From: Withheld under section 9(2)(a)
Sent: Wednesday, 13 October 2010 8:55 am
To: Michael_Hampl@moh.govt.nz
Cc: Withheld under section 9(2)(a); Bryce Wigodsky; Ministerials
Subject: Incoming briefing/speech note request Funding for Enzyme Replacement Therapies - Briefing request BR10-026, DUE 3 November
Attachments: Discussion paper on NZ funding arrangement - draft 4 October.doc; 10-026 Advice on the proposal from Genzyme Australasia for funding of treatment for patients with Lysosomal Storage Disorders.doc

Hi Michael

Below is an incoming briefing/speech note request Funding for Enzyme Replacement Therapies - Briefing request BR10-026, **DUE 3 November**

Could you please let me know who in your team will be responding to this

many thanks
Christina

	Dt Due	Ref Number	Section	Subject	AssignedTo	Status	DB Number	Due Dt Extension
Link	03/11/2010	201010/13 (BR10-026)	Strategy and System Performance Directorate, Policy Unit	**Advice on the proposal from Genzyme Australasia for funding Enzyme Replacement Therapies for people with Lysosomal Storage Disorders**	Michael Hampl	With Analyst	H201004042	

Christina O'Connell
Support Officer
Hours Mon-Thurs 6.30am to 2.00pm
Friday 6.30am to 12.00pm
Ministerials 1
Government Relations
Corporate Services Directorate
Ministry of Health
DDI: Withhe

http://www.moh.govt.nz
Withheld under section 9(2)(a)

----- Forwarded by Christina O'Connell/MOH on 13/10/2010 08:19 -----

"Jennifer Langton (MIN)" <Withheld under section 9(2)>

12/10/2010 14:47

To "Briefings@moh.govt.nz" <Briefings@moh.govt.nz>
cc
Subject FW: Funding for Enzyme Replacement Therapies - Briefing request 10-026

Hello

Please see attached briefing request and proposal from Genzyme Australasia.

Many thanks
Jenny

Jenny Langton
Private Secretary - Health

From: P Dunne (MIN)
Sent: Wednesday, 6 October 2010 1:59 pm
To: Jennifer Langton (MIN)
Subject: FW: Funding for Enzyme Replacement Therapies

FYI - please refer to Health for comment

Hon Peter Dunne
MP for Ohariu /Leader of United**Future**
Minister of Revenue/Associate Minister of Health
Visit our website at www.unitedfuture.org.nz
UnitedFuture

From: Withheld [Withheld under section 9(2)(a)]
Sent: Tuesday, 5 October 2010 5:43 pm
To: P Dunne (MIN)
Cc: Jennifer Langton (MIN); Withheld under section 9(2)(a)
Subject: Funding for Enzyme Replacement Therapies

Dear Minister

Thank you once again for the opportunity to discuss access to highly specialised medicines and how Genzyme can contribute to the development of innovative policy solutions. Following on from our discussions with you on 31 August, please find attached a discussion draft of a funding proposal that could allow for expanded access to enzyme replacement therapies in New Zealand. We would welcome the opportunity to discuss these concepts with you in more detail once the NZ Government has had a chance to consider our draft. Please do not hesitate to contact us with any questions or regarding a follow-up meeting.

Kind regards

With

genzyme
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genzyme

Proposal for an innovative funding agreement for treating patients with Lysosomal Storage Disorders

Prepared for the New Zealand Ministry of Health by Genzyme Australasia Pty. Ltd

October 2010

Confidential – Not for distribution

genzyme

Executive Summary

Genzyme Australasia welcomes the New Zealand Government's commitment to addressing the issue of access to high cost, highly specialised medicines. As a world leader in the provision of therapies for ultra-orphan genetic conditions, Genzyme is well aware of the barriers that patients with these diseases face. With our global experience in developing sustainable partnerships and solutions to meeting access challenges, we welcome the opportunity to have a meaningful discussion with the Government about options for New Zealanders suffering from these life threatening conditions.

As we have discussed in our meeting with Minister Dunne on 31 August 2010 and in our submissions to the High Cost Drugs Review, these challenges are significant for treatments for lysosomal storage disorders (LSDs), extremely rare genetic conditions with patient populations over 1000 times smaller than the average pharmaceutical product. The small patient populations for these Enzyme Replacement Therapies (ERTs) mean that the cost of development and production is recouped from relatively few people, leading to high cost therapies. Neither the current Pharmaceutical Schedule nor Exceptional Circumstances schemes provide a solution to funding these life-long, life-saving therapies. Clearly an alternative solution is needed.

Genzyme Australasia believes that it is in a position to deliver such a solution, through a "pan-ERT" agreement that would deliver savings and budgetary certainty to the government across ERTs for 5 LSDs:

- Gaucher disease,
- Fabry disease,
- Mucopolysacharidosis Type I disease
- Mucopolysacharidosis Type II disease
- Pompe disease.

Key components of any such arrangement would be:

- A focus on obtaining the best clinical outcomes for patients
- Coverage of all ERTs supplied by Genzyme
- A partnership in service provision and treatment
- Predictable annual funding over 5-6 years

This draft proposal describes these program elements and shows how benefits to such an arrangement would accrue to the Government, patients, clinicians and Genzyme. It does not constitute an offer to the NZ Government and is confidential, but will allow for future discussions on specific elements.

We look forward to further constructive discussions about the shape of an agreement that will satisfy all stakeholders.

Background

The New Zealand Government has committed through the Review of Access to High Cost, Highly Specialised Medicines to addressing the issue of access to high cost, highly specialised medicines. Genzyme Australasia welcomes this recognition that New Zealanders currently face barriers to access for these medicines and in many cases do not have the same opportunity to receive treatment as those in comparable countries.

This is particularly apparent in the case of patients with extremely rare ultra-orphan disorders, such as Lyososmal Storage Disorders (LSDs), affecting only a few hundred or a few thousand people worldwide. The Enzyme Replacement Therapies (ERTs) developed by Genzyme for LSDs treat patient populations 200 times smaller than a typical orphan drug; 1,000 times smaller than an average pharmaceutical product; and 10,000 times smaller than the largest pharmaceutical product. Importantly, these treatments are life-saving and can provide a normal quality of life for people who have few treatment options and would otherwise experience great suffering and be a large burden on the health and welfare system.

The small patient populations for ERTs mean that the cost of development and production is recouped from relatively few people, leading to high cost therapies. The nature of these therapies means that their value to patients is not captured by cost effectiveness assessment. The Pharmac review of ERT conducted in 2009 concluded that they could not be recommended for listing on the Pharmaceutical Schedule. As a consequence, patients in New Zealand rely on funding under Community Exceptional Circumstances (CEC), which is not well-suited to treating life-long conditions.

In New Zealand, we are aware of approximately 40-45 people with conditions that are potentially treatable with our ERTs. Of these, 19 Gaucher patients are approved for treatment with Cerezyme® (imiglucerase-rch), which is available on the Pharmaceutical Schedule albeit at a much lower dose than elsewhere in the world. The remainder with other LSDs have few if any treatment options. Given the benefit that patients derive from these therapies and the inequity of current arrangements, a new way forward is needed.

Genzyme Australasia is pleased that the New Zealand Government is continuing to explore options for how patients with rare ultra-orphan conditions can receive access to life-saving medicines. At our meeting on 31 August 2010 with Minister Dunne, we discussed the need for solutions that can deliver "win-win" outcomes for patients, the government and for sponsors.

Genzyme Australasia believes that it is in a position to deliver such a solution, through a "pan-ERT" agreement that would deliver savings and budgetary certainty to the government across 5 ERTs. The therapies included would be:

- Gaucher disease,
- Fabry disease,
- Mucopolysacharidosis Type I disease
- Mucopolysacharidosis Type II disease

- Pompe disease

Partnership elements

As we noted in our submission to the High Cost Drugs Review, Genzyme has worked constructively in many countries around the world to develop partnerships that provide sustainability and the best outcomes for patients. Genzyme Australasia has considered the various funding arrangements it has been involved in worldwide and determined the key components that would facilitate the best outcome. These are discussed below.

Coverage of all ERTs supplied by Genzyme

A "pan-ERT", multi-product agreement provides an opportunity to deliver savings across the portfolio that cannot be achieved on drug-by-drug negotiations. This is achieved by creating economies of scale and using a funding mechanism that reflects overall value. It also ensures that patients are treated with equity irrespective of which disease they have.

A focus on optimal outcomes for patients

A comprehensive solution with fixed costs removes disincentives on both sides to focus on anything other than the optimal treatment of patients. For example, clinicians would have the ability to "treat to goal", which could involve increased doses (at no additional cost) for severe patients or reduced doses (and shorter infusion times) for patients with well-controlled disease. This would allow clinicians to identify which patients could experience additional benefit from a higher dose.

Experience in other countries shows that Genzyme's global disease registries can provide treaters with the ability to track patient progress and optimise treatment. This already occurs in Australia, where the Gaucher and Fabry treatment committees use the disease registries to track over With patients and individualise the treatment regimes to drive maximal patient outcomes.

Genzyme Australasia supports treatment decisions being made by expert clinicians, who are supported by registry data and have access to emerging global evidence and appropriate professional development. We would be pleased to include in the agreement support for monitoring of patients and development of local clinical expertise to allow New Zealand to become a "centre of excellence" in treating rare diseases.

Predictable annual funding over 5-6 years

A reasonable term for such an agreement would be 5-6 years. This is long enough to provide predictability and certainty, but recognises that the market for LSDs is likely to change over time, with the emergence of new treatments such as oral therapies.

To provide maximum certainty and financial viability, an agreement could be structured to involve fixed annual payments. These would be calculated based on the expected

number of patients receiving treatment, with any unexpected increase in eligible patients treated at the cost of Genzyme. These fixed annual payments could be structured to increase at a slower rate than patient numbers, thus providing increasing discounts to the government over the term of the agreement.

Alternatively, a fixed "per patient" cost could be negotiated, with payments based on total treated patient numbers. This would be less predictable and would provide less opportunity for discounting over time, but would ensure that payments match growth in patient numbers more closely.

A partnership in service provision and treatment

In addition to supporting the development of an evidence-based and outcomes-driven treatment system, Genzyme Australasia is also committed to improving the efficiency and appropriateness of patient care. As part of a comprehensive agreement, we would be willing to look at additional services such as delivery of treatment and tracking of biomarkers that would be of benefit to clinicians and patients.

Benefits to stakeholders

Genzyme Australasia believes that a comprehensive funding solution for ERTs in New Zealand would have benefits for all stakeholders.

- New Zealand Government
  - Opportunity to deliver improved access to specialised medicines for 5 diseases
  - A focus on obtaining the best clinical outcomes for patients
  - Removes need to make funding decisions on an ad hoc basis under CEC
  - Predictability of funding with potential to manage risk
  - Substantial savings on total treatment costs
  - Delivering on the election promise to increase access to high cost medicines
- Patients with LSDs
  - Access to life-saving therapies across 5 disease states
  - Optimised treatment including appropriate dosing and improved care
- Treaters
  - Professional development
  - Freedom to treat optimally
  - Support from global registries and colleagues
- Genzyme
  - Sustainable business in New Zealand
  - Certainty over reasonable time period

Program funding

The funding needed for such a partnership is related to the expected number of patients. There are currently 40-45 LSD patients known to Genzyme Australasia. Given the variability of disease, an expert treatment committee is likely to deem that not all patients are appropriate for treatment. While the final number would depend of this clinical judgement, an internal Genzyme Australasia review of known patients against treatment guidelines used in Australia anticipated that around 35 would be appropriate for treatment:

- 20 Gaucher patients (including 19 currently approved for Cerezyme);
- 8 Fabry patients;
- 2 MPS I patients (including 1 currently on compassionate treatment);
- 1 MPS II patient (co-funded by CEC and Genzyme at present); and
- 4 Pompe patients.

International literature on prevalence suggests there may be slightly over 100 symptomatic patients in NZ, but not all will be suitable for treatment. Genzyme has undertaken a number of forecasts of likely uptake of treatment. Given the maturity of Gaucher treatments, patient numbers are expected to approach the total prevalence (potentially around 25 patients), while the other diseases will approach 60% of expected symptomatic patients over the course of 5 years leading to 77 total patients (see below). While the mix of patients across diseases may vary and the number of treated patients would depend on local guidelines, this is an indication of the number of patients who could benefit significantly from therapy.

Table: Treated and prevalent patient forecasts over 5 years

	Treatable patients				
Year	1	2	3	4	5
Gaucher	20	22	23	24	25
Fabry	8	16	22	27	32
MPSI	2	2	3	4	4
MPSII	1	1	1	1	1
Pompe	4	8	10	13	15
Total	35	49	59	69	77

Based on the average cost of treatment in Australia, treating the current 35 patients at an appropriate dose would be around Withheld under section 9(2)(b)(ii), or around Withheld under section 9(2)(b)(ii). This would increase over 5 years to around Withheld under section 9(2)(b)(ii), depending on uptake. Genzyme Australasia would be willing to discuss how funding could be arranged to deliver a funding envelope over 5 years that provides a discount to this treatment cost, balancing the New Zealand Government's ability to pay and the need for a sustainable return to Genzyme.

Specific constraints

Genzyme Australasia notes that a comprehensive agreement would be likely to result in [redacted] for the New Zealand Government in comparison to standard global prices. To ensure that a mutually beneficial arrangement is found, [redacted]

In addition, for Genzyme Australasia to agree to a funding deal, the caps and structure would need to be such that risks and uncertainties relating to patient numbers and approvals are shared and not borne solely by Genzyme.

This agreement would also need to include a process to ensure that funding can be renegotiated after the initial term on fair and reasonable terms.

Timeline

Genzyme Australasia is willing to pursue the development of an innovative "pan-ERT" solution in partnership with the New Zealand Government as a matter of high priority. This could potentially lead to a funding solution in the 2011 New Zealand Budget.

Conclusion

Genzyme Australasia is pleased that the New Zealand Government recognises the need for constructive solutions that deliver improved access to medicines for patients with rare diseases. This draft proposal sets out how such a solution might be structured so as to deliver vastly improved health for these patients, while providing certainty and predictability for both the Government and Genzyme. We look forward to future discussions about how such a partnership might be arranged that will deliver these results.

Office of Hon Peter Dunne

MP for Ohariu Belmont
Minister of Revenue
Associate Minister of Health

FROM: Jenny Langton
Health Private Secretary
Telephone Withheld under section
Email: Withheld under section 9(2)(a)

Ref. No: 10-026

TO: Ministry of Health

CC: Oliver Poppelwell / Christina O'Connell
Nigel Allardyce / Catherine Otang
Philip Berghan-Whyman
Briefing Writers Team
Ministry of Health

Briefing Information Request

DATE OF REQUEST: 12 October

TOPIC: **Advice on the proposal from Genzyme Australasia for funding Enzyme Replacement Therapies for people with Lysosomal Storage Disorders**

BRIEFING DUE DATE: 03 November 2010

REASON FOR BRIEFING

Minister Dunne recently met with representatives from Genzyme Australasia to discuss access to Enzyme Replacement Therapies (ERT) in New Zealand. Genzyme Australasia indicated they wanted to work with Government to fund a solution to funding these products. The Minister indicated he was willing to look at a proposal, if they put one forward, which they have now done.

Minister Dunne would like Ministry comment and advice on the attached proposal but would like the proposal and any discussion to remain internal at this stage.

ISSUES TO BE COVERED IN BRIEFING

Please provide advice on the feasibility of this type of approach for funding ERT, how it could work in principle and the risks associated with this.

By hard copy to Jenny Langton

Parliament Buildings, Wellington, New Zealand. Telephone: 64 4 470 6562, Facsimile: 64 4 473 5817
pdunne@ministers.govt.nz

COMMERCIAL – IN CONFIDENCE

21/01/2011

Minister of Health

At your request for information on the pharmaceutical investment pipeline, this email outlines:

- the pharmaceutical investments PHARMAC is likely to take over the coming 18 months; and
- the pharmaceutical innovations in the pipeline that PHARMAC is unlikely to fund, but will come under increasing pressure to fund, over the next 18 to 30 months.

Please be aware that some of the estimates contained in this email (those not previously supplied) have been produced quickly and, therefore, should be considered imperfect.

Likely investments

In the current financial year PHARMAC expects investments in treatments for narcolepsy, multiple myeloma, pancreatic cancer, and epilepsy to be completed. The new funding decisions are expected to benefit up to 700 further patients a year (in addition to the 380,000 we expect to benefit from those decisions already made).

Next year (2011/12), assuming the government allocates an extra $20 million for pharmaceutical expenditure, a similar number of new pharmaceuticals could potentially be funded. Some of the conditions that could be funded include chronic lymphocytic leukaemia, asthma, digestive disorders, and pulmonary hypertension.

We estimate the numbers of patients to benefit in the first full year of access from next year's potential investments to be approximately 2400. This number of new patients is lower than the past two years, because of the types of conditions being treated. In the past two years the unusually large number of new patients treated has been because of treatments for large-population diseases such as donepezil (for dementia and Alzheimer's Disease), widening of access to atorvastatin for raised cholesterol, tramadol (for pain relief), and funding bupropion and nicotine replacement therapy (for smoking cessation).

The investment plans outlined above are based on the current PHARMAC priority list, however our plans are revised monthly and sometimes new proposals can displace some of the current proposals following further clinical advice from PHARMAC's medical committees. For example, a proposal to fund insulin pumps may receive a higher priority than some proposals on the priority list and may, therefore, displace other proposals so it can be implemented sooner.

Patients treated and value for money of investments over three years beginning 09/10

Year	Conditions being treated by newly funded treatments	Patients	Health gain per $1 million spent*
09/10 (actual)	Non-Hodgkin's lymphoma, Crohn's disease, ankylosing spondylitis, smoking cessation, and chronic myeloid leukaemia.	150,000	Wi
10/11 (estimate)	Renal cell carcinoma, multiple myeloma, epilepsy, smoking cessation, and Alzheimer's disease.	380,000	Wi
11/12 (forecast)	Chronic lymphocytic leukaemia, multiple myeloma, metastatic colorectal cancer, and myelodysplastic syndromes	2,400	Wi

*Per $1 million spent (to be spent) on newly funded treatments. Health gain is quantified in quality adjusted life years (QALYs). A higher number indicates greater health gains than a lower number.

The table shows that the value for money of spending on new pharmaceutical investments this year and planned investments for next year are significantly lower than that gained from spending in 2009/10.

Between the years 1998/99 and 2006/07, new pharmaceutical investments made by PHARMAC produced health gains in the order of 170/$1million spent. By comparison, the investments we appear able to afford over the coming 18 months are of very low value for money.

Investment options that will create funding pressure

It is likely that PHARMAC will come under increasing pressure in the next 18 to 30 months to fund factor Xa and direct thrombin inhibitors (these are the next "big thing" internationally and are potentially a game changer in the treatment of atrial fibrillation – a heart condition – and other conditions where warfarin would be used to lower the risk of blood clots). These therapies may potentially benefit in excess of 35,000 patients at a cost to the community pharmaceutical budget, based on current information, of approximately $50 million a year. These are new therapies with a developing evidence base, and we consider we are unlikely to fund them in the next 18 months due to that evidence base being immature as much as their being unaffordable. Beyond 18 months, i.e. in 2012/13, and assuming the evidence of benefit continues to grow, PHARMAC is unlikely to be able to fund these drugs despite them being likely to provide relatively better value for money for some patient groups than the investments made over the last 20 months. This is because without a significant increase in funding, these products will cost too much (even with good competition between similar products, expenditure demands are going to be in the order of $20 to $50 million a year).

While the review of Exceptional Circumstances schemes has not yet been completed, it is likely that an increase in expenditure may occur in the initial stages of any changed scheme. Over time, as these treatments are able to be assessed for schedule listing, the cost would shift into the population-based budget. We anticipate such an increase would be able to be met from within the existing budget provision. Even with this scheme in place, there are also a number of treatments that we are very unlikely to fund outside of very exceptional circumstances because they are extremely expensive per patient and for many patients, provide limited benefits. For example, the enzyme replacement therapies (ERT) for the lysosomal storage diseases promoted by John

Forman's group NZORD. ERT treatment for adult Pompe disease is estimated to cost $500,000 per patient a year with approximately 7 patients known to PHARMAC. It is likely that in most circumstances these treatments would represent very poor value for money (health gain per dollar spent) when compared with previous PHARMAC investments.

PHARMAC
Pharmaceutical Management Agency

BRIEFING

Access to enzyme replacement therapies for New Zealand patients

Date **15 February 2011**

To **The Hon Tony Ryall (Minister of Health)**

Copies to

PHARMAC Board
DHB spokesperson on pharmaceutical issues
Director General of Health
Deputy Director-General, Sector Funding and Performance

Recommendations

It is recommended you:

- **note** the contents of this report
- **agree** that PHARMAC updates Associate Minister Dunne on progress, given his responsibility for Medicines Strategy New Zealand, assisting with PHARMAC and prior interest in this matter;
- **forward** this paper to Associate Minister Dunne.

