC is PHARMAC's decision-making framework that sets out the broad range of considerations PHARMAC will take into account when making a funding decision. The sixteen factors that make up the framework are not weighted or applied rigidly, and not every factor is relevant for every funding decision.

In the context of rare disorders, we know that some FFC are particularly relevant including:

- Health need of the person – rare disorders can often be debilitating and severe, and so individuals with a rare disorder are often considered to have a high health need.
- The availability and suitability of existing medicines, medical devices and treatments – people with rare disorders often have limited alternative treatment options available.
- Health need of others – caring for a person with a rare disorder can have impacts on the health of those with this responsibility.

PTAC Rare Disorders Subcommittee established

PHARMAC has established a Rare Disorders Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC). We sought membership applications through colleges and clinical networks (both New Zealand and Australian based), from people with a special interest in managing patients with rare disorders.

The nine appointed members include some of New Zealand's leading experts in treating rare disorders, from specialties such as paediatric nephrology, metabolic disorders, blood disorders and neurology. One member is an Australian specialist in genetics and metabolic disorders who has been involved in Australia's Life Saving Drugs Programme (LSDP). The Subcommittee also includes two PTAC members (one of whom is the Chair of the Subcommittee), to maintain links between this new Subcommittee and our primary clinical advisory committee. Appendix 1 includes a list of members and their specialities.

The first Subcommittee meeting was held in early November 2018 over two days to ensure that the 13 applications received could all be comprehensively reviewed and discussed. The process that was followed to encourage applications, and more detail of the applications that were considered is explained in more detail in the 'commercial activity' section below.

Subcommittee members were required to review the applications received and make recommendations to PHARMAC about whether the treatments should be funded or not, based on the Factors for Consideration and their clinical appraisal of the information provided. Members were provided with the funding application and briefing papers from PHARMAC staff which included background, context, further clinical evidence and relevant international recommendations. Members were also provided with collated submissions from patients, their families, treating clinicians and consumer groups. All of this information was factored into their recommendation. The range of expertise around the table, including members with international experience in other jurisdictions, added significant value to the assessment process.

Minutes of the Subcommittee's discussion (including its recommendations) will be published on our website and Application Tracker. We expect the minutes to be available in early 2019. PHARMAC may decide it also needs advice from PTAC on some applications. Following clinical advice and completion of our assessment processes, PHARMAC will then determine the next appropriate steps for each application, such as commercial processes, in the light of other priorities for funding.

This process and associated timeframes for next steps, including publication of the minutes in early 2019, have been clearly communicated to stakeholders, as well as on the PHARMAC website.

Publication on funding medicines for rare disorders

Globally many health systems are grappling with the issue of funding medicines for rare disorders. PHARMAC has had a series of enquiries from other jurisdictions about our work and we are increasingly being seen as taking a leading and innovative approach. This was evident in a recent meeting with international funders in Canberra attended by the PHARMAC Chief Executive where funding of rare disorders medicines was a key topic, and there was significant interest in a presentation on the PHARMAC model and our new approach to funding medicines for rare disorders

In response to this interest, PHARMAC is currently developing a report for publication about how PHARMAC has approached the challenges many countries are facing in respect of funding medicines for rare disorders. We intend to share the learnings from our pilot and the subsequent permanent policy changes we have made. The report will focus on the process we followed and what we found, and will be targeted at a policy audience, although we expect there to be wide interest.

The draft report will be shared with you prior to publication, which we expect in early 2019.

Commercial activity

Over the past few years PHARMAC has undertaken commercial activity relating to funding medicines for rare disorders through three separate mechanisms:

- The standard Pharmaceutical Schedule listing process where treatments are comparatively ranked against all other possible funding options.
- The Exceptional Circumstances framework, including the Named Patient Pharmaceutical Assessment (NPPA) process, for making decisions about funding treatments for individuals with exceptional clinical circumstances that are not listed on the Pharmaceutical Schedule.
- The rare disorders contestable funding pilot where PHARMAC ran a competitive process in 2014/15 specifically for treatments for rare disorders.

The largest proportion of the gross annual spend for medicines used to manage rare disorders is through the Pharmaceutical Schedule and Exceptional Circumstances Framework (Table 1). These mechanisms also have the greatest number of individuals receiving funding and most medicines funded. The number of patients and gross spend through the rare disorders pilot has increased over the past three financial years. These figures indicate that all three mechanisms have contributed to meeting some of the diverse health needs of patients with rare disorders in New Zealand.

Table 1 represents the approximate expenditure, number of medicines funded and number of patients accessing medicines for rare disorders over the past three financial years using PHARMAC's definition of 'rare' (population of less than 1: 50,000 in New Zealand). A discussion of the limitations of these data can be found in Appendix 2.

Table 1: Medicines for rare disorders funded through PHARMAC's three funding mechanisms.

