22 June 2011

To the Board of Pharmac

Appeal

Allyson Lock, the New Zealand Organisation for Rare Disorders, Lysosomal Diseases New Zealand and the Muscular Dystrophy Association of New Zealand together (the Appellant) write to present this appeal against the decision (the Decision) of the Pharmac Board on 25 February 2011 to decline funding for alglucosidase alpha (Myozyme) for Allyson Lock.

Our appeal is based on the following grounds (detailed submissions on each ground are attached):

1. Factual errors: In the Decision, Pharmac took into account incorrect information about incidence and prevalence, which assumed a much higher number of likely patients who may require treatment than is accurate, and this had a significant negative impact on the assessment of costs and budget impacts.

2. Additional relevant cost information: The information in the Decision on the cost of the medication is overstated. We are aware of an offer being made from a pharmaceutical company that would cap the total cost for treating all patients with a Lysosomal disease for which that company provides a treatment, thus reducing the cost per patient. It does not appear that the Pharmac Board took this offer into account when making the decision. The omission of this information had a negative impact on the economic analysis and cost effectiveness assessment.

3. Failure to consider "community values": In making the Decision, Pharmac failed to take into account other legislative and policy guidance that puts a duty on Pharmac to incorporate community values into its assessment and decision. The community values that Pharmac should have included in its assessment of the application include reduction of disparities in health outcomes, equitable access, fairness, and moral considerations.

In addition, at the end of the attachment we summarise briefly some other matters which we consider are relevant to this appeal. We look forward to presenting a submission in person in front of the Board of Pharmac.

Yours sincerely,

Allyson Lock
John Forman, Executive Director, New Zealand Organisation for Rare Disorders
Chris Higgins, Chief Executive, Muscular Dystrophy Association of New Zealand
Jenny Noble, Field Officer, Lysosomal Diseases New Zealand

1. Factual errors – The expected number of patients with Pompe disease

Page 6 of the paper to the board of Pharmac with the recommendation to decline funding for Allyson states "using international prevalence data of 1 in 40,000 there could be up to 100 people with Pompe disease in New Zealand". In subsequent correspondence with Allyson, the Medical Director of Pharmac elaborated on incidence versus prevalence and again used the figure of 1 in 40,000 but this time described the figure as representing incidence.

We assume that Pharmac has relied on Ausems et al 1999, *European Journal of Human Genetics, Frequency of glycogen storage disease type II in the Netherlands: implications for diagnosis and genetic counseling*, who report that the combined incidence in the Netherlands of infantile onset and adult onset Pompe disease is 1 in 40 000. This paper also states that adult-onset Pompe disease may have a comparatively high incidence in the Netherlands.

However this is not the complete picture. Further investigations show that an incidence figure of 1 in 40,000 is relevant only to selected populations where a genetic founder effect is likely, including the Netherlands (Ausems et al 1999 and Poorthuis et al 1999) and the United States (Martiniuk et al 1998), the latter being significantly influenced by a high incidence among African Americans (Hirschhorh & Reuser 2001).

There is additional research on incidence and prevalence in Australia. Meikle et al 1999, *Journal of the American Medical Association, Prevalence of lysosomal storage disorders*, put the incidence of Pompe disease in Australia at 1 in 201,000 and the prevalence at 1 in 146,000.

All other population studies show incidence is considerably less in predominantly European populations. See GeneReviews on Pompe Disease http://www.ncbi.nlm.nih.gov/books/NBK1261

It is our view that the Australian figures are far more likely to reflect the actual incidence and prevalence in New Zealand than are the other studies, and the assumed incidence and prevalence figures for New Zealand should be 1 in 201,000 and 1 in 146,000 respectively. At first cut, this would result in less than one third of the likely number of patients than has been assumed in the Decision.

Even then, the number of patients calculated from the assumed incidence and prevalence figures is highly likely to overstate the actual number of patients presenting with symptoms requiring treatment, because there is a very wide heterogeneity in lysosomal diseases and not all those with the genetic mutation that leads to the enzyme deficiency will in fact have any significant disease manifestations that would require treatment.

An appropriate estimate of actual New Zealand patients with adult-onset Pompe disease needing treatment would be 6 patients. This is based on 4 known patients and an allowance for an increase by 50% for symptomatic but undiagnosed patients. This conclusion is supported by the fact that in Australia, with a population about five times that of New Zealand, and where a compassionate access programme has been in place for about 4 years, just 25 adults with Pompe disease have been identified, including 16 who are treated via a compassionate access programme funded by a pharmaceutical company, and 9 other untreated patients who for various reasons have not been included in that programme.