Contact(s)

Matthew Brougham, Chief Executive
Jude Urlich, Manager Corporate & External Relations

Withheld under
Withheld under

Purpose

This briefing provides information to you about issues in relation to providing access to enzyme replacement therapies to New Zealand patients.

Executive Summary

- Lysosomal Storage Diseases (LSD) are rare genetic disorders that affect the body's enzymes, with diagnoses occurring from birth through to old age. These are very distressing conditions for patients as in many cases the condition is life-shortening, particularly for those diagnosed at birth, and patients frequently face significantly reduced quality of life.
- Enzyme replacement therapies (ERTs) cost in the region of $500,000 to $2 million per patient per year. There is a poor evidence base, itself not uncommon with rare diseases, but the publicly-available evidence suggests poor levels of health gain for most indications.
- PHARMAC considers that there is an opportunity to obtain significant health gains for some patients and is very keen to progress funding decisions for these treatments. The challenge lies in identifying the groups of patients likely to benefit from treatment.
- Due to the paucity of publicly-available evidence, data held by the supplier of ERTs, Genzyme, will be critical to reaching an informed and faster decision.
- PHARMAC is seeking to engage with Genzyme to help progress the assessment and potential funding of ERTs. To date, engagement with Genzyme has been difficult, reflecting an international business methodology whereby public funders are by-passed in favour of a direct approach to government.
- Following a funding proposal by Genzyme to Associate Minister of Health, Mr Dunne, we have met with, and written to, Genzyme to outline our willingness to seek a co-operative way forward.
- Two potentially high-profile ERT applications, both under the Community Exceptional Circumstances (CEC) scheme, have annual budget impacts of Withheld per annum or more each. One has already been considered and approved for renewal by the PHARMAC Board. This decision remains commercially sensitive given its intent is to ensure continuity of treatment for the patient by covering any shortfall on the supplier's part in terms of meeting the original funding agreement, and we have not yet been informed of its future intentions. The second case is to be considered at the February Board meeting.
- The current review of Exceptional Circumstances (EC) may be seen by some stakeholders as a solution to current funding issues. However, a changed EC scheme will not see the fundamental nature of ERTs change – they are very expensive and, in many instances, appear to provide tiny benefits.

Background

Lysosomal Storage Diseases (LSD) are a group of approximately 45 rare, inherited genetic disorders that affect the body's enzymes. An enzyme deficiency or malfunction in the patient means a substance the enzyme would usually metabolise builds up in the body, resulting in damage and dysfunction to major organ systems which can be fatal. Different enzyme deficiencies affect different organ systems; thus, symptoms vary depending on the type of

lysosomal storage disease. Symptoms may include developmental delays, movement disorders, seizures, dementia, deafness, blindness, or liver and spleen damage.

LSD affect mostly children and they often die at a young age, many within a few months or years of birth. Other children affected by LSD may die following years of suffering from various symptoms of LSD.

Enzyme Replacement Therapies (ERTs) have been developed to treat a number of LSD. ERTs treat the symptoms of LSD, but do not cure the disease. ERTs are currently expensive, and can cost up to $2 million per year for an adult patient. The cost is significant given ERTs are required throughout a patient's life and dosing is body-weight dependant.

Manufacturers explain that the high prices are necessary to reclaim the high cost of research to develop the drugs. They are also for very small patient populations, so there is no opportunity to spread the cost across large markets. However, there is a lack of clinical studies demonstrating useful clinical end points. Such a lack of data makes it very difficult to assess the long-term effectiveness of these products, and to draw conclusions of their effectiveness in discrete populations. Our assessment of the evidence to date indicates that for some patient groups the benefits are potentially tiny.

Current patient funding

PHARMAC currently funds low doses of treatment for 16 patients with Gaucher's (Type 1) through the Pharmaceutical Schedule.

Two other patients Withheld under section 9(2)(a) have Type 3 Gaucher's disease and have been funded for many years through CEC at a total cost to the Pharmaceutical Budget of $2.6 million.

Another type of funded ERT patient is Withheld under section 9(2)(a). Withheld under section 9(2)(a) Withheld under with this disease without neurological involvement and was approved by the Board in March 2009 under CEC. PHARMAC approved funding of $500,000 over two years. At Withh bodyweight the treatment would cost approx $2 million per annum.

Funding Enzyme Replacement Therapy

There are three mechanisms for potential public funding of ERT:

- Pharmaceutical Schedule – one therapy, imiglucerase (Cerezyme), is already funded under Special Authority for the treatment of Gaucher's disease;
- DHB hospitals; and
- Exceptional Circumstances scheme.

ERT has sufficient evidence to demonstrate that the therapies are effective in some patients, but not all. As PHARMAC has not been able to obtain access to Genzyme's data, each case has had to be examined individually. This has been through a special panel of clinicians who assess individual funding applications. A thorough assessment leading to a Schedule listing would benefit patients in terms of certainty around funding decisions, except in the case of exceptional circumstances where the usual processes would apply.

On a cost-effectiveness basis, the cost per Quality Adjusted Life Year (QALY) is 5 to 10 times greater than investments PHARMAC is currently progressing. On a historical basis, the cost per QALY is 20 to 50 times worse. While Exceptional Circumstances applications for specific

patients can have higher than average costs per QALY, the cost effectiveness of ERT treatment compares unfavourably with other population-based applications PHARMAC has prioritised. However, should it be possible to target treatment to populations most likely to benefit, it is likely the high cost per QALY would reduce. This makes it imperative to obtain up-to-date health benefit information from the supplier of ERTs.

Current issues

Genzyme engagement

Genzyme is the company that almost exclusively manufactures ERTs. Genzyme is keen to have more of its products funded in New Zealand, however, in line with its business practices internationally, it appears not to want to engage with PHARMAC to do so, preferring to make a direct approach to government.

We have sought to engage with Genzyme in order to evaluate the evidence and to obtain pricing information. To date, in the many years we have funded Genzyme products, we have not been able to agree to such information being provided, or even to them agreeing a price.

In November 2010, Genzyme put what it said was a `novel funding proposal' to associate health minister Peter Dunne. Mr Dunne's response was to urge Genzyme to engage with PHARMAC.

We met with Genzyme officials in February 2011. At the meeting we gained a greater understanding of the reasons behind its approach to funding products. Genzyme is concerned that using usual funding processes, its treatments are unlikely to compare well to other medicines (due to the very high price and difficulty developing evidence of long-term health benefits in diseases affecting small patient groups).

In response, Genzyme appears to have consciously adopted a strategy of, in effect, testing how much Governments are prepared to pay for its products to make potentially politically contentious problems go away. The political economy of small patient groups tends to work in favour of funding these products. Genzyme has already tested this strategy in New Zealand with its approach to Minister Dunne.

We think it may be possible to identify patients who are more likely to gain substantial health benefits than others. Given the treatments cost $500,000 to $2 million per year, we are keen to ensure health gains flow from any funding. In order to make these assessments, we think it necessary to have co-operation from Genzyme to share information.

We have written to Genzyme to make clear our desire to work together to progress a long-term assessment and funding process. This could involve describing, up front, the patients who are likely to gain most benefit, which may enable us to consider providing some greater access, and to agree a commercial arrangement.

Current exceptional circumstances issues

As outlined above, PHARMAC funds one Withheld under section 9(2)(a) with Withheld under section 9(2)(a), and approved funding of $500,000 in 2009. This decision is due to be revisited in June 2011. When the decision was made, PHARMAC had no pricing information on which to base accurate estimates, and our best guess was that $500,000 would be sufficient to fund the patient for two years. However, funding was exhausted within one year, and Genzyme has since been providing treatment for free.

The PHARMAC Board will make a decision on whether to continue funding. Without pre-judging the Board's decision, our view on funding treatment is that funders have an ethical responsibility to continue treatment as long as the patient continues to benefit. Where a patient is no longer

benefitting, this is assessed against known exit criteria, either notified to the individual as part of an EC approval, or published in the Schedule for high-cost medicines such as Cerezyme, or beta interferon for multiple sclerosis. Clinical advice from our expert panel will play an important part in the Board's decision.

PHARMAC is also considering funding for an adult patient with Pompe Disease who is seeking funded access to Myozyme through the CEC scheme. As the funding decision has a high financial impact (approx $500,000 per year), the Board will also make this decision. Again, expert clinical advice and PHARMAC's cost-utility analysis will be central to the Board's decision. We have advised the NZ Organisation for Rare Disorders, which has the patient's permission to discuss their case, that the decision is being considered by the Board on 25 February. Coincidentally, 28 February is International Rare Diseases Day. NZORD may use this as an opportunity to highlight the issue.

Exceptional Circumstances Review

As you are aware, PHARMAC is currently reviewing the Exceptional Circumstances Schemes and is consulting on a proposal to form one scheme called Named Patient Pharmaceutical Assessment. Stakeholders seeking access to high cost medicines such as ERT will be assessing the proposed scheme to determine whether it offers improved access to medicines than the schemes it is intended to replace.

Even with a revised EC scheme such as the one proposed that will enable a wider pool of applicants, in making a funding decision PHARMAC will still take into account its nine decision criteria such as health benefit and total budget impact, balanced against the lost opportunities to fund other medicines.

Future opportunities

Until now Genzyme has been the only company in the world to manufacture ERTs. However, several of its products are shortly to come off-patent and this may lead to generic competition being available. Should this occur it is likely the price of these treatments would reduce dramatically.

The prospect of generic competition may explain Genzyme's eagerness to enter into a long-term arrangement (six years) with the Government, as outlined in its proposal to Minister Dunne last year.

Genzyme is also in the process of discussing a takeover by French pharmaceutical company Sanofi-Aventis. Sanofi has a long history in New Zealand and many of its products are funded by PHARMAC. Should the takeover proceed, it may offer opportunities to progress issues around ERT. Sanofi has a larger portfolio of products than Genzyme so may be able to leverage off this to create bundled agreements, as we have seen other companies do following mergers. Sanofi employs a constructive approach to its dealings with PHARMAC.

Matthew Brougham
Chief Executive

PHARMAC
Pharmaceutical Management Agency

BRIEFING

Response to NZ Organisation for Rare Disorders' concerns

Date 21 September 2012
To The Hon Peter Dunne (Associate Minister of Health)

Copies to

Hon Tony Ryall, Minister of Health
PHARMAC Board
DHB spokesperson on pharmaceutical issues
Director General of Health
Deputy Director-General, Sector Funding and Performance

Recommendations

It is recommended you:

- **note** the contents of this report

Contact(s)

Steffan Crausaz, Chief Executive
Jude Urlich, Manager Corporate & External Relations
Withheld under
Withheld under

Purpose

Following your recent meeting with John Forman, Executive Director of the New Zealand Organisation for Rare Disorders (NZORD), you asked PHARMAC for further information and clarification on the issues raised by NZORD. It includes an update regarding PHARMAC's consideration of lysosomal storage disorders and the operation of the Named Patient Pharmaceutical Assessment (NPPA) policy.

Executive Summary

- Lysosomal storage disorders (LSDs) are a range of genetic disorders affecting the functioning of the body's cells. LSDs can result in shortened life and decreased quality of life. Some patients may present with a LSD acutely with potentially life-threatening consequences, whereas other LSDs are chronic conditions. There is no known cure, although bone marrow transplant may be performed in some cases with curative intent and varying degrees of success.

- Enzyme replacement therapies (ERTs) are a range of treatment options for the different LSDs. ERTs come with a high asking price, generally costing in the region of $500,000 to $2 million per patient per year.

- Because there are a number of LSDs, each with a different ERT treatment, it is difficult to categorise all ERTs as potentially lifesaving. The LSDs have varying levels of severity and its corresponding ERT has different effects in treating it, where some could be labelled as lifesaving while the evidence for others indicates their treatment effect is not clinically significant.

- The principle of ERT treatment is to provide, by injection/infusion, a fully functioning enzyme to supplement the malfunctioning enzyme. However, because the deficient enzymes operate within structures inside the cells of tissues and organs, it does not generally follow that injection/infusion into the bloodstream will result in correcting the clinical condition or extend life. This is a different scenario from other replacement therapies, such as insulin replacement as insulin is a hormone that naturally works by circulating through the bloodstream.

- While not all applications are approved, all patients seeking ERT funding have the opportunity for their circumstances to be considered, either through the Pharmaceutical Schedule or through Named Patient Pharmaceutical Assessment (NPPA).

- The different clinical circumstances, limited clinical evidence and impact of individual circumstances on the expected treatment effect means that funding on a case-by-case basis is the appropriate approach. This is the advice we have received from the Pharmacology and Therapeutics Advisory Committee (PTAC) and others on a number of occasions.

- PHARMAC funds ERTs for 21 patients through the Schedule and NPPA for a range of LSD conditions. In some cases, there is a small amount of evidence, in others there are good reasons justifying funded treatment in the absence of evidence. In still other cases, there is good evidence of clinically insignificant benefits from treatment.

- While we consider it too early to definitively state the effects of the change from the Exceptional Circumstances schemes to NPPA, we have had an increase in operating costs to manage the increased number and complexity of applications, and have observed an increase in the percentage of approved applications.

- We note that widespread consultation and public discussion informed a report on the review of access to high-cost, highly-specialised medicines in New Zealand that was provided to the Minister of Health in 2010. That report's recommendations are generally not consistent with NZORD's views.

Background

We understand that you recently met with NZORD and a number of issues were raised that you would like PHARMAC clarification on. We understand that NZORD's concerns are about funded access to enzyme replacement therapies (ERTs) for lysosomal storage disorders (LSDs).

We note that on 31 March 2010, the Minister of Health received the report *Review of Access to High-Cost, Highly-Specialised Medicines in New Zealand* prepared by Paul McCormack, Joy Quigley and Paul Hansen. That report followed nine months of consultation with, and submissions from, many interested parties from around New Zealand and also overseas.

The authors considered that if more funds were to become available for spending on medicines, it is not obvious that they should necessarily be spent on high cost medicines per se. One of the report's main recommendations is that prioritisation and funding decisions concerning high-cost, highly-specialised medicines continue to be made in the same way as such decisions for other medicines (subject to other recommendations aimed at improving how such decisions are made in the future). They did not recommend that new prioritisation processes and pools of funding be established for high-cost, highly-specialised medicines. In arriving at this view, the authors considered submissions from NZORD expressing views consistent with those currently being put forward.

The report recommended a single Exceptional Circumstances scheme be established. This has been actioned with the establishment of the NPPA process. Since NPPA began in March 2012, two patients with LSDs have received approval for funded ERT treatment.

Enzyme Replacement Therapies

LSDs are a range of genetic disorders whereby enzymes within the body's cells do not function properly, resulting in these cells being unable to process material correctly. Clinical presentation of LSDs occurs from birth through to old age and these can be very distressing conditions for patients and their families. In some cases, the condition is life-shortening, particularly for those presenting in infancy or childhood, and patients frequently face significantly reduced quality of life.

There are approximately 45 known LSDs, occurring with a combined incidence rate of about 1 in 5000 to 1 in 10,000, or about 1 in 100,000 for each LSD individually. According to Lysosomal Diseases New Zealand, there are approximately 180 New Zealanders who currently have one of these conditions.

ERTs are a range of treatment options for patients with LSDs. ERTs can cost in the region of $500,000 to $2 million per patient per year, depending in part on body weight. Primarily, these treatments are supportive, treating the symptoms of LSDs as there is no known cure (though bone marrow/stem cell transplants may be given in some cases with curative intent and varying degrees of success).

In theory, ERTs function by replacing an enzyme in the structures within a cell that is missing or deficient. However, because these malfunctioning enzymes are located within cells, it does not follow that injecting or infusing an ERT into the bloodstream will replace that enzyme within cells. This is a different scenario from other replacement therapies, such as insulin replacement as insulin is a hormone that naturally works by circulating through the bloodstream.

There are other reasons ERTs may not effectively replace deficient enzymes, including:

- the absence of the enzyme may have caused tissue damage during the formative years of a patient's life, which may have ongoing implications;
- some tissues have a poor response to treatment;
- there is variability in uptake across cell types and between patients; and
- some patients develop antibodies to the enzymes in ERT.

In general, treating a patient early is more successful than later as organs with a more advanced disease state respond poorly.

ERTs are aimed at improving the quality of life of those with a LSD through treating the symptoms of the condition. We are aware that NZORD frequently refers to ERTs as "lifesaving" treatments. Due to the range of LSDs and the variety of treatments for these, there is varying evidence and expectation of whether the different ERTs are lifesaving or life extending in specific cases. Each ERT, used to treat a particular LSD, will have different effectiveness on treating that LSD. As such, not all ERTs are the same, just as some LSDs are less severe than others. PHARMAC considers the evidence for this when assessing funding applications for these treatments.

Some LSDs present more acutely in some children. In these cases, the children often have significantly shorter life expectancies. The clinical circumstance of each child is critical to the expectation of benefit. For example, a child patient with a LSD, but whose neurological system is not yet affected, could receive benefit from an ERT treatment. Neurological involvement is an important factor to account for because ERT treatment does not pass into the brain. PHARMAC is currently funding an ERT for a child patient in such a situation.

PHARMAC's funding consideration of ERTs

In both 2009 and 2011, the Pharmacology and Therapeutics Advisory Committee (PTAC) discussed ERTs for listing in the Pharmaceutical Schedule. In both cases, PTAC recommended declining Schedule listing of these treatments; however, it also recommended PHARMAC continue to consider individual applications for ERTs through the Exceptional Circumstances (EC) scheme.

In May 2011, PHARMAC issued a Request for Information (RFI) seeking further evidence of the clinical effectiveness and outcomes of ERTs, including information about dosing and pricing of these treatments. PTAC reviewed the information provided in response to the RFI at its November 2011 meeting. In summary, PTAC recommended declining funding for five ERTs for six LSDs, stating:

> *that even if the evidence of effectiveness were to improve, at the current costs of ERT treatment it would be challenging to make their cost effectiveness argument. The Committee considered that at the present time best supportive care should be the treatment option.*

The relevant advice from this meeting is attached to this Brief and the full minutes are available online at http://www.pharmac.govt.nz/2012/01/25/2011%2011%20PTAC%20web%20minutes.pdf.pdf.

We continue to assess new information about ERTs as it becomes available to inform our decision making. As a case in point, at its next meeting, PTAC will be reviewing recent evidence provided by a specialist.

PHARMAC has considered, and continues to consider, a number of funding applications for ERTs for both individual patients under NPPA and for Pharmaceutical Schedule listing. Some patients have been approved under the NPPA policy, as in the case of three patients whose applications were approved as Withheld under section 9(2)(a). Additionally, a special access panel applies the Special Authority criteria for Schedule-listed treatments for the Gaucher's disease LSD.

The table below provides a general summary of the funding status of ERTs for LSDs that we have considered.