	Mechanism	Gross spend	Patients	Medicines
2015/ 2016	Pharmaceutical Schedule	$2,648,269	138	17
	Exceptional Circumstances Framework	$1,678,968	125	69
	Rare Disorders Pilot	$184,979	15	10
	TOTAL	**$4,512,216**	**278**	**96**
2016/ 2017	Pharmaceutical Schedule	$2,974,172	149	17
	Exceptional Circumstances Framework	$2,258,167	156	78
	Rare Disorders Pilot	$1,029,017	35	10
	TOTAL	**$6,261,356**	**340**	**105**
2017/ 2018	Pharmaceutical Schedule	$3,013,567	150	16
	Exceptional Circumstances Framework	$2,090,573	160	76
	Rare Disorders Pilot	$1,694,107	38	10
	TOTAL	**$6,798,247**	**348**	**102**

In addition to the medicines for rare disorders that are funded via the three mechanisms above, many people with rare disorders access a range of other funded medicines to manage the symptoms of their illness – for example: pain relief, immunosuppressants, alimentary treatments, muscular or seizure related treatments. PHARMAC is not able to quantify the approximate expenditure on such treatments for specific patient groups.

PHARMAC's standard application processes

Recent commercial transactions that have been completed through PHARMAC's standard Pharmaceutical Schedule process include:

- Taliglucerase for Gaucher Disease: In August 2018, PHARMAC widened access and changed the funded enzyme replacement therapy for Gaucher Disease, a rare inherited enzyme deficiency disorder. PHARMAC is working with clinicians to help approximately 20 patients transition to the new treatment. As a result of this transaction, patients with Gaucher Disease may be able to access higher doses of enzyme replacement therapy.
- Sapropterin for phenylketonuria (PKU): In September 2018, PHARMAC announced the decision to fund sapropterin for women with PKU who are pregnant or actively trying to get pregnant from 1 November 2018. PKU is a rare metabolic condition affecting approximately 160 people in New Zealand. Uncontrolled PKU in pregnancy can cause serious harm to the unborn child. We estimate that six women each year may be eligible for treatment with sapropterin following this decision. Though this treatment does not meet PHARMAC's definition of 'rare', PKU is considered a rare disease in some other jurisdictions. Sapropterin has also subsequently been considered for the wider population with PKU by PTAC and recommended for funding with low priority.

Dedicated rare disorders process: Call for supplier applications

In June 2018, PHARMAC called for supplier funding applications for medicines for rare disorders. By the 3 September 2018 deadline we had received 13 applications, from 8 different suppliers, for 10 different medicines for rare disorders. The list of applications received and their indications, are attached as Appendix 3. Multiple applications for two medicines were received from different suppliers and these were considered together. One medicine had two different indications that were considered. Six of the 13 applications received were for medicines that are not Medsafe approved, two had already been submitted to Medsafe and are under evaluation, and five are Medsafe approved. All 10 medicines were considered by the Rare Disorders Subcommittee of PTAC in November 2018.

Prior to and during the call for applications, PHARMAC undertook pre-engagement with suppliers in Australia and New Zealand. We found this approach helpful in the 2014 pilot process and it has been particularly successful with suppliers that are not based in New Zealand, or where rare disorders products are managed through the Australian business unit. Feedback from suppliers involved in this pre-engagement has been very positive. Suppliers have been particularly supportive of the removal of the requirement for Medsafe approval (principle 1) prior to PHARMAC consideration given this was seen as a significant barrier to entering the New Zealand market. We continue to develop good working relationships with suppliers that are new to New Zealand and to PHARMAC processes.

Horizon scanning of new medicines

PHARMAC is continuously undertaking horizon scans for new rare disorders medicines. As we become aware of new information, we may approach suppliers or even initiate funding applications if opportunities present. Our clinical advisors also stay abreast of clinical advancements in their therapeutic areas, and discussions on future funding opportunities take place regularly at PTAC and Subcommittee meetings. The establishment of the Rare Disorders Subcommittee provides further opportunity for horizon scanning for rare disorders medicines and this will be incorporated into future meetings with this group. We continue to regularly discuss the development pipeline for rare disorders medicines with suppliers.

Through our relationships with suppliers and our clinical advice network we're comfortable that we are aware of the current rare disorders medicines on the market in New Zealand and internationally. We know that there are many treatments in clinical trials potentially entering the market in the near future. With our confirmed policy settings, and flexible approach to running commercial processes as we see fit, the PHARMAC model can adapt to the pharmaceutical market accordingly.

Stakeholder engagement

Regular stakeholder engagement

Some of the applications for treatments received through the call for applications process, are for treatments that have very active consumer groups. We've endeavoured to keep consumer groups well informed about the process we will follow. It is likely that some groups will be dissatisfied with the final outcome.

PHARMAC has developed good relationships with patient advocacy groups and clinicians for people with rare disorders. These relationships have been enhanced through the pilot process and our subsequent ongoing work, and PHARMAC staff regularly make contact with these important stakeholder groups. Members of PHARMAC's Senior Leadership Team continue to meet quarterly with the New Zealand Organisation for Rare Disorders (NZORD) and our staff engage regularly with treating clinicians who manage patients with rare disorders.