Further support for our estimate comes from the history in New Zealand of the number of Gaucher patients actually identified and indicated for treatment, remaining at around 20 after nearly two decades of treatment, when a frequently quoted “raw” statistics for Type 1 Gaucher disease suggests incidence of 1 in 50,000 to 1 in 100,000 in the American population that would in turn suggest possibly around 40 to 80 patients in need of treatment in New Zealand. That is clearly not the case.

As numbers of people with Pompe disease in NZ is a factor in Pharmac’s decision-making process the onus is on Pharmac to ensure relevance and accuracy.

2. Additional relevant cost information - Likely future cost of the pharmaceutical

The paper prepared for the board in response to Allyson's application provides the Board with the estimated annual cost of Myozyme for Allyson as $575,000 per year, despite later information posted on Pharmac's website suggesting the actual price per patient would be even higher at around $770,000 per year. We believe this does not represent the likely typical cost of the treatment for Allyson or for any other patients. We are aware of an offer being made to discount the price and cap the total financial risk, while treating all patients with therapies which the company supplies. However we do not have any details of the offer as it is commercially sensitive.

The offer had its genesis in March 2008 when NZORD met with the Associate Minister of Health, Peter Dunne, to consider ways to improve access to the new enzyme replacement therapies. NZORD's suggestion of approaching the supplier to consider making a package deal offer was greeted with some enthusiasm by the Minister.

Subsequently NZORD met with the company and proposed that it should make such an offer, and NZORD kept up that pressure over time. It transpires that the company did make such an offer to the Associate Minister in August 2010.

We had no knowledge of the existence of the offer at all, until advised by the company in February 2011 after their meeting with Pharmac to discuss the offer, that it had been effectively rejected.

We still have no knowledge of the detail of the offer other than its broad parameters that include treating all eligible patients with the company's enzyme replacement therapies, and limiting the total cost to our health system. We understand that in some instances the cost per patient could be as much as 70% less than the standard dose for body weight, and would effectively cap the cost per patient to a level significantly below that presented in the paper to the Board.

Pharmac is obliged to ensure its decisions are well informed and rely on accurate information. The information in this submission regarding this offer is provided to emphasise that the costs factored into Pharmac's paper to the Board, in order to be accurate, should have included possible discounts and caps on financial risk as those are relevant considerations in making the Decision.

3. Failure to consider "community values".

There is numerous legislative and policy guidance that puts a duty on Pharmac to incorporate community values into its decision, yet there is no analysis of such matters in the paper leading to the Board's Decision. The guidance from these instruments produces strong direction to Pharmac to respond to these issues in its actual decision-making.

A – The NZ Public Health and Disability Act 2000, including:

- section 3 (1) (b) ... the reduction in health disparities by improving health outcomes for Maori and *other population groups* (emphasis added),
- section 22 (1) ... the objectives of DHBs on whose behalf Pharmac acts as an agent when making decisions about pharmaceuticals, and which spell out:
    - reduction in health outcome disparities between population groups
    - exhibit a sense of social responsibility
    - uphold ethical .. standards .. expected of .. public sector organisations.

B – The NZ Health Strategy provides a framework within which organisations in the health sector including Pharmac must operate, and provides the principle:

- Timely and equitable access for all New Zealanders to a comprehensive range of health and disability services, regardless of ability to pay
    - This principle reflects the fact that fairness is a fundamental value for most New Zealanders, and the health sector must ensure that New Zealanders with similar health conditions are able to achieve similar outcomes.

C – The Best Use of Available Resources – an approach to prioritisation developed by the Joint DHB and Ministry of Health Working Group on Prioritisation, March 2005, and providing significant commentary on the application of equity principles in decision making in the health sector. See this publication online at http://www.moh.govt.nz/moh.nsf/0/68AA2F8C455F19BECC2571310007E137/$File/best-use-of-available-resources.pdf

D – The NZ Medicines Strategy provides an overarching policy direction:

- Medicines to be allocated in a manner that reduces inequity of outcomes
- New Zealanders in similar need of medicines have an equitable opportunity to access equivalent medicines
- New Zealanders to have confidence that the medicine system is fair
- Ensuring equitable and affordable access
- The health status of those currently disadvantaged is improved
- "Greatest possible value" is inclusive of efficacy, equity and cost
- Taking account of and reflecting community values