LSD	Description	Funding status
Gaucher's disease	Gaucher's disease has three common clinical subtypes: Type I – the most common subtype, occurring in about 1 in 50,000 births. Symptoms may begin early in life or in adulthood, and include enlarged liver and spleen, with the possibility for the spleen to rupture; skeletal weakness and bone disease; blood disorders; lung and kidney impairment. Depending on disease onset and severity, these patients may live well into adulthood. Many patients have a mild form of the disease or may not show any symptoms. Type II – typically begins within 6 months of birth and has an incidence rate of approximately 1 in 100,000 births. Symptoms include an enlarged liver and spleen; extensive and progressive brain damage; eye movement disorders; spasticity; seizures; limb rigidity; and a poor ability to suck and swallow. Affected children usually die by age 2 and funded treatment is generally not available as ERT is not effective in treating their brain damage (as discussed above). Type III – can begin at any time in childhood or adulthood and occurs in approximately 1 in 100,000 live births. Type III is characterised by slowly progressive, but milder, neurologic symptoms compared to Type II. Major symptoms include an enlarged spleen or liver; seizures; poor coordination; skeletal irregularities; eye movement disorders; blood disorders; and respiratory problems. Patients often live into their early teen years and adulthood.	**Pharmaceutical Schedule:** Imiglucerase (Cerezyme) funded for 16 patients with type 1 Gaucher's and two patients with type 3. Miglastat (Zavesca) was recommended for funding by PTAC with a low priority. This has been prioritised against all other investments available for funding.
Mucopolysaccharidosis II (Hunter's disease)	Like other LSDs, there is a disease continuum for Hunter's disease between two extremes (severe/type A and attenuated/type B). Symptoms include upper airway obstruction and an enlarged tongue; decreased lung functionality; heart disorders; liver and spleen enlargement; skeletal deformities; limited joint mobility; severe learning difficulties and	**Community Exceptional Circumstances:** Idursulfase (Elaprase) is currently funded on an on-going basis for one patient via the former Community Exceptional Circumstances (CEC) (patients approved for ongoing funding under EC continue to be assessed under EC criteria following introduction of NPPA).

	progressive neurological decline. Death usually occurs in the first or second decade of life for the severe/type A, but patients with attenuated/type B can survive into early adulthood.	**NPPA:** Idursulfase (Elaprase) funding was approved in June 2012 for one patient for short-term use as Withheld under section 9(2)(a) Withheld under section 9(2)(a).
Mucopolysaccharidosis I (Hurler, Hurler-Scheie and Scheie syndromes)	Hurler syndrome is the most severe form of this LSD, with onset occurring in the first year of life. The central nervous system is affected, resulting in intellectual impairment. Lifespan is shortened and children with Hurler syndrome rarely survive the first decade. Treatment is a stem cell transplant, with the best outcomes occurring with early transplantation. Hurler-Scheie syndrome is the intermediate form, with onset in the first few years of life. Intellectual development is usually not affected. Lifespan is shortened, with patients usually surviving into their teens or young adulthood. Scheie Syndrome is the mildest form of this LSD and may not be detected until adulthood. The primary condition is joint disease.	**Community Exceptional Circumstances:** Laronidase (Aldurazyme) funding declined in 2006 for two patients with Hurler disease by the PHARMAC Board on the basis of a lack of evidence of immediate clinical benefit and long term benefit, and poor cost effectiveness. Laronidase funding was approved in January 2012 for one patient for short-term use as Withheld under Withheld under section 9(2)(a) Withheld. **NPPA:** Laronidase funding was approved in August 2012 for one patient for short-term use as W Withheld under section 9(2)(a) Withheld under section 9(2)(a).
Pompe disease (Juvenile onset, Adult onset)	Late onset (or juvenile/adult) Pompe disease is the result of a partial deficiency of the gene that produces enzymes to help the body's cells break down complex material. Onset of Pompe disease can be as early as the first decade or as late as the sixth decade of life. The primary symptom is muscle weakness progressing to respiratory weakness and death from respiratory failure after a course lasting several years or more.	**EC/NPPA:** Alglucosidase alfa (Myozyme) funding was declined under EC and NPPA by the PHARMAC Board for five individual patients with adult onset Pompe disease on the basis of lack of evidence of clinical benefit and poor cost effectiveness. PHARMAC is currently considering an application for alglucosidase alfa for a patient with juvenile onset Pompe disease.
Pompe disease (Infantile onset)	Early onset (or infantile) Pompe disease is the result of complete, or near complete, deficiency of the gene that produces enzymes to help the body's cells break down complex material. Symptoms begin in the first months of life, with feeding problems, poor weight gain, muscle weakness, floppiness, head lag and an enlarged heart. Respiratory difficulties are often complicated by lung infections. Most babies with Pompe disease die from cardiac or respiratory complications in the first year of life. Infantile onset Pompe disease is	**EC/NPPA:** Infantile onset Pompe disease is a very rare disorder and PHARMAC has never received an application for the treatment (alglucosidase alfa) of it. Were such a case to present, it would be considered under the NPPA policy with urgency due to the acute nature of the presentation. Alglucosidase alfa is funded in Australia for this indication under that country's Life Saving Drugs Programme (LSDP), used to provide subsidised access for eligible patients to high cost drugs

	generally treated with the drug alglucosidase alfa (Myozyme).	for rare life threatening conditions. Treatments funded under LSDP are not recommended for inclusion in Australia's Pharmaceutical Benefit Scheme due to unacceptable cost-effectiveness.
Fabry's disease	Fabry's disease is a genetic disorder which results in an enzyme deficiency. This results in a build-up of enzymes in most non-neural tissues and body fluids.	**Exceptional Circumstances:** Eight applications for agalsidase beta (Fabrazyme) were submitted and declined under the former Exceptional Circumstances between 2002 and 2009 due to not meeting rarity criteria and limited available evidence of efficacy.

NPPA and EC

To provide further context and information for you, we are aware of NZORD's interest as to whether the NPPA policy has improved patient access to consideration of treatments over the previous EC schemes. NPPA is likely to be the process by which most patients with a LSD are considered for funded treatment.

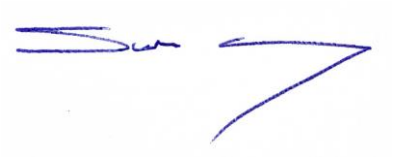
It is too early to definitively determine whether there is a substantial difference in access or expenditure between EC and NPPA. There is an added dimension in that as the NPPA policy is implemented, PHARMAC expects more treatments for smaller groups to be listed on the Pharmaceutical Schedule. This will have the impact of reducing the amount spent overall on NPPA.

There has been an increase in operating costs to manage the increase in number and complexity of applications. Although the total number of applications to NPPA has increased modestly compared to EC (16%), the number of applications approved for funding from the CPB as a percentage of applications has increased significantly from 39% under EC to 68% under NPPA. The table below provides a further breakdown of the application and decision rates between NPPA and EC.

Number of Applications	**NPPA** 1/3/2012-31/08/2012	**NPPA Pathways**				**EC**	**EC Schemes** 1/3/2011-31/08-2011		
		HPC	**UA**	**UCC**	**Other**		**CEC**	**HEC**	**CaEC**
Approved	345	111	161	46	27	340	49	235	56
Declined	14	0	10	1	3	108	72	33	3
Pending	146	N/A	N/A	N/A	N/A	5	4	1	0
Subtotals	**505**					**453**	**125**	**269**	**59**
Withdrawn	71					45	12	31	2
Total applications	**576**					**498**			

We recognise that patients with a LSD, and their families, are in very difficult and distressing situations. With the implementation of NPPA, more of these patients can have their case considered for funded treatment than under EC.

PHARMAC is willing to continue dialogue and a working relationship with NZORD to discuss its concerns. We note that we are currently reviewing our Operating Policies and Procedures, which provides a further opportunity for NZORD to comment more formally on our processes.



Steffan Crausaz
Chief Executive

Attached: November 2011 PTAC minute on ERTs

Minute of the Pharmacology and Therapeutics Advisory Committee

November 2011

Enzyme Replacement Therapies

Application

The Committee considered an application from PHARMAC staff that sought advice on whether to list six Enzyme Replacement Therapies (ERTs) for five lysosomal storage diseases on the Pharmaceutical Schedule.

Recommendations

The Committee **recommended** that the proposal to fund agalsidase alpha (Replagal) for the treatment of Fabry disease be declined.

The Committee **recommended** that the proposal to fund agalsidase beta (Fabrazyme) for the treatment of Fabry disease be declined.

The Committee **recommended** that the proposal to fund laronidase (Aldurazyme) for the treatment of Mucopolysaccharidosis I (Hurler, Hurler-Scheie and Scheie disease) be declined.

The Committee **recommended** that the proposal to fund idursulfase (Elaprase) for the treatment of Mucopolysaccharidosis II (Hunter disease) be declined.

The Committee **recommended** that the proposal to fund galsulfase (Naglazyme) for the treatment of Mucopolysaccharidosis VI (Maroteaux-Lamy disease) be declined.

The Committee **recommended** that the proposal to fund alglucosidase alpha (Myozyme) for the treatment of Pompe disease (infantile, juvenile and adult-onset) be declined.

The Decision Criteria particularly relevant to all recommendations are: *(i)The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (v)The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services and (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

Discussion

The Committee considered an application from PHARMAC staff that sought advice on the funding of various Enzyme Replacement Therapies (ERTs) generated following receipt of responses to a Request for Information (RFI) issued by PHARMAC on the 9 May 2011. The RFI sought evidence to support: the causal association between improved surrogate markers and clinical outcomes that ERTs reduce mortality, further information regarding optimum doses and dosing protocols, and proposed pricing for New Zealand supply. The Committee noted responses and all evidence provided by pharmaceutical suppliers, the National Metabolic Service, NZ Organisation for Rare Disorders, Mayo Clinic and two patients.

The Committee noted that it had previously reviewed the funding of six ERTs at its February 2009 meeting, and again, specifically the funding of alglucosidase alpha for adult-onset Pompe disease at its February 2011 meeting. The Committee noted that it was aware of funding applications for ERT treatments for individual patients received through the Exceptional Circumstances scheme.

The Committee considered that in general ERTs comprised high cost, highly specialised medicines and noted that a recent review of the process of evaluating the funding of high cost, highly specialised medicines, which is published online at www.beehive.govt.nz, recommended that

'prioritisation and funding decisions concerning high-cost, highly specialised medicines continue to be made in the same way as such decisions for other medicines'.

The Committee noted the severe nature of these lysosomal storage diseases. It was noted that even if the evidence of effectiveness were to improve, at the current costs of ERT treatment it would be challenging to make their cost effectiveness argument. The committee considered that at the present time best supportive care should be the treatment option.

The Committee's discussion of various disease settings and ERTs are detailed separately below:

Fabry disease

Agalsidase beta

The Committee considered evidence submitted by Genzyme, the supplier of agalsidase beta (Fabrazyme), in relation to the optimum dosing regimens. The Committee considered that the standard dose in trials of agalsidase beta (Fabrazyme) is 1mg/kg/fortnight, although members noted that one study (Lubanda et al 2009; 11:256-264) used this dose for 6 months then 0.3mg/kg/fortnight thereafter. Members noted that in this two year trial 70-90% of patients maintained their initial clearance of globotriaosylceramide (GL-3) from the kidney. The Committee considered this data suggested that dose reduction following an initial treatment phase may offer similar efficacy and would significantly reduce the cost of treatment compared with standard dosing.

The Committee considered evidence provided by Genzyme regarding the effect of agalsidisase beta treatment on renal outcomes. The Committee considered a multicentre, randomised, double-blind, placebo-controlled study published by Banikazemi et al. (Ann Intern Med 2007; 146:77-86) designed to assess the effectiveness of agalsidase beta compared with placebo on time to clinically significant progression of renal, cardiac, cerebrovascular disease and/or death in 82 patients with advanced Fabry disease. Members noted that patients were randomised (2:1) to receive treatment with either 1 mg/kg/fortnight of agalsidase beta or placebo for up to 35 months. The Committee noted that although there appeared to be a trend in favour of agalsidase beta there was no statistically significant difference in the rate of clinical progression between the two treatment groups for any efficacy endpoint over the duration of the study suggesting that agalsidase beta treatment may take years before significant clinical benefits are seen, if any. Other than this trial, the Committee considered that there was little new evidence to support any effect of agalsidase beta on renal outcomes.

The Committee also considered evidence regarding the effect of agalsidase beta on cardiac disease. The Committee considered a five month, double-blind, randomised, placebo controlled trial (Thurberg et al. Circulation 2009;119:2561-2567) followed by an open-label extension study which demonstrated that agalsidase beta was effective in clearing globotriaosylceramide (GL-3) from capillary endothelial cells of the heart and this effect was sustained for up to five years. However, the Committee noted that in this study no effect was seen on GL-3 deposition in cardiomyocytes and there was no evidence of improved cardiac function, or other clinically meaningful end points such as reduction of myocardial infarction or cardiac death.

The Committee also considered evidence from three small, single arm, open label, studies (Imbriaco et al. Heart 2009;95: 1103-7, Weidemann et al. Circulation 2009; 119: 524-529, Collin et al. Euro J Cardio Prev & Rehab 2011), all published since its last review which showed a reduction in left ventricular hypertrophy, reduction in aortic stiffness and improvement in baroreflex function with agalsidase-beta treatment. Overall, the Committee considered that, despite evidence of effect of agalsidase beta on some cardiac measures, there was no evidence to support its effect on clinically meaningful endpoints.

The Committee also considered evidence from a single arm, open label, study published by Watt et al. (Genet Med 2010:12 703-712) regarding effect of agalsidase beta treatment on quality of life in 130 patients treated with agalsidase beta. Members considered that agalsidase beta improved quality of life measures over two years of treatment, however, these improvements were not sustained beyond three years of treatment.

Agalsidase alpha

The Committee considered evidence submitted by Shire, the supplier of agalsidase alpha (Replagal). The Committee noted that the standard dose of agalsidase alpha in all trials was 0.2mg/kg/fortnight (five times lower than the dose of agalsidase beta). The Committee considered that agalsidase alpha and agalsidase beta were functionally indistinguishable and that no convincing evidence had been provided demonstrating any significant difference between the two enzymes in their effect on surrogate markers and clinical end points, despite algalsidase beta at 1mg/kg/fortnight producing a higher percentage of antibodies than algalsidase alpha at 0.2mg/kg/fortnight (Vedder et al. Mol Genet Metab 2008; 94:319-25; reviewed by PTAC previously).

The Committee considered evidence supplied in support of the clinical effect of agalsidase alpha treatment comprising two studies that used data obtained from the Fabry Outcome Survey observational (FOS) database. The Committee reviewed evidence from a single arm observational study (Mehta et al. Lancet 2009; 374:1986-96) of 181 patients enrolled in FOS who were treated with agalsidase alpha for 5 years. Members noted that in patients with baseline cardiac hypertrophy, treatment with agalsidase alpha significantly reduced left ventricular mass (LVM) and increased midwall fractional shortening (MFS). However, in patients without baseline hypertrophy LVM and MFS remained stable. Members noted that patient quality of life and pain were improved significantly, and the rate of decline in glomerular filtration rate (GFR) was less than that seen in historical controls. The Committee also considered a 3 year analysis of renal function outcomes in 165 patients enrolled in the FOS (Ferriozzi et al. Am J Nephr 2009; 353-361). Members noted that the authors found a significant increase in serum creatinine, decreased GFR and increased proteinuria, but reported that the rate of decline in renal function was less than historical controls. A baseline proteinuria of >500mg/24 hours and, to a lesser extent hypertension predicted acclerated loss of renal function. The Committee noted that in both studies, concomitant use of ACE-inhibitors and angiotensin II receptor blockers were common and may have influenced outcomes.

The Committee noted that there were no new safety concerns published in the FOS annual report from 2010. The database contained 1,903 patients, of whom 1,120 had been treated with agalsidase alpha. Safety statistics reported showing 18% of patients had serious adverse events, 9% had infusion related reactions (IRRs) and 5% died. Overall, the Committee considered that the evidence for agalsidase alpha was weak and its effect on clinically meaningful endpoints was unclear.

Migalastat

The Committee considered a submission from Amicus, the supplier of the pharmacological chaperone migalastat (Amigal), which targets misfolded endogenous enzymes, as a result of specific mutations, in patients with Fabry disease. The Committee considered evidence from a non-randomised, single arm, extension study (Schiffman et al. J Peds 2011) which examined the long-term safety, tolerability and renal function of migalastat treatment in patients with Fabry Disease. Members noted that 26 patients completed the primary 12-24 week treatment period, and 23 patients completed 24-84 week initial extension period and were then enrolled in a separate long term extension study. Members noted that the authors reported that migalastat reduced levels of kidney globotriaosylceramide compared with baseline in patients with Fabry disease with responsive mutations of alpha-galactosidase A. Members also noted that glomerular filtration rate remained stable and some subjects with responsive mutations observed reduced proteinuria compared with baseline. The Committee noted that these effects were maintained out to 3-4 years and are comparable to results reported for ERT. The Committee noted that migalastat is currently in Phase III development and is not registered in New Zealand.

Meta-analysis

The Committee considered evidence from a Cochrane review (El Dib et al. Cochrane Database of Systematic Reviews 2010; Issue 5) of a meta-analysis five randomised controlled trials of ERT (agalsidase alpha or beta) in Fabry disease. The Committee noted that it had previously reviewed evidence from four of these studies (Banikazemi et al. Ann Int Med 2007;146:77-86, Eng et al. New Eng J Med 2001; 345:9-16, Hughes et al. Heart 2008;94: 153-8 and Schiffman et al. JAMA 2001; 285:2743-9) with the fifth being a small study comprising 15 patients (Bierer et al. J Inh Metab Dis 2006;29:572-9). The Committee noted that the authors reported a non-statistically significant

improvement in serial cardiopulmonary exercise testing following 18 months treatment with agalsidase beta compared with placebo. Members noted, and agreed with, the authors conclusion that "five small, poor quality randomised controlled trials provide no robust evidence for use of either agalsidase alpha or beta to treat Anderson-Fabry disease".

The Committee considered evidence from a review article submitted by the National Metabolic Service (NMS) (Lidove et al. Genet Med 2010;12:668-679) of the clinical efficacy of ERT in Fabry disease, however, members noted that the end points considered were all surrogates and considered their relevance to clinical outcomes was questionable.

General Discussion – Fabry disease

The Committee considered that agalsidase alpha and agalsidase beta are expensive treatments with limited evidence for clinical benefit and poor cost-effectiveness. The Committee considered that whilst evidence demonstrates that agalsidase (beta and alpha) clears GL-3 from plasma and organs, and that this occurs in all ages, genders and different ethnicities, this has not been shown to translate to improved organ function or delayed clinical progression in patients with Fabry disease. The Committee considered that many years of ERT treatment may be necessary before meaningful clinical benefits, if any, would be seen in patients with Fabry disease.

The Committee considered that overall the evidence provided in the various submissions was poor in quality and weak to moderate in strength. The Committee noted that the evidence reviewed to date suggests that the most beneficial use of ERT is likely to be early in the course of disease, potentially in childhood, before the onset of proteinuria, left ventricular hypertrophy or other organ involvement and that treatment of established disease may not be clinically beneficial.

The Committee considered that there remained concerns around serious adverse effects, infusion related reactions and neutralising antibody formation with agalsidase. The Committee considered it to be still only a hypothesis that the higher dose of 1 mg/kg agalsidase beta may saturate existing antibodies overcoming the negative effect of neutralising antibody formation leading to greater effectiveness of the therapy (Vedder et al. Mol Genet Metab 2008; 94:319-25). The Committee considered that there are important unanswered questions about the optimum treatment for reversal, maintenance and prevention of Fabry's disease, optimum dosing protocols, including the frequency of infusions, and the long term risks and benefits of ERT treatment.

Mucopolysaccaridosis I (Hurler, Hurler-Scheie and Scheie syndrome)

The Committee considered a submission from Genzyme, the supplier of laronidase (Aldurazyme). Members noted that the recommended dose of laronidase in patients with mucopolysaccridosis I (MPS I) is 100U/kg weekly by IV infusion. The Committee further noted that this dose was established by Giugliana et al. (Mol Genet Metab 2009; 96:13-19) in a dose-optimisation study and that this dose provided the best benefit to risk ratio. The Committee noted that there is no data on the effect of dose reductions for laronidase once a patient is stabilised.

The Committee noted that the supplier did not provide any relevant new evidence for consideration. The Committee considered evidence from 2010 MPS I Registry Report (www.mpsiregistry.com) however, members noted that this did not contain any information on the ongoing clinical benefits of laronidase for MPS I patients. The Committee considered that although the supplier claimed that surrogate markers in clinical trials of 6 minute walk test (6MWT) and forced vital capacity (FVC) were "increasingly understood as predictors of survival in diseases such as MPS I" no published reference was provided to support this view.

The Committee also considered evidence from a case series observational study (Wynn et al. J Pediatr 2009; 154:135-9) of outcomes of stem cell transplantation in 18 consecutive patients with MPS I Hurler syndrome under two years old. Patients received weekly IV infusions of laronidase at 100U/Kg for 12 or more weeks pre-transplantation and until donor cell engraftment post-transplantation. The survival rate after first transplantation was 100%, however, 4 patients developed graft failure, all of whom required a second transplant and one a third. Of these 4 patients, two died and two successfully grafted the second time, thus overall, survival was 89%. Members noted that

the authors considered that historically, 15% children with MPS I Hurler syndrome do not survive transplantation and engraftment is unsuccessful in 44% of cases. The authors attributed the higher engraftment and survival results seen in the study as being due to the accumulated effect of full-intensity conditioning regimens, well matched donors, individualisation of GVHD prophylaxis and good supportive care. The authors' conclusion that the benefit of laronidase is linked to improvement in a patient's pre-transplantation condition and thus their tolerance of such intensive therapy was noted.

The Committee considered a submission from the National Metabolic Service (NMS) suggesting that laronidase could be targeted for patients with MPS I pre- and post-transplant. The Committee considered the evidence submitted by the NMS which comprised case studies reporting variable improvement in some patients in various end points: including exercise tolerance, respiratory function, joint pain and range of motion, sleep disorder, mobility, quality of life and mood.

The Committee considered that there was little new data provided since its previous review in 2009 and the strength and quality of evidence reviewed was weak. The Committee considered that laronidase may not improve organ systems when irreversible changes have already developed and it is ineffective in neurological disease. The Committee considered that virtually all patients develop IgG neutralising antibodies and more than half exhibit infusion related reactions. The Committee considered that use in the pre and post transplant setting requires further evidence and noted that such new evidence could be reviewed by them in the future.

Overall, the Committee considered that laronidase has a consistent but small effect on study end points out to 3.5 years and possibly 6 years although members noted the studies were small and considered that the effect may not be clinically meaningful. However, the Committee considered that the long term benefit of laronidase, and its effect on morbidity and mortality, is unknown at this time and requires longer term studies.

Mucopolysaccharidosis II (MPS II) – Hunter's disease

The Committee considered a submission from Genzyme, the supplier of idursulfase (Elaprase) for the treatment of Hunter's disease. The Committee noted that idursulfase is administered by weekly IV infusion at a recommended dose of 0.5mg/Kg over 3 hours to treat non-neurological manifestations of the disease.