Additionally, PHARMAC has been invited to present at conferences on our rare disorders work and this has helped continue to build our broader networks. We also continue to work with and provide advice to the Ministry of Health.

Consumer voice engagement

During 2018 PHARMAC initiated a review of how consumers' voices are incorporated into PHARMAC's processes. People with rare disorders, and advocacy groups, were well represented at community events, and through written submissions.

The outcome of this review will be some changes to our current processes to make it easier for consumers to be informed and engaged in our decision-making processes. This will include considering ways consumers can provide input earlier. PHARMAC will also be undertaking work to better understand who our consumers are, including those consumers who PHARMAC is not currently reaching. Finally, PHARMAC will be reviewing the role and function of our Consumer Advisory Committee, to ensure all our current mechanisms for consumer input into our work remain fit for purpose.

PHARMAC is committed to continuing our work to progress funding medicines for rare disorders. Our work programme (Appendix 4) provides an overview of our recent and upcoming progress, and we will continue to update you on progress.

Sarah Fitt
PHARMAC Chief Executive

Appendix 1: Rare Disorders Subcommittee members

Prof Tim Stokes, (Chair, PTAC member) Professor of General Practice, University of Otago.

Melissa Copland, (PTAC member) PhD, Pharmacist, Queenstown.

Dr Howard Wilson, General Practitioner, Akaroa.

Dr William Wong, Paediatric Nephrologist, Auckland DHB.

Dr Callum Wilson, Metabolic Physician, Auckland DHB.

Dr Dylan Mordaunt, Clinical Geneticist, Auckland DHB.

Dr Janice Fletcher, Clinical Director – Genetics and Molecular Pathology, SA Pathology, Adelaide.

Dr Humphrey Pullon, Haematologist, Waikato DHB.

Prof Carlo Marra, Dean of the School of Pharmacy, University of Otago, Dunedin.

Dr James Cleland, Neurologist and Neurophysiologist, Bay of Plenty DHB.

Appendix 2: Limitations of analysis for figures shown in Table 1

Analysis such as that provided in Table 1 always has limitations. The intent of the table is to provide as accurate a picture as possible of the mechanisms through which PHARMAC funds medicines for rare disorders. Given the data available these figures are an underrepresentation of the actual medicines PHARMAC funds for rare disorders. Below is further explanation of the limitations:

- The Pharmaceutical Schedule and Exceptional Circumstances Framework figures use PHARMAC's definition of 'rare' (prevalence less than 1:50,000). Disorders that may be widely held as 'rare' but do not meet this threshold have been excluded from these figures e.g. phenylketonuria has been excluded.

- The figures presented are different to that which was provided in May 2018. Data has been updated to reflect our definition of rare. The Pharmaceutical Schedule and Exceptional Circumstances Framework mechanism figures do not include medicines for rare cancers and infections. The Rare Disorders Pilot includes one medicine used for the treatment of highly resistant tuberculosis (bedaquiline). The pilot data reflects the medicines approved for funding through the pilot and now listed on the Schedule, or via the Exceptional Circumstances Framework pending Medsafe approval.

- The Pharmaceutical Schedule and Exceptional Circumstances Framework analysis is limited to those medicines where a distinct rare disorder could be identified. This was derived from the accompanying clinical information for patients applying under the Exceptional Circumstances Framework or by using the medical indications specified in Special Authority criteria in the Pharmaceutical Schedule. The analysis excludes expenditure on some medicines used to manage rare disorders where the indication data is not available (i.e. open listed) or is not available at a sufficiently detailed level. In cases where treatments are open listed, they may be used for a variety of purposes.

- The analysis excludes hospital purchases expenditure of medicines under either the normal Pharmaceutical Schedule (Hospital Medicines List) or the Exceptional Circumstances Framework mechanism, due to the limitations of the datasets from the hospital setting. Many of the medicines approved for hospital use under these mechanisms are high cost medicines (e.g. biologic medicines used for rare autoimmune diseases such as rituximab).

Appendix 3: Applications received following 2018 call for funding applications

Application	Indication	Supplier
Agalsidase alfa (Replagal)	Fabry disease	Shire
Alglucosidase alfa (Myozyme)	Late-onset Pompe disease	Sanofi-Genzyme
Carglumic Acid	Hyperammonaemia due to urea cycle disorders	Max Health
		Te Arai BioFarma
Elosulfase (Vimizim)	Mucopolysaccharidosis (MPS) type IVA	BioMarin
Ivacaftor (Kalydeco)	Cystic fibrosis - with G551D mutation	Vertex
Migalastat (Galafold)	Fabry disease	Amicus
Miglustat	Gaucher disease	Te Arai BioFarma
Miglustat	Niemann Pick Type C	Te Arai BioFarma
Nitisinone	Tyrosinaemia type 1	Max Health
		Te Arai BioFarma
Nusinersen (Spinraza)	Spinal muscular atrophy	Biogen
Teduglutide (Revestive)	Short bowel syndrome intestinal failure	Shire

Appendix 4: PHARMAC's work in funding medicines for rare disorders July 2018 – February 2019