E – Pharmac's Statement of Intent and the Minister's letter of expectations

- Pharmac is to perform its functions within the amount of funding provided to it and in accordance with its statement of intent. The SOI and the letter of intent require Pharmac to continue working on improving access to highly specialised medicines. A key part of improving this access will be consideration of community values in exceptional circumstances applications. Improving access cannot be achieved by simply rolling out a new policy for exceptional circumstances. Rather, it requires Pharmac to identify any aspects of its current process that implicitly deny access to highly specialised medicines. To deliver on the Statement of Intent, Pharmac should be taking positive steps to ensure that the process for any applications for highly specialised medicines fully considers community values. This would be a key step towards creating a framework that will more appropriately assess such applications consistent with the underlying policy frameworks.

F – International support. There are many examples of community values being factored into public policy. It is arguable that public policy is seriously deficient if not grounded in the values of the community it serves. The most recent and relevant reference is the Eurobarometer survey reported 28 February 2011 by the European Commission. http://ec.europa.eu/health/eurobarometers/index_en.htm Findings include:

- More than nine in ten Europeans (93%) agree with the statement that the cost of developing drugs to treat people suffering from rare diseases should be fully reimbursed by the national health care system even if they are expensive.
- Almost all Europeans (96%) agree that resources should be allocated to ease the access to drugs for people suffering from a rare disease with only 2% opposed.

G – International instruments including the Universal Declaration of Human Rights (UDHR), and the International Covenant of Economic, Social and Cultural Rights (ICESCR). Though limited in their reach and enforceability, both of these provide sound guidance about "the right of everyone to the highest attainable standard of physical and mental health" (Article 12.1).

H – Academic support

Andrew Moore, Department of Philosophy, University of Otago, founding chair of National Ethics Advisory Committee (2002-10) (personal communications about the particular value "a fair go" or "fairness").

- A "fair go" is a value persistently expressed and endorsed by a very wide range of New Zealanders over a very long period, alongside more tepid and more occasional endorsement of other values, such as benefit, value-for-

money, and so on. It is no accident, for example, that the name of one of New Zealand's most popular and long-running television shows was "Fair Go".

- The importance of a fair go is repeatedly endorsed, usually as "fairness", throughout the several decades of recent New Zealand health policy work by several different organisations, including the National Health Committee (e.g. in its *The Best of Health* documents), the Health Funding Authority, and in more recent years the Ministry of Health. This has remained so even through various changes in terminology for the process that this value should inform - "resource allocation", "prioritisation", "rationing", etc.
- Note that the fairness that is most importantly in question here is a value to be included within criteria on which actual medicine funding decisions are made. It is not a more peripheral matter, such as fair opportunity to put one's case.

New Zealand Medical Association, Health Equity Position Statement, NZMJ 4 March 2011, Vol 124 No 1330; http://www.nzma.org.nz/journal/124-1330/4568

- This position statement uses the term equity in preference to equality because it better recognises that people differ in their capacity for health and their ability to attain or maintain health. Consequently, equitable outcomes in health may require different (i.e. unequal) inputs to achieve the same result. This is the concept of vertical equity (unequal, or preferential, treatment for unequals) in contrast to horizontal equity (equal treatment for equals).

Maurice Ormsby, Philosopher, writing in the Access to Medicines Coalition submission to the Ministry of Health on the development of a Medicine Strategy, 2007

- Drawing on Rawls on "Justice as Fairness" – the difference principle, Ormsby states "cases with serious impacts and severe outcomes need special consideration" and "treating like cases alike can be rephrased as treating unequal cases unequally".
- Ormsby again, from the same submission, discusses utilitarian analysis [often crudely stated as the greatest good for the greatest number and which appears to be Pharmac's dominant driver], and concludes that utilitarianism "needs a level of sophistication in its analysis, and must incorporate social context and community values if it is to be a useful tool for analysis and decision making."