The Committee considered three studies published since its last review which assessed the efficacy and safety of idursulfase. The Committee considered evidence from a prospective observational cohort study of idusulfase in 94 patients with MPS II, published after its last review in 2009 (Muenzer J et al. Genet Med 2011; 13:95-101). Members noted that all patients received IV idursulfase at a dose of 0.5 mg/kg weekly for 2 years. Members noted that no change from baseline in the percent predicted forced vital capacity was seen, but absolute forced vital capacity demonstrated sustained improvement and was increased by a mean of 25.1% by the end of the study ($p<0.05$). Members further noted statistically significant improvements in 6-minute walking test distance were observed at most time points with the greatest absolute improvement seen at 20 months (42m), but at 3 years the gain, although statistically significant ($p<0.01$), was only 25m ($p<0.01$). Members noted that mean liver and spleen volumes remained stable throughout the 2-year extension study. The Committee noted that infusion-related adverse events occurred in 53% of patients and peaked at month 3 of treatment and declined thereafter and that neutralising IgG antibodies were detected in 23% of patients and seemed to attenuate the improvement in pulmonary function.

The Committee considered evidence from a 12 month retrospective observational cohort study (Okuyama et al. Molecular Genetics and Metabolism 2010; 99:18–25) in 10 Japanese adults aged 21-53 years who received weekly idursulfase. Members noted that treatment with idursulfase resulted in significant reductions compared with baseline in urinary glycosaminoglycan, liver and spleen volume, but non-statistically significant reductions in forced vital capacity, the 6 minute walk test, left ventricular mass index, left ventricular ejection fraction and joint range of motion.

The Committee considered evidence from a study published by Muenzer J et al. (Genet Med 2011; 13:102-9), which used the Hunter Outcome Survey to carry out a retrospective analysis of open-labelled treated patients and included 124 patients younger than 6 years old, and 287 patients older

than 6 years. Members noted that treatment with idursulfase resulted in significant reductions in urinary glycosaminoglycans and liver size. Members noted that IgG neutralising antibodies were detected in 53.5% and 42.8% of patients younger and older than 6 years respectively. The Committee noted that the study authors concluded that long term observation would be required to determine whether early initiation could prevent progression of clinical disease.

The Committee considered evidence from by Glamuzina et al. (J Inherit Metab Dis 2011; 34:749-54) provided in the NMS submission, which retrospectively compared the populations enrolled in two studies (Muenzer et al. Genet Med 8:465–473, Muenzer et al. Mol Genet Metab 2007 90:329–337) to a treatment population from Great Ormond Street Hospital, London. The authors concluded that the end points used in the trials may not be applicable to everyday practice and could not be used as an indicator of treatment efficacy in the clinical setting. The Committee noted that the weaknesses of this study were its retrospective design and that the populations differed particularly in age, height and CNS disease. The Committee noted that these weaknesses mitigate the authors' conclusions.

The Committee noted that the supplier of idursulfase agreed with international guidelines that patients with neurological disease should not be treated, and made reference to a recent paper which demonstrated that in this population brain MRI features worsen despite ERT treatment (Manara et al. J Inherit Metab Dis 2011, 34:763 – 780).

Overall, the Committee considered that the quality and strength of the evidence provided for the idursulfase for MPS II was weak. The Committee considered that the most improvement, if any, occurred in the first 12-18 months of treatment with idursulfase, with little improvement thereafter. The Committee considered that infusion related reactions can be serious and life threatening. The Committee considered that the long term safety and efficacy of idursulfase remained unknown at this time and longer term studies were required.

Mucopolysaccharidosis VI (Maroteaux-Lamy disease)

The Committee noted that the supplier of galsulfase (Naglazyme) for MPS VI did not submit any relevant new information. The Committee considered the submission by the NMS in which it suggested that patients with severe MPS VI would probably be best managed by bone marrow transplantation, mild cases do not warrant ERT, and moderate cases should be assessed on a case by case basis. The Committee considered that the evidence previously reviewed was weak and showed no significant effect of galsulfase on respiratory, cardiac or musculoskeletal function, and has no effect on central nervous system disease.

Pompe disease

The Committee considered evidence submitted by Genzyme, the supplier of alglucosidase alpha (Myozyme) to support its use in the treatment of infantile, juvenile and adult-onset Pompe disease.

Infantile-onset Pompe disease

The Committee noted that it has previously reviewed evidence for infantile-onset Pompe disease in 2009. The Committee considered evidence from a retrospective observational cohort study by Chakrapani et al. (J Inherit Metab Dis 2010;33:747-50) which reported the outcome of all patients with infantile-onset Pompe disease treated in the United Kingdom since the availability of alglucosidase alpha. The Committee noted that a total of 20 infants were treated from 2000 to 2009 with median ages at diagnosis and treatment of 5.75 months and 6.5 months respectively and the median duration of treatment was 31 months. The Committee noted that overall ventilator free survival was 35%, while 35% died at a median age of 10 months and 30% were alive but ventilator dependent. The Committee considered that overall the outcomes in this study were worse than in the pivotal clinical trials, possibly due to later diagnosis and patients being at the severe end of the clinical spectrum.

The Committee also considered evidence from a retrospective observational cohort study by Chien et al. (Pediatrics 2009;124:1116-25) which reported outcomes for six patients with infantile Pompe disease, five of whom were screened at birth, diagnosed with a rapidly progressive form of Pompe disease and treated soon after diagnosis (12-34 days old). Members noted that the sixth patient was

started on treatment at 14 months of age because of progressive muscle weakness. The Committee noted that the five screened infants who had early cardiac involvement demonstrated normalisation of cardiac size and muscle pathology with normal physical growth and age-appropriate gains in motor development and survival was significantly improved compared with those in an untreated reference historical cohort (p=0.001). The Committee noted that the sixth patient who started on treatment at 14 months of age due to progressive muscle weakness also achieved normal motor development with treatment. The Committee noted that all patients were cross-reactive immunologic material (CRIM) positive.

The Committee noted that CRIM status may affect treatment outcomes in patients with infantile-onset Pompe disease. Members noted that the NMS agreed with this view and also noted that the response to ERT treatment is very variable. The Committee noted that to identify CRIM status in New Zealand takes approximately two months but the Adelaide LSD lab may be able to provide results in two weeks. However, members noted that the rationale to test for CRIM status at birth is weaker, in the absence of a funded treatment.

Overall, the Committee considered that the evidence suggests that early diagnosis and treatment, preferably before 6 months of age may be important in determining longer term outcomes and that alglucosidase alpha treatment may improve respiratory and motor function and lifespan in some patients, however the long term effect on morbidity and survival is unknown.

Juvenile and adult-onset Pompe disease

The Committee noted that it had reviewed the evidence to support the treatment of adult-onset Pompe disease with alglucosidase alpha most recently in February 2011. The Committee considered evidence from a prospective observational cohort study specifically looking at the effect of alglucosidase alpha treatment on juvenile-onset Pompe disease (Van Capelle et al. Neuromuscul Disord 2010; 12:775-82). The Committee noted that the authors reported that five patients aged between 5 and 16 years treated with 20 mg/kg alglucosidase alpha every two weeks over a three year period showed no deterioration was seen in lung function and muscle strength and small gains were made by some patients.

The Committee considered a long term prospective observational, non-randomised cohort study involving 24 patients including 7 juveniles and 17 adults in which patients received bi-weekly infusions of alglucosidase alpha (20 mg/kg) for at least 36 months (Bembi et al. J Inherit Metab Dis 2010; 33:727-35). Members noted that the authors reported that compared to baseline, patients had significant improvements in motor function (as assessed by Walton scale) and 6 minute walk test at 3 years. The Committee noted that there was a great variation in results, especially for the adult population. Committee considered that in both juvenile and adult patients, gains were made in the first 12 months and then stabilised over the next 2 years (which is similar to the pattern observed in the pivotal Van der Ploeg et al. 2010 trial which PTAC reviewed in Feb 2011). The Committee noted that muscle strength improved only in juvenile patients and adult patients with mild to moderate disease severity while the 6 minute walk test response improved across all patients. The Committee noted that forced vital capacity and FEV1, remained stable and fewer patients required ventilator support and for less time compared with baseline. The Committee considered that there appeared to be a consistent effect on surrogate endpoints in all groups but the effect across patients was very variable.

The Committee considered a retrospective observational cohort study by Güngör et al. (J Inherit Metab Dis 2011; 3: 441 abstract and poster) which looked at the impact of alglucosidase alpha treatment on survival in 196 patients with adult-onset Pompe disease compared with an historic control group of 75 patients who had never received ERT. The Committee noted that the authors suggested that ERT extended lifespan with mortality reported to be 36% in the untreated group compared to 9% in the treated group. The Committee noted the data it was reviewing was abstract and poster only and so it could not review the quality of the study. The Committee noted that the median treatment duration was 4 years and median follow up time was 6 years. The Committee noted the authors concluded that a longer follow up was needed to elucidate the relationship between ERT, disease severity and survival of adults with Pompe disease.

The Committee considered that the evidence suggests that the optimum dose of alglucosidase alpha is 20mg/kg with no added benefit of higher doses. The Committee noted that PHARMAC have carried out a cost utility analysis for alglucosidase alpha in patients with adult-onset Pompe disease which indicated that it was cost-ineffective relative to other funding options.

The Committee considered that the claim by the supplier that alglucosidase alpha was 'life-saving' is misleading to patients and not supported by the evidence.

Overall, the Committee considered that the quality of the evidence for alglucosidase alpha in the treatment of infantile, juvenile and adult-onset Pompe disease was poor and the strength weak to moderate. The Committee considered that the evidence supports the benefit of treatment on some surrogate end points, however the long term effect on morbidity and mortality is still unknown. The Committee considered that there is little evidence to support treatment of patients with established disease and with irreversible end organ disease. The Committee noted the significant unmet health need faced by patients with Pompe disease, but considered this to be outweighed by the lack of evidence for clinically significant benefit and the disproportionately high cost of disease-modifying treatment.

From: Rachel Melrose
Sent: Tuesday, 8 April 2014 10:19 am
To: Michael Johnson ([redacted])
Cc: [redacted]; Jude Urlich
Subject: No surprises - discussion documents being released today
Attachments: 2014-03-19 PHARMAC's Review of the Named Patient Pharmaceutical Assessment Policy (NPPA) - Seeking Your Views#2.docx; High Cost Treatments for Rare Disorders - Seeking Your Views.docx

No surprises – Discussion documents on NPPA and high cost medicines being released by PHARMAC today

PHARMAC is seeking feedback on our Named Patient Pharmaceutical Assessment (NPPA) policy as part of the rolling review of our Operating Policies and Procedures (OPPs). The NPPA policy has been in place for two years, and in that time it's also been updated to manage hospital medicines. We are seeking views on the NPPA Policy, and any other issues the public and sector may have with PHARMAC's provision of subsidies for exceptional circumstances. The consultation document is attached, and can be found on our website from 11am today: www.pharmac.health.nz/link/nppa-review

We are also releasing a discussion document outlining our plans for a contestable fund, intended to give people better access to medicines for rare disorders. The discussion document shares our thinking on the topic to date, and invites stakeholders' input to iron out the details about how the fund would work. Our intention is to seek commercial offers for access to the fund by the end of this year. The discussion document is also attached, and can be found on our website from 11am today: www.pharmac.health.nz/link/high-cost-medicines

Kind regards,

Rachel

Rachel Melrose | Senior Policy Analyst, Engagement & Implementation

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High Cost Medicines for Rare Disorders

Discussion document and a request for your input

We've been doing some thinking about access to high cost medicines for rare disorders, and we want your input to help us develop an alternative commercial approach.

EXECUTIVE SUMMARY

There is on-going public interest on the topic of access to high cost medicines for rare disorders. Feedback we've received as part of our ongoing consultations has led us to again consider this issue.

The issue of access to high cost medicines for rare disorders is likely to be an on-going one. It's likely that medicines in the future will be increasingly expensive and targeted at relatively few patients. Although PHARMAC does fund some expensive medicines, a high price reduces the likelihood that a medicine will be funded, all else being equal, because of the impact that price has on two decision criteria – cost effectiveness and budgetary impact. Suppliers understand the consequences of this, and know that medicines that cost many tens of thousands of dollars per year are less likely to be funded unless clear delivery of substantial health benefits can be proven. Given that they charge these prices overseas, suppliers have little incentive to cut their prices here in New Zealand, in part because doing so would raise questions about their high prices elsewhere.

We've been doing some thinking about whether a contestable fund and bidding process specifically for high cost medicines for rare disorders could demonstrate to suppliers that we want to improve access to these treatments, and could encourage them to propose more competitive pricing offers than they have done to date. If successful this could lead to better pricing for these medicines, resulting in improved access and, ultimately, better outcomes for patients with rare disorders. We're proposing to use an existing funding pool to avoid having to make direct trade-offs within each annual budget cycle against other medicines that with the current approach offer better value for money.

Establishing a contestable high cost medicine fund would create risks, and regardless of what approach we take, there will always be some treatments that we can't fund within our fixed overall budget. We're proposing to establish a contestable fund to help establish whether a different approach might be able to improve competitive tension and reduce prices. We still need to work out the scope, process and entry criteria for the fund, but we intend to run it as a Request for Proposals (RFP), whereby suppliers of medicines that meet the pre-requisites would be invited to bid for a capped fund. The approach adopted will need to be consistent with PHARMAC's statutory objective.

The commercial approach could be evaluated in terms of whether we receive good commercial offers, whether access to effective pharmaceutical treatments and health outcomes for patients are improved, and whether the risks to the overall PHARMAC model are managed.

We're aiming to have something ready by the end of this year, and we want input from the public and suppliers to help us design the RFP. We encourage you to give us your feedback on our approach and to meet with us to discuss how it might work.

DISCUSSION

We've heard the public's concern about access to high cost medicines for rare disorders…

There is on-going public interest on the topic of access to high cost medicines for rare disorders. Feedback we've received as part of our consideration of eculizumab for paroxysmal nocturnal haemoglobinuria (PNH) and alglucosidase alfa for adult late-onset Pompe disease, along with our Decision Criteria consultation, has led us to again consider this issue. Patient groups and their representatives also raised the issue during the 12 community forums we held from July to September 2013, with one group proposing that PHARMAC establish a separate, competitive, high cost medicines pool.

…which is likely to increase in the future.

The issue of access to high cost medicines for rare disorders is likely to be an ongoing one. Some commenters (such as the McCormack Panel in 2009[1]) have noted that in the future medicines will be increasingly targeted at relatively few patients; more expensive than the ones currently available; and there will not be many new 'blockbuster' medicines that have a high uptake and are sold at a relatively low cost over time. The Nature Reviews journal noted in 2012 that the pharmaceutical industry has been moving from a blockbuster model towards 'niche-buster' opportunities[2]. In the past few years, medicines for rare conditions accounted for over 35% of the new drugs approved by the US Food and Drug Administration (FDA), 22% of the new chemical entities, and 31% of the biologics[3]. The global orphan drugs[4] market reached $84.9 billion in 2009, growing from $58.7 billion in 2006. The market is expected to grow at a compound annual growth rate of nearly 6% to reach $112.1 billion by 2014[5].

The Treasury has noted in its Long Term Fiscal Statement (2009) that "the main drivers of health spending have been and will continue to be income growth and technological change – both of which affect the demand for, and the cost of supplying, health care". Public expectations of the health system increase as technology progressively extends the range of possible treatment options. This suggests that not only is it likely that medicines will become increasingly expensive, public expectations about access to pharmaceuticals are also likely to increase.

PHARMAC does fund some high cost medicines…

PHARMAC does fund some expensive medicines. In the 2012/13 financial year, 86% of PHARMAC's expenditure was spent on 20% of patients[6]. The highest amount spent in

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[1] McCormack, P; Quigley, J; Hanson, P; *Review of Access to High-Cost, Highly-Specialised Medicines in New Zealand. 2009*

[2] Melnikova, I: *Rare Diseases and Orphan Drugs*. Nature Reviews – Drug Discovery, Volume 11, (April 2012)

[3] Melnikova, I: *Rare Diseases and Orphan Drugs*. Nature Reviews – Drug Discovery, Volume 11, (April 2012)

[4] Orphan drugs are pharmaceuticals that have been developed specifically to treat a rare medical condition.

[5] Sharma, A et al. *Orphan Drug: Development Trends and Strategies.* Journal of Pharmacy and BioAllied Sciences (2010).

[6] To respect the commercial arrangements PHARMAC has with some suppliers, these figures do not reflect any rebates.

2012/13 on one patient (for one treatment) was approximately $450,000[7]. Out of the six medicines that New Zealand has received applications for[8] that are funded by the Australian government as part of their Life Saving Drugs Programme, three have been funded, either on the Schedule or for particular named patients.

In New Zealand, the definition of what medicines are considered to be 'high-cost' will continue to change over time. Funding a medicine 10 years ago at $20,000 for each person per year was considered to be very high-cost, while now it is more in the order of $20,000 to $100,000. In 2013, PHARMAC received applications for pharmaceuticals costing over $500,000 per patient per year.

…but because treatments for rare disorders are often priced very highly…

Treatments for rare disorders are often priced very highly, and suppliers claim this is due to the need to recoup the fixed costs of research and development (R&D) across lower volume or patient numbers.

However, the BMJ journal noted in 2012 that more than four fifths of all funds for basic research to discover new drugs and vaccines come from public sources[9]. Many countries have supported the development of drugs for rare conditions through public funding of research, lowered registration costs, and extensions to market exclusivity. These incentives, combined with developments in genetic targeting and in human monoclonal antibodies, have led to a rapid rise in the number of products available for relatively limited populations. However, despite the incentives and subsidies, many of these new products are priced at a level that makes them very poor value for money compared to other treatments used in wider populations, or even to other therapies used to treat the same condition.

Suppliers also claim that it is often difficult to build sufficient clinical evidence due to natural limitations on the size of randomised controlled trials (RCTs), because of the rarity of the conditions. However, this also means that orphan drugs potentially offer some financial advantages to pharmaceutical companies over conventional medicines, including faster development timelines, lower research and development expenses, a higher likelihood of clinical and regulatory success, premium pricing, lower marketing costs and a lower risk of generic competition[10].

According to the Tufts Centre for the Study of Drug Development, companies reported that 22% of their programmes designated as orphan drugs led to FDA approvals between 2000 and 2009, whereas the clinical approval success rate for mainstream drugs was 16%[11]. Arguments about high prices being necessary to recoup research have also been discredited by several commentators,[12] concerned that the true cost of research is masked by access to Government research subsidies, calculations of profits

[7] To respect the commercial arrangements PHARMAC has with some suppliers, these figures do not reflect any rebates.
[8] Nine medicines are listed as part of the LSDP programme, but PHARMAC has not received applications for three.
[9] *BMJ*2012;345doi: http://dx.doi.org/10.1136/bmj.e4348 (Published 7 August 2012)
[10] Melnikova, I: *Rare Diseases and Orphan Drugs*. Nature Reviews – Drug Discovery, Volume 11, (April 2012)
[11] Melnikova, I: *Rare Diseases and Orphan Drugs*. Nature Reviews – Drug Discovery, Volume 11, (April 2012)
[12] Roger Collier, "Drug development cost estimates hard to swallow", CMAJ, 3 February 2009, 180(3): 279-280

foregone rather than out-of-pocket expenses, and payments to doctors. PHARMAC is also aware that not all medicines for rare diseases are priced highly.

… they often don't compare favourably to other medicines…

A high price can reduce the likelihood that a medicine will be funded because of its impact on two different decision criteria: cost effectiveness (PHARMAC decision criterion five[13]) and affordability / budgetary impact (decision criterion six). Because price is a large component of cost, an expensive medicine is less likely to be cost-effective, all else being equal. Price also affects affordability, along with the size of the population group, the likely uptake rate, and the average dosage. It is possible for a medicine to be cost-effective but not affordable, or to be affordable but not cost-effective.

This means that very high cost treatments often do not compare favourably to other medicines that benefit larger populations and achieve greater overall health gains for less money. In the case of eculizumab for PNH for example, we estimate that at the current price, funding eculizumab instead of other treatments would mean tens of thousands of New Zealanders would miss out on new medicines that offer more health gain overall.

…and suppliers are dis-incentivised to make competitive offers.

New Zealand is only 0.1% of the global pharmaceutical market, and many other countries fund high-cost treatments for rare disorders. In our experience New Zealand is generally a price taker for these treatments and has been unable, with our current commercial approach, to influence pricing to an extent that would see such treatments compare favourably to other medicines we consider.

Suppliers are aware that PHARMAC's current funding approach means that very highly priced medicines are less likely to be funded, and so they may be dis-incentivised to propose competitive offers that could undermine their global pricing strategy, especially where there may also be a limited likelihood of such activity being successful in securing funding.

A fixed contestable pool could improve competition….

PHARMAC is intending to develop an alternative commercial approach. The idea is that a separate funding pool and bidding process specifically for treatments for rare disorders could demonstrate to suppliers that funding is available to improve access to these medicines, and incentivise them to propose more competitive offers than they have done to date. If successful this could lead to better pricing offers for these medicines, which may result in better outcomes for patients.

We're still working out the details of the scope, process and entry and exit criteria for the proposal, although we intend to run it as a Request for Proposal (RFP), whereby suppliers of treatments that meet the pre-requisites would be invited to bid for a capped fund.

[13] Our current nine decision criteria are currently under review. Refer to our website for more information http://www.pharmac.health.nz/about/operating-policies-and-procedures/decision-criteria-consultation

The proposal could be evaluated in terms of whether it incentivises suppliers to provide better commercial offers, whether access to effective pharmaceutical treatments and health outcomes is improved, and to ensure the approach supports PHARMAC's ability to secure the best health outcomes that are reasonably achievable from the funding provided in accordance with our statutory objective.

... but bring new risks.

Establishing a high cost treatment pool would create risks. Key among them is the risk that funding some high-priced treatments establishes a new, higher benchmark for pricing of new products, and reduces incentives on suppliers to develop and sell products that offer good value for money and continue to improve the cost-effectiveness of public health spending in New Zealand.

Regardless of what approach PHARMAC takes, there will always be some treatments that we are not able to fund as there will always be more investment options available than funds. Consequently the discussion about access to funded pharmaceuticals is likely to always exist in some form.

CONTESTABLE FUND PROPOSAL

We still need to work out the detail of how a contestable fund would work, but some of our current ideas are outlined below. These ideas are only provided to give a sense of how the proposal could work - we're seeking your input to help us decide on the best process, prerequisites and evaluation criteria.

Process

Suppliers could be invited to submit funding proposals for medicines[14] that meet the prerequisites (listed below) by a set deadline.

Suppliers could be required to submit proposals that can be managed from within a fixed funding provision i.e. they would need to involve some form of risk-sharing that manages the risk to PHARMAC of a significant growth in patient numbers. Suppliers could bid, for example, for a fixed amount of funding for which they would supply all patients regardless of the size of the patient population, so that the risk of the patient group being lower than forecast would be borne by PHARMAC, and the risk of the patient group being higher than forecast would be borne by the supplier.

Suppliers would also be able to propose patient entry and exit criteria, but these would need to ensure that patients with the same clinical circumstances receive the same level of access, to ensure equity of access for patients. Further consideration would need to be given to the ways in which suppliers' commercial sensitivities about pricing could be managed, given the small patient numbers and the fixed nature of the fund.

All eligible proposals could then be considered and clinical advice obtained, before they are prioritised against each other and the size of the fund. The current Decision Criteria[15] could be used for this purpose, or we could consider alternative prioritisation methods.

On-going eligibility for patients could be considered at appropriate intervals, based on whether there has been a clinical improvement in the patient or a stabilisation of the

[14] The scope of the proposal would include medicines, but not medical devices, as the issue is one of improving access to high cost medicines.
[15] We note that the current decision criteria are being reviewed.

patient's condition. Any entry and exit criteria would need to be agreed before the treatment is started.

Prerequisites

Entry prerequisites would need to be considered in more detail, but prerequisites along the following lines could be considered:

Disease related:

1. There is a rare[16] but clinically defined disease for which the drug is regarded as a proven therapeutic modality (i.e. has been approved by Medsafe for that indication).
2. The disease is identifiable with reasonable diagnostic precision.
3. Epidemiological and other studies provide evidence that the disease causes a significant reduction in either absolute or relative age-specific life expectancy or quality of life, for those suffering from the disease.

Treatment related:

4. Clinical advice suggests the treatment is likely to be clinically effective.
5. The patient's lifespan or quality of life could be substantially improved as a direct consequence of the treatment[17].

Alternatives related:

6. The treatment or chemical is not indicated for the treatment of another, non-rare, disease (or if it is, the combination of prevalence still falls within the definition of rare)[18].
7. There is no alternative treatment on the Pharmaceutical Schedule.
8. There is no suitable[19] alternative non-drug therapy for the rare disorder.

Cost / market related:

9. Total market value, based on the price and the supplier's proposed expenditure cap, is less than a set figure.

Funding

PHARMAC has been successful in transferring 26 medicines that we received Named Patient Pharmaceutical Assessment (NPPA) applications for in 2012/13 (and 16 so far in 2013/14) onto the Pharmaceutical Schedule. This has the effect of providing greater access to patients, reducing administrative workload for clinicians, and providing greater certainty for patients and clinicians alike. The agreed funding provision for NPPA is $8 million per annum, although, as stated in our original policy objective, we anticipated this expenditure level would reduce as we listed more medicines on the Schedule. We

[16] 'Rare' would need to be defined. In the UK an orphan disease is defined as a disease with a prevalence of less than five cases per 10,000 and an ultra-orphan disease as 1:50,000. In the USA, it is defined as 1:1,500, in Japan as 1:2,500 and in the EU as 1:2,000. The UK's definition of ultra-orphan (1:50,000) is probably the most useful definition for the purposes of the proposal, which would imply fewer than 90 people per condition across the whole of New Zealand.

[17] This could be measured by absolute or proportional QALY gain.

[18] Bidders could be required to reveal their overseas approved indications, their phase 3 development program and any relevant patents.

[19] Further consideration could be given as to how 'suitable' could be defined. It could be defined as a treatment that provides a comparable health outcome.

anticipate a projected surplus of up to $5 million in this NPPA funding provision next year, which means this funding could be made available for use in a contestable fund for high cost medicines.

Evaluation Criteria

The success of the proposal could be evaluated against the following criteria:

- Access to effective pharmaceutical treatments is improved.
- Health outcomes for those patients who receive funded treatments via the proposal
- Financial risk is managed, and expenditure does not exceed the value of the funding provision.
- PHARMAC receives better commercial proposals for eligible treatments than those that have been received in the past.
- PHARMAC's ability to negotiate good prices for the rest of the Pharmaceutical Schedule is maintained, for the purposes of securing the best health outcomes for New Zealanders.

WE WANT TO HEAR FROM YOU

The purpose of this discussion document is to share our thinking, and to seek your feedback on how a contestable fund could work. We still need to work out the detail, and we would appreciate your input to help us do that. We're working towards requesting commercial proposals by the end of this year. We're interested in meeting with suppliers, patient groups and anyone else that has an interest in this work.

If you would like to meet with us, please contact us via email, fax, or letter to:

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Please note that any feedback we receive from you is subject to the Official Information Act 1982 (OIA). This means it, and your identity, may need to be disclosed in response to a request under the OIA. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information, please advise us of this and clearly identify the relevant sections of your feedback that you would like withheld. PHARMAC will give due consideration to any such request.

From: Jenny Langton
Sent: Monday, 22 September 2014 2:13 pm
To: Michael Johnson
Cc: Jude Urlich; Withheld under section
Subject: No surprises update - Myozyme for Pompe Disease

No surprises update - Myozyme for Pompe Disease

PHARMAC has completed its consideration of funding of Myozyme for two patients with Pompe Disease. PHARMAC has reconfirmed its view, to decline funding these treatments.

This process followed an initial decision to decline funding for one patient, after which the patient and support groups – including the NZ Organisation for Rare Disorders – complained to the Ombudsman about the decision and PHARMAC's process for reaching it.

In 2013 the Ombudsman reviewed the case and, while upholding the PHARMAC decision, suggested PHARMAC consider any further representations about allowing funding for Myozyme on a trial basis for the patient.

PHARMAC received further representations including some new information, completed a new analysis using the most positive view possible on the potential clinical benefits of treatment and sought fresh advice from its clinical advisory committee PTAC. PTAC considered the new evidence insufficient to warrant a change in the Committee's previous recommendation to decline funding for alglucosidase alfa for patients with Pompe disease.

PHARMAC would like to be in a position to make an effective, reasonably priced, treatment available to people with Pompe disease. Having considered all nine criteria, the main issue for Myozyme is that the evidence shows only limited, if any, clinically relevant effectiveness. This, combined with the very high price of Myozyme (about $500,000 per patient per year), means that PHARMAC cannot justify making funding available. If it were to do so, it would potentially mean many thousands of New Zealanders missing out on other more effective treatments.

The request on behalf of the two patients, was for the PHARMAC Board to reapply its nine decision-criteria to the applications. PHARMAC staff have carefully reviewed the further representations and information, including seeking further advice from PTAC, and concluded that it is not necessary or appropriate at this time to reapply a full PHARMAC decision process to these applications, as there is nothing available that could reasonably support a different outcome. As a result it was not considered necessary or appropriate to refer the matter to the Board.

We will be writing to the patients and their supporters (including NZORD and the Lysosomal Disorders NZ group) to outline the decision. It is possible these groups will continue to press for funding via media coverage and/or approaching politicians.

Kind regards
Jenny

Jenny Langton | Manager, Policy
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From: Simon England
Sent: Monday, 17 October 2016 11:56 am
To: Michael Johnson
Cc: Peter Alsop; Kerri Osborne
Subject: No surprises, proposal for medicines for rare disorders

Hi Michael

Below is information provided on a no surprises basis regarding a consultation we are beginning this afternoon, regarding medicines for rare disorders (including Pompe Disease).

PHARMAC has reached a provisional agreement with Sanofi Genzyme to list three medicines on the Pharmaceutical Schedule for rare enzyme deficiency disorders, for defined uses. This is part of our funding pilot for medicines for rare disorders.
Medicines proposed are:

Alglucosidase alfa (Myozyme) for infantile-onset Pompe Disease (proposed listing date 1 December 2016).
Idursulfase (Elaprase) for Hunter Syndrome (MPS II) to stabilise patients awaiting stem cell transplant (proposed listing date 1 December 2016).
Laronidase (Aldurazyme) for Hurler Syndrome (MPS 1-H) to stabilise patients awaiting stem cell transplant (to be listed once registered by Medsafe).

Listing laronidase and idursulfase would make these medicines more readily available and reduce the administrative task for clinicians wanting to access them. We've previously approved their use through exceptions policies.

Alglucosidase alfa would be funded for infantile-onset Pompe Disease, because evidence shows this is where there is the greatest potential for patients to benefit. Our expert clinical advisers told us that, because the disease can progress very quickly in children, treatment can be potentially life-saving. This, combined with a lower cost in children (dosage is weight-based) makes a funding proposal possible.

If approved, this agreement would mean we would have listed nine medicines from our rare disorders RFP.

We're anticipating a further consultation on another medicine occurring. We will then begin evaluating the rare disorders pilot.

PHARMAC remains open to considering funding for Myozyme for other forms of Pompe Disease. We have received a new funding application for Myozyme for late-onset Pompe Disease, and will seek further clinical advice from PTAC in November. This application, which is not related to the rare disorders RFP, is the first time a supplier has made a Schedule funding application for Myozyme.

Please let me know if you need further information.

Kind regards

Simon England APR | Senior Communications Advisor

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From: Peter Alsop
Sent: Wednesday, 8 February 2017 11:40 am
To: Kerri Osborne; Rebecca Elliott
Subject: FW: No surprises update - release of Myozyme PTAC minute

Sorry I didn't check recipient list on this to let you know …
Thx for checking
P

Peter Alsop | Director of Engagement and Implementation

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From: Simon England
Sent: Tuesday, 31 January 2017 11:48 AM
To: Michael Johnson <Withheld under section 9(2)(a)>
Cc: Peter Alsop <Withheld under section 9(2)(a)>; Jude Urlich <Withheld under section 9(2)>
Subject: No surprises update - release of Myozyme PTAC minute

Hi Michael

This is a no surprises update regarding information we will be releasing this week on our consideration of funding for the enzyme replacement treatment alglucosidase alfa (Myozyme). This has been an issue for some years and the release of this information will be of high interest to stakeholders with an interest in medicines for rare disorders.

Our clinical advisory committee, PTAC, has conducted a thorough review of all the evidence about alglucosidase alfa for late-onset Pompe Disease (LOPD). PTAC has recommended to PHARMAC that funding for Myozyme for LOPD be declined. This will likely come as a disappointment to patients and supporters of people with Pompe Disease.

While we'd very much like to provide a funded and effective medicine for people with Pompe Disease, the evidence for Myozyme doesn't show that it would benefit patients sufficiently to justify the price asked by the supplier.

We've recently decided to fund Myozyme for infantile-onset Pompe Disease - because evidence shows this is where there is the greatest potential for patients to benefit. However, in late-onset Pompe Disease the evidence shows limited and uncertain benefits and raises questions over whether benefits last very long.

We continue to be in discussions with Sanofi-Genzyme regarding pricing and other information that may become available.

This funding application has been progressed separately to our rare disorders contestable funding pilot, which resulted in medicines being funded for 10 rare disorders, including infantile-onset Pompe Disease.

Please let me know if you need anything further.

Kind regards

Simon England APR | Senior Communications Advisor

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From: Rebecca Elliott
Sent: Wednesday, 8 February 2017 2:16 pm
To: 'Withheld under section 9(2)(a)'
Cc: Angela Mansell; Jenny Langton
Subject: RE: Urgent briefing for the Minister on rare disorders

Hi David,

The bullets below summarise current work or BAU activity that would be useful context for the Minister to include in the Ministry's briefing. For your information, the Minister has been briefed on the rare disorders evaluation and the Myozyme minute through No Surprises briefings.

- PHARMAC's contestable funding trial for medicines with rare disorders came to a close in December 2016, and the evaluation of this process is now underway. PHARMAC is seeking an external service provider to undertake the evaluation through the All of Government procurement process. PHARMAC is also seeking feedback from external stakeholders who were involved in the RFP process. This feedback will feed into the external evaluation which we may release publicly at the end of the evaluation process which we expect will be May-June.

- The results of the evaluation will contribute to PHARMAC's deliberations on what should occur in future. Broadly, the outcomes would be further utilisation of the approach used in the pilot; adoption of a modified approach; or use of no special approach at all. We will brief the Minister at the completion of this evaluation on the outcome, and proposed next steps. PHARMAC is meeting with NZORD on Thurs 9 February to get their feedback in person on how the process ran.

- On 31 January, the minute from PHARMAC's clinical advisory committee (PTAC) was published on the application from Sanofi Genzyme for alglucosidase alfa (Myozyme) for the treatment of late onset Pompe disease (LOPD). PTAC has recommended that the application be declined, as evidence shows limited and uncertain benefits for LOPD and raises questions over whether benefits last very long. The next stage in the decision-making process is for PHARMAC to compile any further information relevant to our Factors for Consideration and then rank this application against all other applications for funding (our prioritisation process). Applications with a relatively high ranking are more likely to be progressed for negotiation and a listing decision than those with a low ranking.

- PHARMAC has funded Myozyme for infantile-onset Pompe Disease through the rare disorders contestable funding pilot because evidence shows this is where there is the greatest potential for patients to benefit. PHARMAC was in contact with NZORD and the relevant patient groups following the publication of this minute.

- PHARMAC's Medical Director has been invited, and will be attending, the rare disorders day cocktail evening later in February.

- PHARMAC has assisted the Ministry of Health with a response to NZORD and the Health & Disability Intelligence group regarding the estimated prevalence and total annual costs for a select list of rare disorders. The Ministry provided the data which PHARMAC approved the use of, and we emphasised that important explanatory detail associated with the information should accompany its use.

Please let me know if you have any questions or need any clarification on the below. As noted earlier I will follow up with you if anything further comes from our meeting with NZORD tomorrow that may be useful to add.

Kind Regards
Rebecca

Rebecca Elliott | Senior Policy Analyst

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From: Withheld under section 9(2)(a)
Sent: Wednesday, February 8, 2017 10:21 AM
To: Rebecca Elliott <Withheld under section 9(2)(a)>; Angela Mansell <Withheld under section 9(2)(a)>
Subject: Fw: Urgent briefing for the Minister on rare disorders

Hi Rebecca and Angela,

I just received an "out of office" reply to my email to Jenny Langton (immediately below).

Can one of you answer the question about approximately when the PHARMAC information about rare disorders will be sent to me today?

Cheers,

David

Dr David St George
Chief Advisor
Office of the Chief Medical Officer
Ministry of Health
Wellington
New Zealand

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Mobile: Withheld
http://www.health.govt.nz
Withheld under section 9(2)(a)

---- Forwarded by David St George/MOH on 08/02/2017 10:17 a.m. ----

From: David St George/MOH
To: Jenny Langton <Withheld under section>,
Date: 08/02/2017 10:16 a.m.
Subject: RE: Urgent briefing for the Minister on rare disorders

---

Hi Jenny,

Do you happen to know approximately what time today the information for the Minister's briefing will be sent to me?

Cheers,

David

Dr David St George
Chief Advisor
Office of the Chief Medical Officer
Ministry of Health
Wellington
New Zealand

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Mobile: Withheld
http://www.health.govt.nz
Withheld under section 9(2)(a)

From: Jenny Langton <Withheld under section >
To: Withheld under section 9(2)(a)
Date: 03/02/2017 11:53 a.m.
Subject: RE: Urgent briefing for the Minister on rare disorders

---

Great, thanks David.

We actually have a meeting with Letitia on the 9th so there may be some additional comment that we need to provide after that (alternatively we can give a heads up directly to the Mins office).

Best
Jenny

From: Withheld under section 9(2)(a)
Sent: Friday, February 3, 2017 9:43 AM
To: Jenny Langton <Withheld under section 9(2) >
Subject: RE: Urgent briefing for the Minister on rare disorders

Yes, that will be fine.

From: Jenny Langton <Withheld under section >
To: Withheld under section 9(2)(a)
Cc: Rebecca Elliott <Withheld under section >, Angela Mansell <Withheld under section >
Date: 03/02/2017 09:41 a.m.
Subject: RE: Urgent briefing for the Minister on rare disorders

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Hi David

Thanks for this, I've copied in Rebecca and Angela – between us we can definitely provide you with some advice to include in the Minister's briefing. Of key interest to Letitia will be our rare disorders funding pilot and our intended evaluation of that.

If we got some words to you by Wednesday 8 Feb would that be ok?

Best
Jenny

From: Withheld under section 9(2)(a)
Sent: Friday, February 3, 2017 9:33 AM
To: Jenny Langton <Withheld under section 9(2)>
Subject: Urgent briefing for the Minister on rare disorders
Importance: High

Hi Jenny,

I'm not sure if you are the right person to contact - if not, could you please forward this to the right person.

The Minister is meeting with Letitia O'Dwyer, CEO of NZORD, on 16th February and I have been asked to do a briefing for the meeting (to be in the Minister's office by Friday 10th February).

Are there any current PHARMAC issues (e.g., about rare disorders and orphan drugs) that the Minister should be made aware of in advance of the meeting? Or anything else of relevance that PHARMAC would like to put into the briefing?

Many thanks,

David

Dr David St George
Chief Advisor
Office of the Chief Medical Officer
Ministry of Health
Wellington
New Zealand

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http://www.health.govt.nz
Withheld under section 9(2)(a) **********

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PHARMAC

Pharmaceutical Management Agency

BRIEFING

Improving access to effective treatments for rare disorders

Date 3 November 2017
To The Hon Dr David Clark (Minister of Health)

Copies to

PHARMAC Board
DHB spokesperson on pharmaceutical issues
Director General of Health
Deputy Director-General, Corporate Services
Manager Governance & Crown Entities

Recommendations

It is recommended you:

- **note** the findings from the evaluation of the contestable funding pilot to improve access to funded treatments for rare disorders were favourable; and
- **note** PHARMAC will run a regular, dedicated approach from mid-2018 to improve funded access to treatments for rare disorders.

Contact(s)

Steffan Crausaz, Chief Executive
Jude Urlich, Director of Engagement and Implementation

Withheld under
Withheld under

Purpose

To provide you with an overview of PHARMAC's contestable funding pilot for rare disorders medicines and discuss next steps to improve access to funded medicines for rare disorders.

Executive Summary

- Medicines for rare disorders are often priced very highly and high launch prices are a matter of global debate. There is no competition for branded products which are on patent and for which there are no alternative medicines available. Suppliers can command premium prices that usually pressure public funders to pay the high price or occasionally to exercise the option to decline to fund any access. Due to the price premium obtained from selling products with market exclusivity, research expenditure on medicines for rare disorders has increased relative to medicines for common conditions.

- To tackle this global issue and improve access to effective treatments for rare disorders PHARMAC trialed a contestable funding pilot 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 – as a result of the pilot better commercial proposals were received, there were new suppliers to the New Zealand market and funded access to treatments for rare disorders improved. Stakeholders including suppliers, clinicians and consumers were supportive of the pilot and their feedback is published on PHARMAC's website alongside the evaluation report.

- PHARMAC undertook to advise stakeholders by the end of the year on our view as to the future use of contestable funding for medicines for rare disorders. During the pilot we adopted a high-trust model with clinicians and consumer advocacy groups by having regular contact in advance of the public release of information.

- PHARMAC's own assessment was consistent with the external evaluation. We were pleased to have funded 10 medicines through the RFP and a related medicine for a rare disorder through our regular process, we removed administrative hurdles for clinicians and attracted two suppliers new to New Zealand. However, in a small number of cases decisions were made that did not compare favourably to alternative uses of the funding through our regular process. Our future process would be designed to avoid this, whilst retaining the overall benefits.

- PHARMAC appreciates there is Government interest in improving access to treatments for people with rare disorders, including greater consumer engagement. PHARMAC has been working on similar objectives, and has obtained some insights from our recent experience trialing a new approach to improve access which has informed our current view.