Community values relevant to this funding decision include:

- "Rule of rescue" – there is no other medicine available for treatment of Allyson's life-threatening disease. This situation produces a morally distinct situation, for example, from that where a new medicine has become available which offers a potential improvement to an existing therapy. Application of this rule challenges narrow economic evaluation and should give priority to treating a life-threatening disease that has no

alternative treatment. See Pharmac: a Prescription for Pharmacoeconomic Analysis, Version 1.1 September 2004 http://www.pharmac.govt.nz/2004/11/03/pfpa.pdf

- Government as the "insurer of last resort"- a sub-set of the "fair go" value, that the government holds responsibility for the community's wish not to be abandoned in serious situations and in the face of catastrophic healthcare costs. In this respect we refer to the government's response to Christchurch post-earthquake, and the decision to provide funding for successive multiple organ transplants for a young child.
- Justice as fairness – in the allocation of health care resources. Beauchamp & Childress: Principles of Biomedical Ethics 2001, the four principles approach to health care ethics, provides the most enduring ethical framework for health service delivery, including Justice in distribution of benefits, risks and costs. These principles bring equity and fairness sharply to the fore, for consideration.
- Action in the face of uncertainty – in relation to Pharmac's questioning "is there enough evidence of the benefit of the drug" – the three part framework of Bernheim, Nieburg and Bonnie 2007 states that the consequences of not acting must also be weighed up. Specifically, this would rate as "unfair" the notion that access be denied until long term evidence provides certainty of benefit.

How application of community values should influence the Decision:

- The fact that an innovative new treatment has been developed for Allyson's previously untreatable disease, produces a morally different situation compared to other situations for other diseases where alternative treatments may already exist but investment in new treatments is also under consideration. This difference should be addressed differently to standard assessment criteria for comparing cost-effectiveness of possible investments.
- Justice as fairness would address the significant inequity of access and disparity of health outcomes that results from the present situation and which would continue if treatment is denied.
- Given that there is no other treatment for the underlying disease she has, it is unfair and morally repugnant to decline the treatment for Allyson. The rule of rescue would justify favourable consideration despite some usual criteria not being met.
- Levels of evidence of benefit that are usually expected for investment in medicines need to adapt according to the principle of action in the face of uncertainty, and the difference principle can accept different (lesser) levels of evidence in such cases of rarity, seriousness, and difficulty of obtaining evidence.

Some practical ways to implement this:
Rare disease patients are realistic and practical people. They accept the solution is not simply to list the medicine on the schedule with access guaranteed subject only to a prescriber's authorisation, nor to approve an Exceptional Circumstances application for an expensive highly specialised medicine without some detailed monitoring of its use and effects. Funding of the medicine for Allyson (and other patients with adult-onset Pompe disease) could reasonably be subject to:

- Entry and exit criteria specific to use of the medicine for treating the disease
- A special panel to oversee treatment of each patient and apply the criteria
- Close monitoring and evaluation of response to therapy to provide more data on long term benefit
- For example, if the monitoring showed continued decline in Allyson's condition after a 24 month period of treatment then there would be likely to be few moral issues regarding the withdrawal of funding.

Other matters Pharmac should take into account in reviewing this appeal:

A "hard look" - Under existing legislation and policy frameworks governing medicine access and funding, Pharmac is the final arbiter. We submit this puts a great onus on Pharmac when reviewing this appeal to take a very "hard look" at all of the issues involved, giving detailed and serious consideration to its obligations, specific and general, and Pharmac must be prepared to judge its own policy in the process of that scrutiny. This "hard look" is based on the legal principle followed by courts when very serious issues are at stake.

In particular, while the absence of any other treatment for this life-threatening disease is noted, the moral or legal implications of that fact were not evaluated in the decision-making process.

Pharmac must ensure its decision making criteria takes into account all considerations relevant to the particular decision. Pharmac can not just assume that the 9 decision criteria it uses can simply be applied without further consideration of their being fit-for-purpose and assume they will comply in all cases with all of Pharmac's legal and policy requirements.

Pharmac should consider in the light of these points of appeal, whether matters need to be considered in addition to those Pharmac usually covers within the application of its 9 criteria, and whether its current approach and the information provided to the board for its decision, is an adequate and compliant process.

We submit, of course, as outlined above that there are other matters of importance that Pharmac must take into account, and that Pharmac's consideration of this application has not been adequate or compliant.

Appeal Summary

We consider it is a serious problem to have a government agency allocating scarce health resources on the basis of narrow Pharmacoeconomic analysis and budget management only. A moral compass is essential. There are numerous historical examples where things have got out of control where decision makers have followed established processes without considering important moral issues.

As the decision maker, Pharmac has an ability to set its processes. This includes an ability to expand existing processes and analysis to include additional factors as the case requires. We submit that it is crucial when making medicine funding decisions to also consider the moral dimension.

End