- We have decided to adopt a set of dedicated features for considering rare disorders medicines through our existing processes:
    - a standing PTAC expert subcommittee for rare disorders to be established;
    - a regular call for rare disorders funding applications commencing in late 2018;
    - undertaking dedicated pre-engagement with new, as well as existing, suppliers prior to each call for funding applications (ie commencing early in 2018);
    - confirming our adjusted policy settings for rare disorders treatments on which we had consulted, in particular the definition of 'treatments for rare disorders' and removal of the requirement for Medsafe approval prior to making applications;

- regular review of the portfolio of rare disorders treatments with good or reasonable opportunities for investment to be progressed through our routine process, or where a portfolio of rare disorders investments offers an opportunity to better obtain health gain, a contestable funding process or alternate commercial approach would be used, dependent on circumstances with the amount available to vary as needed.

- PHARMAC notes that you may wish to obtain further information regarding our future use of a contestable funding process, prior to our view being shared with stakeholders.

Highly-priced medicines for rare disorders

Rare disorders are any disease that affects a small percentage of the population. Nearly all genetic disorders are rare disorders and there are also very rare forms of infectious diseases. Rare disorders are often chronic and progressive.

Different countries adopt difference prevalence ratios or thresholds for rarity, partly because a disease can be rare in one region but common in another, but also in order to target policies. For example, the US the orphan drug designation programme is for diseases or disorders that affect fewer than 200,000 persons; the UK Strategy for Rare Diseases (2013) identifies between 5,000 and 8,000 rare diseases, with each one affecting less than 0.1% of the UK population.

PHARMAC defines a rare disorder as a disease with a prevalence of less than 1:50,000, a ratio at which we estimate to be fewer than 90 people *per condition* across the whole of New Zealand. This is consistent with the United Kingdom definition of an "ultra-orphan" disease being 1:50,000. Consultation revealed that people were comfortable with the definition.

Why are some rare disorder medicines so expensive?

Medicines for rare disorders are often priced very highly and high launch prices are an ongoing matter of global interest. The Commonwealth Fund recently noted that between 2012 and 2014, the prices of 45 orphan drugs increased 30 percent on average and seven of the top 10 best-selling drugs in the USA are approved for at least one orphan disease[1]. From our experience, where there are substitutes for patented medicines prices will reduce, even for rare disorders treatments. For example, treatments for Gaucher's disease affecting 20 New Zealanders have recently undergone a tender process with significant financial savings on offer and the potential for greater dosing flexibility, and consumer advocacy groups have been comfortable with this process given it is based on sound clinical advice.

Suppliers claim the price is due to the need to recoup the fixed costs of research and development (R&D) across lower volume or patient numbers. However, evidence indicates that more than four fifths of all funds for basic research to discover new drugs and vaccines come from public sources[2].

Many countries have supported the development of drugs for rare conditions through public funding of research, lowered registration costs, and extensions to market exclusivity. These incentives, combined with developments in genetic targeting and in human monoclonal antibodies, have led to a rapid rise in the number of products available for relatively limited populations. Orphan drugs accounted for a third of all new chemical entities launched in Europe over 2014[3,4]. Higher proportions have been estimated for new product launches in the US[5].

[1] http://www.commonwealthfund.org/~/media/files/publications/fund-report/2017/jul/waxman_high_drug_prices_drivers_solutions_report.pdf
[2] BMJ2012;345doi: http://dx.doi.org/10.1136/bmj.e4348 (Published 7 August 2012)
[3] Angela McFarlane (2017) Trends of the pharmaceutical industry following British withdrawal (QuintilesIMS: US; 2017).
[4] European Medicines Agency (2017c) Annual report on the use of the special contribution for orphan medical products, Year 2016; EMA (2017d) Orphan medicines figures 2000-2016.
[5] QuintilesIMS (2017) Lifetime trends in biopharmaceutical innovation (QuintilesIMS: US; 2017)

Suppliers also claim that it is often difficult to build sufficient clinical evidence due to natural limitations on the size of randomised controlled trials because of the rarity of the conditions. This does also mean that orphan drugs potentially offer some financial advantages to pharmaceutical companies over conventional medicines. This is due to faster development timelines, lower research and development expenses, a higher likelihood of clinical and regulatory success, premium pricing, lower marketing costs and a lower risk of generic competition[6].

PHARMAC does fund some expensive medicines for small groups of people; in 2016 81.5% of the Combined Pharmaceutical Budget expenditure was spent on 10% of people – up from 71.7% in 2011. While what we consider to be expensive changes over time, a high price does reduce the likelihood that a medicine will be funded (all else being equal) because of the impact that price has on cost effectiveness and affordability.

Suppliers understand the consequences of this and know that medicines that cost many tens of thousands of dollars per year are less likely to be funded unless clear delivery of substantial health benefits can be proven. Given that they are enabled to charge high prices overseas, suppliers have little incentive to cut their prices in New Zealand, as doing so may raise questions about their rationale for high prices elsewhere. PHARMAC lists products at high prices by negotiating confidential rebates or bundled pricing arrangements across a portfolio of a supplier's products to spread the discount. For medicines for rare disorders this is possible where the supplier also offers medicines for common conditions. This can put pricing pressure on other suppliers' products, creating further value through flow-on effect as other suppliers drop their prices to maintain market share.

Why a contestable funding pilot?

Over many years PHARMAC has carefully considered the issue of highly priced medicines and listened to public expectations concerning the funding of treatments for rare conditions. In late 2003, PHARMAC undertook a high cost medicines review to address concerns about the ethics of allowing high cost medicines for a few patients to compete with lower cost treatments, often for larger numbers of patients. These concerns were particularly focused on emerging cancer therapies and 'named patient' applications via the Exceptional Circumstances process.

Continuing public discussion led to a former Minister of Health seeking an expert and independent panel review of access to high-cost, highly-specialised medicines in New Zealand[7].

In 2013, PHARMAC released a discussion paper requesting public input to develop an alternative commercial approach to help address the issue of access to treatments for rare disorders. PHARMAC then consulted on a draft Request for Proposals (RFP) before considering feedback and issuing a final RFP in August 2014. This invited suppliers of medicines that met a set of pre-requisites to provide proposals within a capped contestable funding provision - the aim of which was to introduce competitive tension and reduce prices in the area of medicines for rare disorders.

PHARMAC consulted on the definition of products that would be able to compete in the contestable funding pilot. Following feedback, a set of pre-requisites established the parameters of a rare disorder treatment - covering such elements as the need for the disorder to be a clinically defined long-term disorder identifiable with reasonable precision, that the disorder causes a significant reduction in life expectancy or quality of life, the medicines is proven and clinically effective for that patient group, that length or quality of life could be substantially improved, and that the medicine was registered here or overseas. The definition also excludes products for which there are funded treatment alternatives and products used to treat non-rare disorders.

A funding provision of $25 million over five years was identified by PHARMAC and made available to run the pilot. People accessing funded medicines under the pilot would continue to receive treatment as long as they continue to benefit from the treatment, which in many instances may be life-long access.

[6] Melnikova, I: Rare Diseases and Orphan Drugs. Nature Reviews – Drug Discovery, Volume 11, (April 2012)
[7] McCormack, P; Quigley, J; Hanson, P; Review of Access to High-Cost, Highly-Specialised Medicines in New Zealand. 2010

Results

PHARMAC received 28 proposals from eight suppliers, and funded 10 medicines for rare disorders either through the New Zealand Pharmaceutical Schedule, or for named patients under the Named Patient Pharmaceutical Assessment (NPPA) policy. These products are:

- Icatibant (Firazyr) for hereditary angioedema
- Galsulfase (Naglazyme) for Maroteaux-Lamy syndrome (mucopolysaccharidosis VI)
- Siluximab (Sylvant) for HIV-negative idiopathic multicentric Castleman's disease
- Bedaquiline (Sirturo) for multidrug-resistant tuberculosis
- Sodium phenylbutyrate (Pheburane) for urea cycle disorders
- Cholic acid (Cholebiol) for the treatment of rare forms of bile acid synthesis disorders in infants with metabolic liver disease
- Alglucosidase alfa (Myozyme) for infantile-onset Pompe Disease
- Idursulfase (Elaprase) for Hunter Syndrome (mucopolysaccharidosis II) to stabilise patients awaiting stem cell transplant
- Laronidase (Aldurazyme) for Hurler Syndrome (mucopolysaccharidosis 1-H) to stabilise patients awaiting stem cell transplant
- Betaine (Cystadane) for homocystinuria.

Evaluation of the pilot

Grant Thornton New Zealand was commissioned to complete an external evaluation of the funding pilot using the evaluation criteria previously consulted on. Grant Thornton was provided with all the relevant documentation as well as the external stakeholder feedback sought following the close of the pilot. The evaluation report was published on the PHARMAC website in June 2017[8].

The conclusions drawn by Grant Thornton were favourable:

(1) Funded access to effective treatments for rare disorders has improved.

(2) Anecdotal evidence suggests that patients who have received treatments through the RFP have had improved health outcomes.

(3) Financial risk was managed as PHARMAC has not exceeded the maximum amount allocated in the pool. If any further investments had been made, the maximum amount would have been exceeded.

(4) PHARMAC received better commercial proposals than were received in the past. There were significant improvements in price for those products that were previously considered through the Schedule listing process. Commercial proposals were also received from suppliers new to the New Zealand market – though this wasn't part of the criterion it demonstrated the broader impact of introducing competition into the rare disorders market.

(5) PHARMAC's ability to negotiate good prices was maintained, however, it was acknowledged that the QALYs gained through the products funded via the RFP were substantially lower than most of the pharmaceuticals that could have been achieved through the Pharmaceutical Schedule listing process.

[8] https://www.pharmac.govt.nz/assets/2017-06-final-Grant-Thornton-evaluation.pdf

PHARMAC's view of the pilot

At the time of the release of the external evaluation PHARMAC committed to forming a view on the future use of this approach by the end of 2017. PHARMAC looked at the wider benefits, resource use and opportunity costs of the pilot to form this view.

Opportunity costs of the pilot

Compared to an average of 4.5 QALYs[9] per $million for those treatments under the RFP (a total of 22.5 QALYs per $5 million), the next best spend for $5 million through the Pharmaceutical Schedule process (based on the prioritisation list at the time) could have led to the funding of 11 treatments at 236 QALYs per $million (a total of 1180 QALYs per $5 million) (see Figure 1).

The estimates of QALYs per million (for both rare disorders and Pharmaceutical Schedule listings) do not include those transactions that are cost saving to the health system, only those that offered benefits, but at a net cost. There were Combined Pharmaceutical Budget cost-saving decisions that may have progressed sooner using the same staffing resource – the implication being that savings were not released that could have enabled further investment in other new medicines.

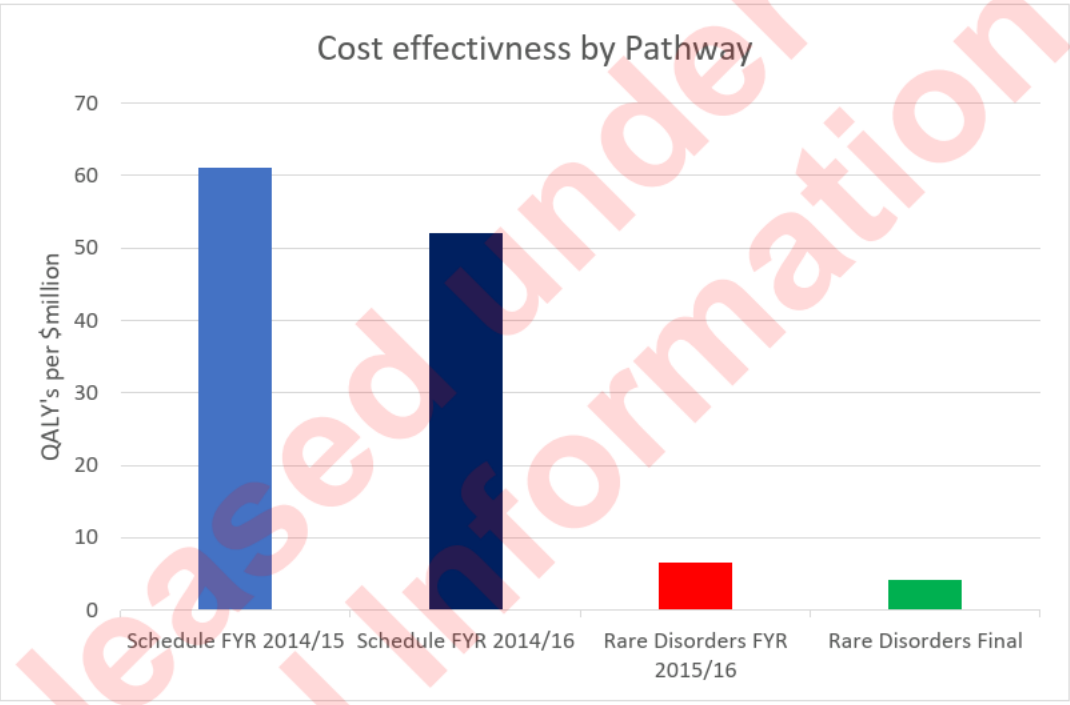

Figure 1. Comparison of cost-effectiveness between Pharmaceutical Schedule listings and RFP

The severity of illness experienced by patients with illnesses treated through the funding pilot was generally higher than patients that would have used the 11 treatments that may have otherwise been funded. The health need[10] of rare disorders patients ranged from 9 to 80 QALY loss per person when compared with expected life expectancy at full health. For the 11 other treatments, the severity of illness ranged from 0 to 60 QALY loss (see Figure 2).

Due to further budget increases and savings transactions, the 11 treatments that were crowded out were subsequently funded. The opportunity cost of funding treatments for rare disorders still exists, but would be measured on the basis of the decisions that are currently being displaced.

[9] One of the components of our decision-making is to estimate the benefits of medicines in cost-utility analysis by calculating the change in QALYs - Quality-Adjusted Life Years. QALYs are a measurement that can be used to compare in standardised way, the benefits of different treatments. QALY's combine a treatment's effects on both the quantity and quality of life (one QALY equates to one year in perfect health).

[10] Health need is a measure of how unwell a person with the disease, condition or illness is, compared with the average health New Zealander.

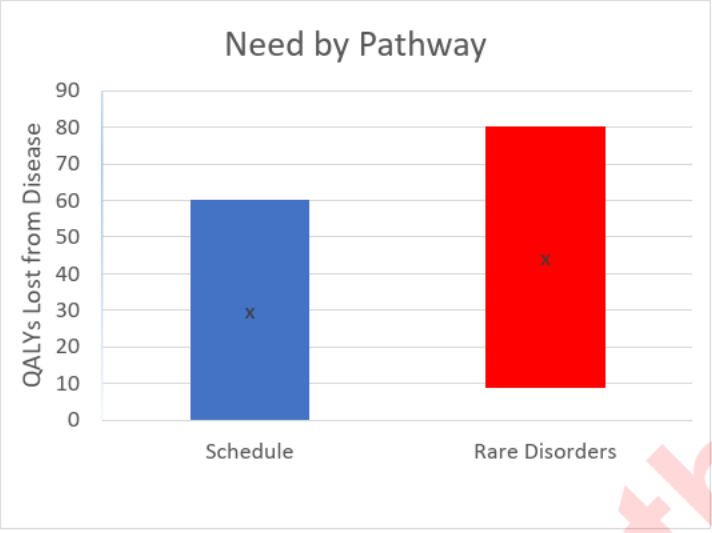

Figure 2. Comparison of health need (QALY loss) between Pharmaceutical Schedule listings and RFP

At the time of the RFP release it was acknowledged there would be a marked difference in the cost-effectiveness between rare disorders treatments and Pharmaceutical Schedule listings. This was borne out, notably the final RFP transactions were of significantly poorer cost-effectiveness than initial transactions (consistent with a prioritised process).

In June 2016 the funding pilot had achieved an average cost effectiveness of 6.5 QALYs per $million and by the final transaction this had reduced to an average of 4.1 QALYs per $million.

Factors for consideration

Cost-effectiveness measures only some of the Factors for Consideration. In relation to rare disorders, other Factors such as the health need of patients, their families and whānau and the availability and suitability of existing subsidised medicines or other treatments, are important to our decision-making as to what constitutes 'best' in terms of health outcomes.

Five of the products (to be) listed via the pilot were already funded via the Named Patient Pharmaceutical Assessment (NPPA) pathway for some patients. NPPA provides a pathway to consider those patients whose clinical circumstances cannot be met through the Pharmaceutical Schedule at a given point in time. However, prices are almost never negotiated for NPPA approvals and the supplier is paid their commercial market rate, both for the first and any subsequent NPPA approvals. While the expenditure on existing NPPA approvals was not counted from the pilot allocation, there are additional financial benefits to PHARMAC from the decision to list on the Schedule - in terms of caps on expenditure, lower pricing, and reduced administration.

How much funding to make available?

The size of the fund and the process itself was sufficient to attract new bids, new suppliers and a sufficiently broad scope of interest. The commitment of $25 million over 5 years (up to $5 million per annum) funding provided certainty and a useful anchor for suppliers. However, specifying a maximum spend created unhelpful expectations for stakeholders (suppliers and consumers) that PHARMAC would commit that level of funding regardless of the quality of proposals. As a result, there were a small number of pilot decisions that, even considering the breadth of the Factors for Consideration, compare poorly with alternate uses of the funding through our regular process.

Modifications have been made in the future approach, primarily through commitment to using extensive pre-market engagement. This would enable PHARMAC to gauge the level of interest and likely medicines proposals available at that time to determine the likely value of investment able to be considered. As the level of investment funding available varies from year to year and even within the year, the amount would similarly differ each time a funding round was opened.

Other benefits

Over time, as more suppliers of rare disorders medicines are attracted to New Zealand, or existing suppliers attracted to participate, larger portfolios of medicines would be funded. This would further enable suppliers to negotiate across bundles of products and over time further increase access to medicines.

Wider benefits were realised from the pilot, including an enhanced understanding of the standard of care for some rare disorders (as a result, an additional product for urea cycle disorders was funded via the Schedule decision-making process outside of the rare disorders RFP), relationships with suppliers and patient advocacy groups improved, and new suppliers were attracted to the New Zealand market.

Future approach for rare disorders medicines

PHARMAC appreciates there is Government interest in improving access to treatments for people with rare disorders, including greater consumer engagement. PHARMAC has been working on similar objectives, and has obtained some insights from our recent experience trialing a new approach to improve access which has informed our current view.

That key objectives were achieved during the pilot demonstrates that New Zealand's PHARMAC model can be applied creatively to resolve medicines access challenges other public funders face.

Suppliers are comfortable with the approach and have contacted us to find out when the next RFP is to be issued. Consumer advocacy groups welcomed the results and wish to see further funding rounds. We understand there is some consumer interest in participating in the pharmaceutical assessment process beyond our public consultation and consumer advisory committee. PHARMAC would be interested to further understand your views in this area, as we intend to conduct a community engagement process in 2018 to further explore options.

PHARMAC considers we can build on what was learned in the pilot and leverage further from changes in supplier behaviour - in order to provide ongoing improved funded access to, and commercial proposals for, treatments for rare disorders.

We have decided to adopt a set of dedicated features for considering rare disorders medicines through our existing processes:

- a standing PTAC expert subcommittee for rare disorders to be established;
- a regular call for rare disorders funding applications commencing in late 2018;
- undertaking dedicated pre-engagement with new, as well as existing, suppliers prior to each call for funding applications (ie commencing early in 2018);
- confirming our adjusted policy settings for rare disorders treatments on which we had consulted:
  - to further encourage applications and remove barriers, Medsafe registration for treatments for rare disorders would no longer be required for participation in the funding application assessment process, but it would be required prior to any listing on the Pharmaceutical Schedule;
  - the definition of 'rare' used in the pilot RFP confirmed along with the entry prerequisites established in the pilot;
  - PHARMAC will consider funding applications for medicines administered in DHB hospitals or in the community;
- regular review of the portfolio of rare disorders treatments with good or reasonable opportunities for investment would be progressed through our routine process or,

if a portfolio of rare disorders investments offers an opportunity to better obtain health gain, a contestable funding process or alternate commercial approach would be used, dependent on circumstances with the amount available to vary as needed.

Implementation

PHARMAC committed to forming and communicating its view on future use of the contestable funding process before the end of 2017. Our intention is to personally contact the consumer advocates and clinicians with whom we have remained in contact, to email all suppliers, consumer and clinicians who took part in the various consultations, and to update the information on our website relating to the pilot evaluation. Our statutory committees, the Consumer Advisory Committee and the Pharmacology and Therapeutics Advisory Committee, will also be advised.

It is appreciated that you may wish to meet to obtain further information regarding our view prior to us sharing it with stakeholders; both the Board Chair and I would be pleased to do so at your convenience.

Steffan Crausaz
Chief Executive

6 September 2018

Summary of the proposal from Lysosomal Diseases NZ to establish a separate funding process for medicines that treat some rare disorders

Context

Mr John Forman, a rare disease advocate and Chair of Lysosomal Diseases NZ has expressed concern about the current processes for funding medicines for rare disorders and has proposed that there be a process for funding some of these medicines, partly separated from the PHARMAC process. He considers that these medicines are not funded because of cost concerns and that, in turn, there is a weakness in the way the funding system works. That is, he is concerned that it lacks 'equity' and excludes some patient groups. The Minister of Health has asked the Ministry to work with Mr Forman to explore the feasibility of the ideas. The purpose of this note is to describe Mr Forman's proposal for the purposes of ensuring the Ministry's analysis is informed by a clear understanding of it.

The proposal would be a significant shift from the current approach for determining access to publicly funded pharmaceuticals[1] and there are important policy and implementation issues that need consideration. This note does not attempt to go into these matters.

The proposal

The proposal is to establish a process to determine individual eligibility to access those publicly-funded pharmaceuticals contained in a defined list. It borrows elements from the Pharmaceutical Benefits Scheme and the Life-Saving Drugs Programme in Australia. The key elements of the proposal are set out below:

a) Medicines: Mr Forman's initial suggested list of medicines is set out in table one. These medicines are for the treatment of some rare disorders including lysosomal storage disorders. The diseases treated are genetic/metabolic conditions, and the treatments are expensive. The initial suggested list in Table 1 are those that are on the Australian LSDP or PBS but are not funded by Pharmac[2] or have been recommended for 'decline' by PTAC. This is proposed as the criteria for medicines to be included on the list.
b) Eligible patients: the proposal provides that all patients with a relevant condition would potentially be eligible. Additional criteria are likely to be needed depending on disease characteristics and available funding.
c) Decision maker: the proposal is that there be a committee[3] established to:
    i. Determine which medicines/disorders should be on the list
    ii. Identify patients with each of the diseases in question
    iii. Confirm an individual's eligibility for access and review this periodically
    iv. Decide of all eligible individuals who is 'most in need' and therefore should have priority access to treatment. Criteria would need to be developed and could include lack of access to any effective treatment for their condition, and assessment of their

[1] At present PHARMAC determines access for the New Zealand population and the Pharmaceutical Schedule contains the list of publicly-funded pharmaceuticals. It also considers individual access to medicines not on the Pharmaceutical Schedule in exceptional circumstances through the Named Patient Pharmaceutical Access programme (known as NPPA).

[2] Work is needed to confirm the funding status of the suggested list of medicines.

[3] The High Cost Treatment Pool process has been suggested as potentially useful in this regard.

clinical circumstances as factors used in setting priorities. The committee would aim to spread the available funds across all these diseases and to treat the highest priority patients for each disease.

v. Determine on an ongoing basis whether new medicines should be added to, or removed from, the list

vi. Provide information on likely future treatment needs and priorities for patients with these diseases, to assist planning and budget setting

d) Funding: it is proposed that funding from the Pharmaceutical Budget be set aside to fund these medicines and that it be ring-fenced from being used for other purposes. Initially $5m per year has been discussed ($20m/four years) (acknowledging that additional funding could be used if it were made available). Note: the funding proposed is based on statements made by the Minister of Health about what would be available. The prioritisation process is suggested only in the event that the funding is inadequate to meet the treatment needs of patients with these diseases.

e) Procurement: it is proposed that PHARMAC be tasked with procuring the medicines using, as far as it is able, its experience in commercial pharmaceutical negotiation to leverage the best price. Note: this provision is included because the Minister of Health has stated that he wanted PHARMAC to be involved. The preference of patient groups is that the scheme should reflect the earlier political promises and remove all responsibility for this scheme to the separate committee.

Table 1: Medicines proposed for Round 1 of the alternative process [Indicative]	
Agalsidase alfa (Replagal) and beta (Fabrazyme) for Fabry disease	
Alglucosidase alfa (Myozyme) for Pompe disease	
Eculizumab (Soliris) for PHN and aHUS	
Elosulfase alfa (Vimizim) for Morquio disease	
Idursulfase (Elaprase) for Hunter disease	
Ivacaftor (Kalydeco) for mutation-specific cystic fibrosis	
Laronidase (Aldurazyme) for Hurler disease	
Nitisinone (Orfadin) for Tyrosinemia Type 1	
Sapropterin dihydrochloride (Kuvan) for PKU	

Appendix 1 Background to the proposal, independently prepared by Mr Forman

Access to "orphan" drugs for rare diseases has been a contentious issue for many years. Numerous discussion documents and reports have been prepared since 2005. In 2014 Pharmac set new policy and sought proposals under a $5 million pilot scheme to improve the number of proposals received for funding of these medicines.

The 2014 RFP indicated a number of diseases that appeared to be likely candidates for consideration under the pilot. Mr Forman maintains that of a then estimated 120 patients with these diseases, fewer than 5 would likely be treated now by approvals made from the pilot. He noted that several approvals under the pilot were in fact shifts of funds from exceptional circumstances (NPPA) to the schedule, and so not new funding for medicines not previously funded. Numbers in need of available treatments that are not funded, will be higher now – estimated about 150. The obvious implication is that policy to date has not made a significant impact and is unlikely to in the future unless there are changes, leaving a growing group of patients abandoned without treatment.

The tension in this debate is between a focus on equity, and a focus on health outcomes from a limited budget. Pharmac's policy and decisions have consistently maintained a strong focus on health outcomes as measured by QALY gains and alternative investments with available funds. This is consistent with their interpretation of their statutory mandate. In contrast, John refers to a variety of publications on universal healthcare, the sustainable development goals, distributive justice in health, the NZ PH&D Act, and the NZ health strategy, as the basis for an equity approach that deals more adequately for those who tend to miss out in the current policy settings.

Leading up to both the 2014 and 2017 general elections, policy positions from the three parties now forming the government, all stated an intention to develop a separate fund for orphan drugs, to manage that away from Pharmac, and to have consumer involvement in decisions. The 2017 confidence and supply agreement did not include such a decision. But the Minister has stated his commitment to progress in funding treatments for rare diseases and his agenda for this is equity. (Radio NZ interview with Dr Collette Bromhead, CE of NZORD 21 Feb 2018).

A meeting between Mr Forman and the Minister on 3 April 2018 resulted in the outline of a proposal being put to the Minister on how a fairer system could be developed for funding of orphan drugs, and equity achieved. The Minister reinforced his concern for the plight of these patients and stated his intention that equity needs to be more specifically addressed in funding decisions. He asked the Ministry to work with Mr Forman to investigate the practicalities of how such a system could work.

Other considerations

In initial conversations, the Ministry has discussed several related matters with Mr Forman and his responses are:

- The focus on rare genetic/metabolic diseases follows the Australian policy which specifically targets a group of diseases and their treatments that regularly fail standard cost-effectiveness evaluations in the PBAC and get referred to their LSDP.

- Rare cancers and other diseases where small subsets of patients might raise similar issues, may need separate consideration and a similar scheme, though they could be considered under this scheme if the budget allocation was adequate to deal with them too.
- Consumer engagement in this process is occurring now in the design of it, and would ideally continue in the special committee which determines funded access. This will be consistent with commitments frequently made by the 3 parties in pre election policies.
- For Pharmac to manage the whole process under their recently announced RFP for medicines for rare diseases (a follow up to their earlier pilot), there would need to be a significant change of focus on their part regarding equity. In the past they have been very determined in rejecting any special consideration of equity.
- Though Pharmac's new factors for consideration can include equity, they give no indication that an outcome like this proposal is even remotely likely. Requests to Pharmac by Mr Forman for an update on work they are doing on equity in their funding decisions, he says, show they are not doing any work in this regard. They are limiting equity considerations to an outcome focus on whether funded drugs are being accessed across the whole population.

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

Contact(s)

Sarah Fitt, Chief Executive
Alison Hill, Director of Engagement and Implementation

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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

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.

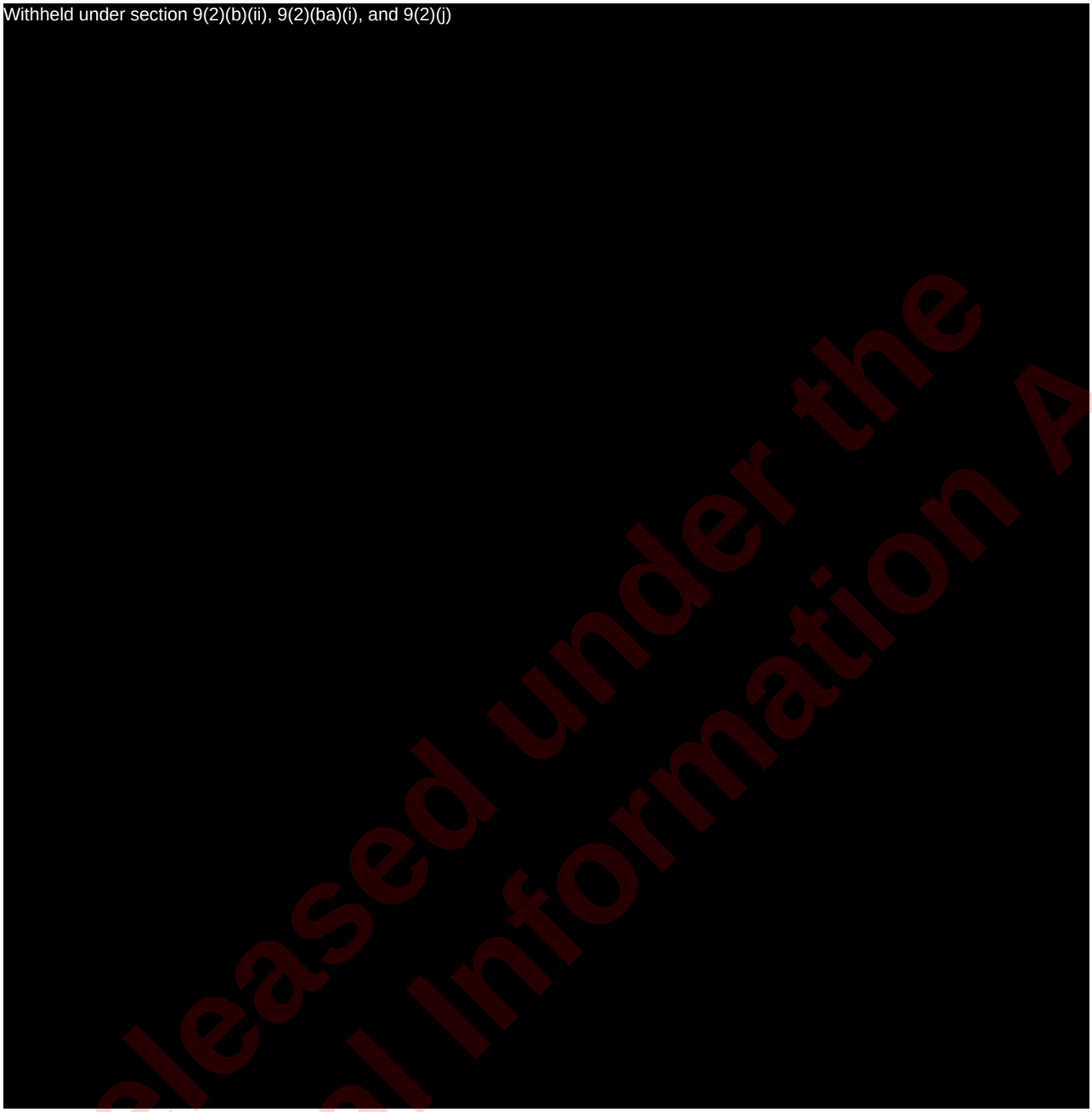
- The figures presented are different to that which was provided in May 2018. Data has been updated to reflect our definition of rare. The Pharmaceutical Schedule and Exceptional Circumstances Framework mechanism figures do not include medicines for rare cancers and infections. The Rare Disorders Pilot 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.

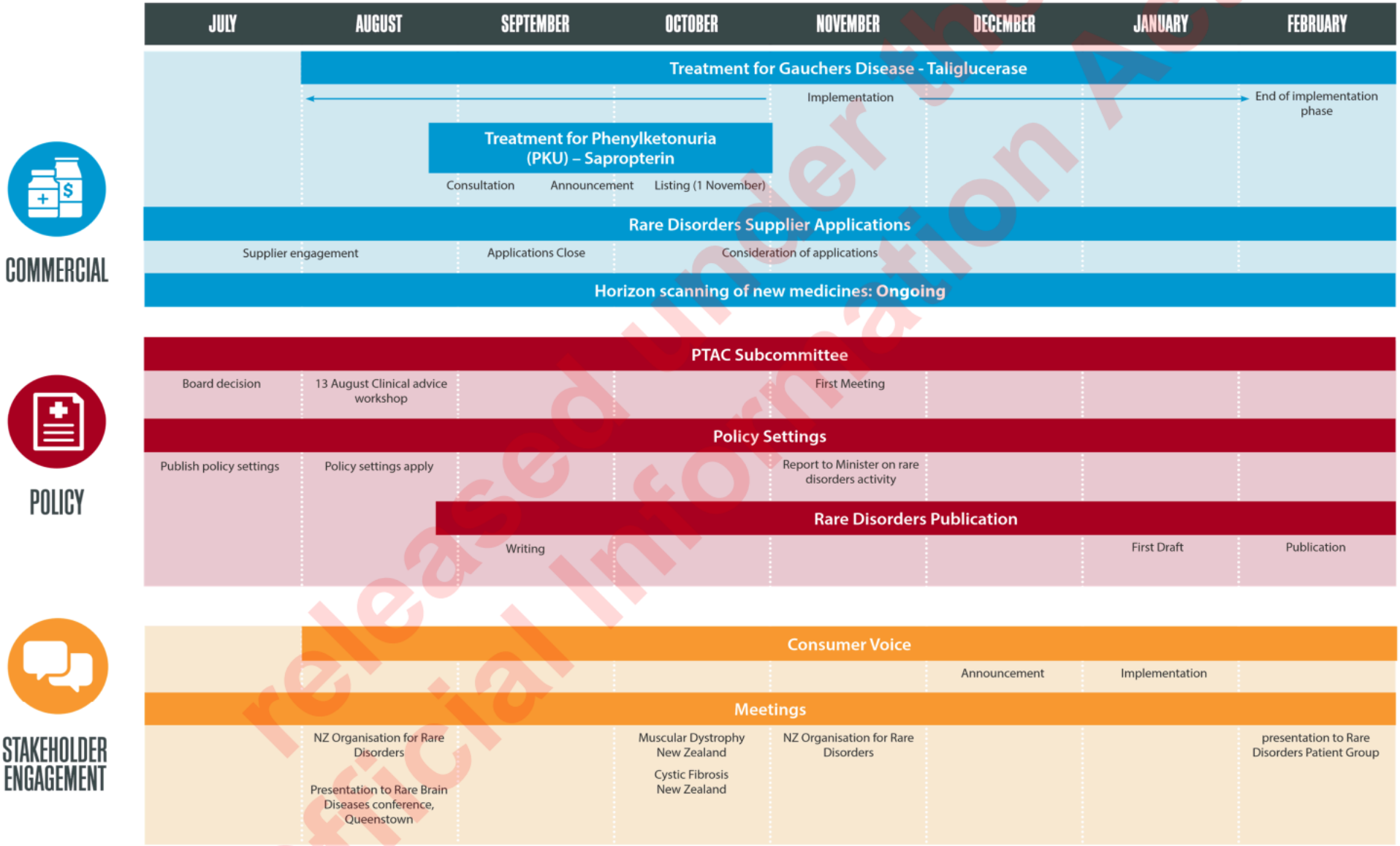
- The analysis excludes hospital purchases expenditure of medicines under either the normal Pharmaceutical Schedule (Hospital Medicines List) or the Exceptional Circumstances Framework mechanism, due to the limitations of the datasets from the hospital setting. Many of the medicines approved for hospital 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

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i), and 9(2)(j)



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



MINISTRY OF HEALTH
MANATŪ HAUORA

Health Report: Funding medicines for rare disorders: further advice

14 December 2018		Report No:	HR 20181462
		File Number:	AD62-14-2018

Action Sought

	Action Sought	Deadline
Minister Clark	Note	N/A

Contact for Telephone Discussion (if required)

Name	Position	Telephone	Contact Order
Todd Krieble	Acting Deputy Director - General, System Strategy and Policy	Withheld under section 9(2)(a)	1st Contact
Kimberly Gilmore	Manager, System Stewardship, System Strategy and Policy	Withheld under section 9(2)(a)	2nd Contact

Actions for the Minister's Office Staff

Return the signed report to Ministry of Health

Note any feedback on the quality of the report

Health Report number: 20181462

File number: AD62-14-2018
Action required by: N/A

Funding medicines for rare disorders: further advice

To: Hon Dr David Clark, Minister of Health

Purpose

This paper provides analysis of a proposal from Lysosomal Diseases New Zealand to establish a separate fund for medicines for rare disorders in New Zealand.

Key points

- Mr John Forman, Chair of Lysosomal Diseases New Zealand (LDNZ) has proposed a process for funding treatments for rare disorders that is separate from the process used by PHARMAC. You asked the Ministry to explore this further with Mr Forman, and report back. Our advice takes into consideration the recent update by PHARMAC about their rare disorders work programme (you received this update on 26 November 2018).
- Mr Forman is concerned that medicines for rare disorders are not funded because they are costly, and that cost-effectiveness analysis should not always be used where a medicine is shown to be effective. We understand he considers the process used by PHARMAC lacks equity, because it excludes this patient group (who suffer poor health outcomes and have high needs).
- The Ministry remains of the view that the current system settings we have in New Zealand for the funding of medicines for rare disorders are effective. We do not recommend any further work be completed on Mr Forman's proposal at this time.
- The Ministry of Health supports PHARMAC's work because it can address many of Mr Forman's concerns, whilst ensuring a robust and fair process remains in place.

  For example:

  - medicines assessed by the rare disorders sub-committee are not required to have Medsafe approval prior to being considered, meaning they do not face the approval costs until it is established that they will be listed on the Pharmaceutical Schedule
  - PHARMAC's rare disorders sub-committee has access to PHARMAC infrastructure and resource to provide expert advice, prepare materials to help inform their decisions
  - submissions can be made during the decision making process by members of the public
  - PHARMAC has the ability to conduct horizon scanning and engage early with suppliers to ensure potential treatments are identified.
- The Ministry will continue to engage with PHARMAC about its rare disorders work to understand its effectiveness in meeting the needs of people with rare disorders, and how equity is accounted for in their processes and decisions.

Contacts:	Todd Krieble, Acting Deputy Director - General, System Strategy and Policy	Withheld under
	Kimberly Gilmore, Manager, System Stewardship, System Strategy and Policy	Withheld under

Health Report number: 20181462

Recommendations

The Ministry recommends that you:

a) **note** that in April 2018 you requested the Ministry work with Mr Forman of Lysosomal Diseases New Zealand to write up his proposal for separate funding for medicines for rare disorders

b) **note** that the Ministry does not recommend further work be undertaken on Mr Forman's proposal at this time

c) **note** that the Ministry supports PHARMAC's work on medicines for rare disorders, and considers this approach can meet many of the concerns voiced by Mr Forman

d) **agree** to write to Mr Forman thanking him for his efforts, encouraging him to remain engaged in the work of PHARMAC, but indicating that the Ministry will not be taking his proposal forward (if you agree a letter will be provided for your signature). **YES/NO**

Todd Krieble
Acting Deputy Director- General
System Strategy and Policy

Minister's signature:

Date:

Contacts:	Todd Krieble, Acting Deputy Director - General, System Strategy and Policy	Withheld under
	Kimberly Gilmore, Manager, System Stewardship, System Strategy and Policy	Withheld under

Health Report number: 20181462

Funding medicines for rare disorders: further advice

1. This paper provides analysis of a proposal from Lysosomal Diseases New Zealand to establish a separate fund for medicines for rare disorders. It follows:
   a. a briefing provided to you in March 2018 with background on medicines for rare disorders (HR20180376)
   b. a meeting between you and Mr John Forman, Chairperson of Lysosomal Diseases NZ (LDNZ). At your meeting Mr Forman outlined a proposal for establishing a funding process for some of these medicines separate from PHARMAC's processes.
2. You requested that the Ministry explore this further with Mr Forman. The Ministry and PHARMAC have engaged with him and Collette Bromhead from the New Zealand Organisation for Rare Disorders (NZORD) a number of times, to discuss his proposal. The Ministry has also met with PHARMAC to understand what they have achieved through their rare disorders work programme. We understand you were provided with an update on this work on 26 November 2018.
3. This advice considers the specific proposal put forward by Mr Forman, but also considers the problem from the wider point of view of funding medicines for all rare disorders (not bound by specific conditions, or medicines).

Access to medicines for rare disorders - what is the problem?

4. Mr Forman is concerned that medicines for rare disorders are not funded because of cost concerns. We understand he considers the process used by PHARMAC lacks equity, because it excludes this patient group (who suffer poor health outcomes and have high needs). Equity is discussed further on page eight of this paper.
5. Considerable debate has taken place internationally regarding government funding of these medicines. The Asia Pacific Economic Cooperation (APEC) Rare Diseases Network has just launched 'APEC Action Plan on Rare Diseases' on the 19th of November 2018. The Action Plan's vision is much wider than access to medicines. One of its objectives is to 'establish policies and fit for purpose protocols for orphan product assessment, including international alignment and expedited registration pathways' with the associated action to 'maintain and fair and transparent decision making process to assess orphan products'. Access to medicines is one area where New Zealand is ahead of most countries.
6. Mr Forman has also raised concerns about the level of consumer engagement in decisions made by PHARMAC historically, and the ability for them to be challenged. We consider significant engagement has been undertaken by PHARMAC with respect to its rare diseases work.
7. The Ministry agrees that medicines for rare disorders have unique characteristics and it can be harder for them to be approved by Medsafe and funded on the Pharmaceutical Schedule in New Zealand. This is because they are impacted by:
   a. demand factors – lower levels of demand (due to a small patient group) can weaken incentives for suppliers to develop these medicines, and submit them for regulatory approval when there may only be a small market
   b. supply factors – prices for these medicines tend to be very high. Even where there is an increasing number of products being developed for rare disorders, they can remain unaffordable
   c. product characteristics – because of the small number of affected people, it can be difficult to conduct clinical trials to gather a full data set on the safety, quality and

efficacy of these products. As a result they can be harder to bring to market and may be of lower quality.

8. PHARMAC has noted some of these challenges in its recent paper to you on 26 November 2018. They state that medicines for rare disorders can be very highly priced despite relatively low efficacy. Because these products can command premium prices, research expenditure on medicines for rare disorders has in fact increased relative to medicines for common conditions.

The proposed solution - a separate fund for medicines for rare disorders

9. Officials worked with Mr Forman to write a description of his proposal for a fund for medicines for rare disorders (the Fund). This description is attached as Appendix A.

10. As we understand it, the overall aim of the Fund would be to provide a process and the infrastructure for approval and funding for some medicines for some rare disorders, independent of PHARMAC. It would aim to overcome cost barriers to access and improve equity. Mr Forman describes wanting to take a 'rights based' approach to the issue.

11. The proposal's key characteristics are:
    a. funding – it would be a ring-fenced fund of initially $5 million per year
    b. scope – the Fund would apply to a sub-set of medicines for some rare disorders (those that treat rare metabolic conditions that are genetically inherited)
    c. decision making body – the Fund would be administered by a Committee separate to those administered by PHARMAC
    d. decision-making process – the Committee would determine what medicines are available, and identify which patients were eligible. It would confirm eligibility and prioritise those patients most in need. Patients would be ranked, and as many treated as possible within the budget
    e. purchasing – this was initially described as being separate from PHARMAC, but it is now agreed PHARMAC would have responsibility for purchasing.

12. We note that the level of detail provided in the proposal is very limited. This particular proposal would require substantial work and resource from the Ministry to be developed to a point where it could be progressed in any way.

13. In assessing Mr Foreman's proposal, we have considered the likelihood of:
    a. an application being made to Medsafe (the regulator) and subsequent approval in terms of clinical safety
    b. the medicine being assessed as a successful candidate for funding through PHARMAC, on the basis of likely benefit and cost.

The current settings - how do they address the problem?

14. There are two steps for a medicine to be funded in New Zealand. First, Medsafe must approve the medicine as being safe, of high quality, and effective. New Zealand currently offers reduced regulatory costs for medicines for rare disorders to address barriers to entry related to cost.

15. The second step is that a medicine must be assessed by PHARMAC, through its 'Factors for Consideration' as a candidate for public funding. As part of the 'Factors for Consideration' framework, PHARMAC's decisions about what medicines should be publicly funded are informed by an assessment of four broad dimensions:

a. need – the impact of the disease, condition or illness on the person, their family/whānau, wider society, and the broader New Zealand health and disability system
b. health benefit – the potential gain from the medicine or medical device
c. costs and savings – the costs and savings to the person and their family/whānau and to the health and disability system and wider society
d. suitability – the non-clinical features of the medicine or medical device that might impact on health outcomes.

16. Each of these dimensions has sub-categories of analysis, some of which are:
    a. the health need of individuals, measured by the lifetime severity of the condition
    b. health outcomes of populations with health disparities
    c. the availability and suitability of other funded treatments (including non-pharmaceutical treatments).
17. There are no current barriers to PHARMAC including an 'equity-lens' in their funding decisions, for example, through the sub-category 'health outcomes of populations with health disparities'. The depth and breadth of analysis that may be undertaken using the 'Factors for Consideration' process is substantial. However, how factors are weighed up against each other, including impact on equity, is not always visible to those outside of the process. PHARMAC has recognised this and is already advancing work on equity to ensure it is able to address it.
18. Medicines for rare disorders are funded by PHARMAC through two additional channels to the Pharmaceutical Schedule listing process through:
    a. the Exceptional Circumstances Framework, which includes the Named Patient Pharmaceutical Assessment (NPPA) process, which is designed for making decisions about funding treatments for individuals with exceptional clinical circumstances that are not listed on the Pharmaceutical Schedule
    b. a new defined pool of contestable funding for medicines for rare disorders. This is detailed below.
19. Note that a substantial amount of PHARMAC's spend on medicines for rare disorders is through the NPPA process (in 2017/18, approximately 31%), and the pharmaceutical listing process itself (approximately 44%).
20. People with rare disorders access a range of publicly funded health and disability services, including pharmaceuticals. Many receive disability support services (DSS) such as equipment and home supports. DSS are designed to support a person and their family to live an independent life, rather than to treat their condition.
21. Improving quality of life, whether it be through access to medicines and/or support services, is a significant part of how the health and disability system can assist people with rare disorders.

PHARMAC's rare disorders work programme

22. In its report to you, PHARMAC outlined progress it has made with its pilot for funding rare disorders. PHARMAC's report notes that it has now made its rare disorders policy settings permanent, using three principles for entry in to its rare disorders funding process.
23. By the September 2018 deadline PHARMAC had received 13 applications, from 8 different suppliers, for 10 different medicines for rare disorders. Decisions on these applications are expected in early 2019.

24. The Ministry is encouraged by PHARMAC's work, and considers many aspects of its programme of work address the concerns raised by Mr Forman, and provide a promising way forward for this group of medicines. In particular:
    a. medicines assessed by the rare disorders sub-committee are not required to have Medsafe approval prior to being considered, meaning they do not face the approval costs until it is established that they will be listed on the Pharmaceutical Schedule
    b. the rare disorders sub-committee has access to PHARMAC infrastructure and resource to provide expert advice and prepare materials to help inform their decisions
    c. submissions can be made by members of the public
    d. PHARMAC has the ability to conduct horizon scanning because of its expertise and engage early with suppliers to encourage applications.

25. The table below records the funding allocated to medicines for rare disorders under each of the three available mechanisms over the last three years. It demonstrates that the level of funding has already surpassed the indicative $5 million per year identified by Mr Forman as a suitable level of funding. There would need to be very clear parameters around the suitable level of funding allocated to a rare disorders fund if it were to be separate from the rest of the Combined Pharmaceutical Budget.

Table 1: Medicines for rare disorders funded through PHARMAC's three funding mechanisms (from PHARMAC's report of 26 November 2018).

	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**

Our assessment

26. The Ministry remains of the view that PHARMAC applies a robust decision-making framework to all funding applications, and that a process independent of PHARMAC is not required to make decisions about funding medicines for rare disorders.

27. The Ministry supports the work programme PHARMAC has in place to support access to medicines for rare disorders. We note that this work is relatively new, and may not have become a visible part of their operating model. We intend to work with them to ensure that the rare disorders work is effective in improving access to medicines for this group, noting that there is likely to be renewed interest in 2019 following PHARMAC's release of its decisions about funding any current applications.

28. There is international movement towards increased research, assessment and funding of medicines for rare disorders. Some international comparisons are provided in Appendix B. Developments in this area are something New Zealand will need to keep a watching brief over, to ensure that our current model remains fit for purpose and is future proofed.

29. We have recommended a number of other options for strategic analysis within access to medicines that will be able to encompass the issues that arise in the context of rare disorders (refer to HR 20182511).

Equity and Cost-effectiveness

30. Mr Forman is concerned that the current system is inequitable and biased against medicines for rare disorders. People with rare disorders do on average have greater health needs when compared to the general population, and as a group will be more reliant on health and disability services to achieve improved health outcomes.

31. However, people with rare disorders are only one group within the population whose needs are taken into account through PHARMAC's decisions. PHARMAC's decision-making framework is underpinned by the right principles and concepts. This is demonstrated in its 'Factors for Consideration' through which it ensures that the need for the medicine (including the severity of the condition for individuals, their ability to benefit, and impact on their family) the medicine's health benefits, as well as its cost effectiveness are taken in to account. PHARMAC is working to understand how equity is addressed and should be reflected within its decisions. PHARMAC is also very engaged in the wider issue of access to medicines.

32. One of PHARMAC's bold goals is to 'Eliminate inequities in access to medicines by 2025'. Our discussion with PHARMAC about its work on access to medicines and equity will be a key feature of the relationship in 2019, to ensure this informs it operating model and decision-making in a meaningful and effective way.

33. The need for a separate fund for rare disorders medicines is premised on the idea that the current system lacks equity because cost-effectiveness underpins decisions about whether medicines are funded. Mr Forman is concerned that where cost-effectiveness is the key consideration, medicines for rare disorders are less likely to be funded, as they are expensive.

34. The Ministry acknowledges that medicines for rare disorders are less likely to be funded if subject to the standard pharmaceutical listing process. However, we do not consider it appropriate to remove cost-effectiveness as a requirement for funding. As a publicly-funded health and disability system we cannot fund treatments at any cost. We also do not consider it appropriate to forgo consideration of effectiveness and ability to benefit.

35. The work that PHARMAC has completed under its rare disorders work programme demonstrates the benefits that can be achieved if PHARMAC uses its infrastructure and networks to address issues related to cost and a small market.

Next steps

36. Should you wish the Ministry to undertake further work on issues related to people with rare disorders, this will require the re-prioritisation of other work.

37. The Ministry has discussed its advice with Mr Forman and Ms Bromhead. We recommend that you formally write to Mr Forman to advise him of your intended course of action. The Ministry can provide a letter (with this report attached) for your approval and signature should you wish to.

38. The Ministry intends to publish this health report under its proactive release policy.

END.

Health Report number: 20181462

Appendix A: Summary of the proposal from Lysosomal Diseases NZ to establish a separate funding process for medicines that treat some rare disorders

Context

1. Mr John Forman, a rare disease advocate and Chair of Lysosomal Diseases NZ has expressed concern about the current processes for funding medicines for rare disorders and has proposed that there be a process for funding some of these medicines, partly separated from the PHARMAC process. He considers that these medicines are not funded because of cost concerns and that, in turn, there is a weakness in the way the funding system works. That is, he is concerned that it lacks equity and excludes some patient groups. The Minister of Health has asked the Ministry to work with Mr Forman to explore the feasibility of the ideas.

2. The purpose of this note is to describe Mr Forman's proposal for the purposes of ensuring the Ministry's analysis is informed by a clear understanding of it.

3. The proposal would be a significant shift from the current approach for determining access to publicly funded pharmaceuticals[1] and there are important policy and implementation issues that need consideration. This note does not attempt to go into these matters.

The proposal

4. The proposal is to establish a process to determine individual eligibility to access those publicly-funded pharmaceuticals contained in a defined list. It borrows elements from the Pharmaceutical Benefits Scheme and the Life-Saving Drugs Programme in Australia. The key elements of the proposal are set out below:
   a. medicines – Mr Forman's initial suggested list of medicines is set out in table one. These medicines are for the treatment of some rare disorders including lysosomal storage disorders. The diseases treated are genetic/metabolic conditions, and the treatments are expensive. The initial suggested list in Table 1 are those that are on the Australian LSDP or PBS but are not funded by Pharmac[2] or have been recommended for 'decline' by PTAC.
   b. eligible patients – the proposal provides that all patients with a relevant condition would potentially be eligible. Additional criteria are likely to be needed depending on disease characteristics and available funding.
   c. decision maker – the proposal is that there be a committee[3] established to:
      i. determine which medicines/disorders should be on the list
      ii. identify patients with each of the diseases in question
      iii. confirm an individual's eligibility for access and review this periodically
      iv. decide out of all eligible individuals who is 'most in need' and therefore should have priority access to treatment. Criteria would need to be developed and could include lack of access to any effective treatment for their condition, and

[1] At present PHARMAC determines access for the New Zealand population and the Pharmaceutical Schedule contains the list of publicly-funded pharmaceuticals. It also considers individual access to medicines not on the Pharmaceutical Schedule in exceptional circumstances through the Named Patient Pharmaceutical Access programme (known as NPPA).

[2] Work is needed to confirm the funding status of the suggested list of medicines.

[3] The High Cost Treatment Pool process has been suggested as potentially useful in this regard.

assessment of their clinical circumstances as factors used in setting priorities. The committee would aim to spread the available funds across all these diseases and to treat the highest priority patients for each disease

v. determine on an ongoing basis whether new medicines should be added to, or removed from the list
vi. provide information on likely future treatment needs and priorities for patients with these diseases, to assist planning and budget setting.

d. funding – it is proposed that funding from the Pharmaceutical Budget be set aside to fund these medicines and that it be ring-fenced from being used for other purposes. Initially $5m per year. Note: Mr Foreman says the funding proposed is based on statements made by the Minister of Health about what would be available. The prioritisation process is suggested only in the event that the funding is inadequate to meet the treatment needs of patients with these diseases.
e. procurement – it is proposed that PHARMAC be tasked with procuring the medicines using, as far as it is able, its experience in commercial pharmaceutical negotiation to leverage the best price. Note: Mr Foreman says this provision is included because the Minister of Health has stated that he wanted PHARMAC to be involved. The preference of patient groups is that the scheme should reflect the earlier political promises and remove all responsibility for this scheme to the separate committee.

Table 1: Medicines proposed for Round 1 of the alternative process [Indicative]	
Agalsidase alfa (Replagal) and beta (Fabrazyme) for Fabry disease	
Alglucosidase alfa (Myozyme) for Pompe disease	
Eculizumab (Soliris) for PHN and aHUS	
Elosulfase alfa (Vimizim) for Morquio disease	
Idursulfase (Elaprase) for Hunter disease	
Ivacaftor (Kalydeco) for mutation-specific cystic fibrosis	
Laronidase (Aldurazyme) for Hurler disease	
Nitisinone (Orfadin) for Tyrosinemia Type 1	
Sapropterin dihydrochloride (Kuvan) for PKU	

Appendix B: International Comparisons

United Kingdom

1. The United Kingdom run the Highly Specialised Technologies Programme (HSTP) for funding medicines for rare disorders. This only covers rare disorders that have a population sufficiently small that treatment has to be concentrated in a few centres only.
2. The HSTP process examines the disease, clinical efficacy of the medication, cost-effectiveness, and wider impact of the technology.
3. The HSTP recognises that drugs for rare disorders require a different approach to the mainstream, due to issues such as poorer cost-effectiveness, small population sizes, and less robust evidence bases.

Australia

4. The Australian Government has very recently (November 2018) announced its intention to develop a National Rare Diseases Framework and Action Plan. Funding of $170,000 will be provided to Rare Voices Australia through the Government's Public Health and Chronic Disease Program to enable the collaborative development of the action plan and framework.
5. Specific priorities, actions and activities will be identified through consultation including with people with a rare disease, clinical and academic experts, policy makers and state and territory governments.
6. This is in addition to the Australian Life Saving Drugs Programme (LSDP), which subsidises access to medications for eligible people with rare diseases. The LSDP established an alternative process for people to access medications, which are assessed as clinically effective, but are not cost effective. Currently, 14 different life-saving medicines are funded through the LDSP for 400 people.[4]
7. An evaluation of the programme found that although the medications funded under the LSDP are clinically effective, the programme is not financially sustainable. Since these drugs were initially approved, there has been evidence that some of the approved drugs have lower levels of clinical effectiveness, value, and impact than was initially determined during their assessment.
8. Following its review, from July 2018 it is also implementing a number of changes including:
   a. the implementation of transparent and rigorous assessment processes and guidance, including the establishment of an expert panel to advise the Commonwealth Chief Medical Officer
   b. the negotiated application of pricing policies to new and existing medicines, similar to those applied to Pharmaceutical Benefits Scheme medicines.
9. Applying these rigours seems to bring the programme more in line with existing processes for all medications, rather than further separating their consideration from this.
10. Australia does not have an equivalent to the NPPA.

Scotland

11. Scotland assesses whether medicines for rare disorders should be funded through a separate framework to other medicines. A Patient and Clinician Engagement Group (PACE) was convened to assess potential drugs based on qualitative considerations, which include the

[4]http://www.health.gov.au/internet/ministers/publishing.nsf/Content/816B9A9416A23B33CA258346007A1A63/$File/GH156.pdf

potential benefit to patients, efficacy of the drug, impact on the quality of life, and comparisons of cost between other treatment options.

12. A review found that Scotland's rate of acceptance of orphan drugs has increased as a result, with stakeholders (such as clinicians and patients) reporting high levels of satisfaction with the new system.

No surprises

Rare Disorders Subcommittee minutes

PHARMAC has recently established a Rare Disorders Subcommittee of clinical experts to review funding applications for medicines for rare disorders.

At its first meeting, in November 2018, the Subcommittee reviewed 13 applications to fund medicines for ten rare disorders. (There was more than one application for some medicines.)

We are publishing the full minutes of this meeting on our website today.

The Subcommittee has recommended that four of the medicines be funded,

- carglumic acid (for two different groups)
- nitisinone
- agalsidase alfa
- ivacaftor (Kalydeco)

These four medicines are used in hyperammonaemia, hereditary tyrosinaemia type 1, Fabry disease, and cystic fibrosis in patients with a G551D mutation.

The Subcommittee recommended five be declined for funding.

- elosulfase alfa
- migalastat (for three different groups)
- teduglutide
- alglucosidase alfa (Myozyme)

One medicine, nusinersen, for spinal muscular atrophy was deferred to be considered at a later date.

The next step is for our main body of expert clinical advisors, the Pharmacology and Therapeutics Advisory Committee (PTAC) to consider the Subcommittee's assessment of these funding applications at its February 2019 meeting. Following this, PHARMAC will consider these funding applications using our Factors for Consideration framework, and will rank them against other funding applications we have received.

Before the Subcommittee meeting, there were relatively high-profile campaigns to fund the following medicines:

- Kalydeco for cystic fibrosis in patients with a G551D mutation
- Myozyme for late onset Pompe disease

- Nusinersen for spinal muscular atrophy

PHARMAC is not planning any proactive communications, other than liaising with key stakeholders such as suppliers and patient advocacy groups. PHARMAC's Chair, Hon Steve Maharey, is also presenting at a rare disorders meeting on Saturday 16 February.

We do anticipate some media attention, so will ensure that messaging clearly states that, at this stage, we are not making any funding decisions, but have sought expert clinical advice.

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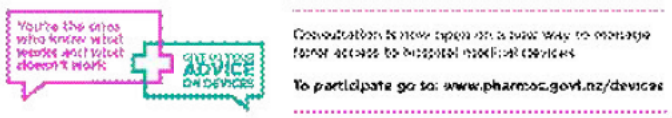

From: Withheld under section 9(2)(a) <Withheld under section 9(2)(a)>
Sent: Tuesday, 16 July 2019 4:16 PM
To: Rachel Read <Withheld under section 9(2)>
Cc: Veronica Adams <Withheld under section 9(2)(a)>; Withheld under section ; Withheld under section 9(2)(a) ; Withheld under section
Subject: PHARMAC related petitions

Hi Rachel

It was great to meet yourself and Veronica yesterday. Many thanks for the interesting overview of Pharmac.

As promised, here is the information on the upcoming Health Committee hearing on 7th August, with our written submission due 5th August.

We have been asked to provide a written and oral submission on the following PHARMAC related petitions:

Petition of Janine Yeoman - Lifesaving treatment for people who suffer from Spinal Muscular Atrophy
Petition of Jeffrey Chan - Fund Osimertinib for lung cancer
Petition of Emma Crowley - fund breast cancer drugs
Petition of Neil Graham - funding of ibrutinib and venetoclax for Chronic Lymphocytic Leukaemia
Petition of Kenneth Romeril - Funding of myeloma treatments for multiple myeloma (blood cancer)
Petition of Rachel Brown on behalf of DJ Whiting - Funding of Lenalidomide for multiple myeloma (blood cancer)
Petition of Rachel Brown - Fund Lynparza and Avastin for ovarian cancer
Petition of Allyson Locke - Fun Myozyme for Late Onset Pompe Disease
Petition of Philip Hope - fund lung cancer medications, including Keytruda, Alectinib, Osimertinib and Crizotinib, for all Kiwis with advanced lung cancer

As discussed, since PHARMAC have not been requested to make a submission in this instance, we will share our written submission with you before it goes to Select Committee on the 5 August.

Melissa Buckle is the main contact who is drafting the written submission and I have cc'd her to this email. She will be in contact in due course with our draft submission on the PHARMAC related positions.

Ngā mihi

Louise

Louise Eunson
Manager (Acting) Government and Executive Advisory
Office of the Director General

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http://www.health.govt.nz
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