Summary of feedback

PHARMAC's proposal to decline a funding application for eculizumab

August 2013

CONTENTS

SUMMARY OF THE REPORT

1. This report summarises the feedback received by PHARMAC in response to its May 2013 proposal to decline funding eculizumab (Soliris) for the treatment of paroxysmal nocturnal haemoglobinuria (PNH).

Description of respondents

2. Feedback was received from 263 respondents: 15 groups with an interest in health, 19 PNH patients, eight clinicians, and 221 other individuals.

3. In addition the notes from two meetings PHARMAC held were included in this analysis:

    a. a meeting with PNH patients and their supporters, and

    b. a meeting with a clinician who is treating patients with eculizumab and with the parent of a PNH patient who is receiving eculizumab on a compassionate basis from Alexion Pharmaceuticals.

4. Two hundred and fifty eight respondents opposed PHARMAC's proposal to decline funding for eculizumab, four supported the proposal, and one was undecided.

5. Two thirds of respondents not supporting PHARMAC's proposal to decline funding submitted standard feedback provided by the PNH Support Association of New Zealand.

6. Most respondents provided their feedback by email. It was not clear in which country 47% of the respondents lived (all of these were 'other individual' respondents).

Reasons for opposing PHARMAC's proposal

Objection to PHARMAC's analysis

7. Overall, respondents opposed to PHARMAC's proposal objected to the analysis PHARMAC had used in forming its proposal. This objection encompassed both the facts presented in the consultation document, and the principles underlying the analysis.

Incorrect or missing information in the consultation document

8. Respondents considered there was incorrect or missing information in the consultation document:

    - the number of PNH patients eligible for treatment with eculizumab was overstated, and consequently so was the cost of treating these patients and the effect on funding available for others
    - it was unclear whether PHARMAC's cost analysis had taken full account of the costs to the public health system of PNH sufferers not receiving eculizumab, and the effect of Alexion Pharmaceuticals' global patent on Soliris expiring
    - the statement about efficacy in the consultation document inadequately reflected how effective eculizumab is in treating PNH
    - the survival improvement for the treatment of PNH with eculizumab was understated
    - there was inadequate explanation of why PHARMAC's haematology subcommittee's recommendation to fund eculizumab had not been accepted.

Equity of access to treatment

9. Another major focus of those opposed to PHARMAC's proposal was on the rights of those with PNH to have equity of access to treatment – this was an area that many respondents considered to have been poorly addressed by PHARMAC.

10. These responses centred on:

- basic human rights as expressed by the United Nations and in New Zealand law
- the obligations of District Health Boards (DHBs) under the New Zealand Public health and Disability Act 2000 and on PHARMAC as DHBs' purchasing agent
- a general social responsibility to provide equity of access to people requiring treatment
- the role of ethics in decision making.

Special decision criteria

11. Most respondents opposed to PHARMAC's proposal stated that PHARMAC should have special decision criteria when considering treatment for rare diseases or particularly high cost pharmaceuticals.

12. Using a standard response template (provided by the PNH Support Association of New Zealand), 60% of respondents stated that PHARMAC:

- 'must amend its operating policies and procedures to acknowledge the right of rare disease patients to access life restoring and life saving treatments as in the specific example of the Soliris treatment,' and
- 'establish fair assessment criteria, based on expert advice from the international haematological community, to assess patient need for the Soliris treatment.'

Managing the cost of eculizumab

13. Respondents considered that PHARMAC had a responsibility to facilitate access to viable therapies in as cost effective manner as possible. Thus PHARMAC must negotiate to supply the treatment.

14. If PHARMAC's budget was not adequate, then it was PHARMAC's responsibility to address the issue by renegotiating with Alexion Pharmaceuticals. Two-thirds of respondents asked that PHARMAC do this, including some who supported PHARMAC's proposal to decline funding. All respondents that suggested this were of the view that Alexion would be prepared to enter negotiations with PHARMAC and to lower the price of eculizumab.

15. It was further suggested that if the pharmaceutical budget was inadequate, it was PHARMAC's responsibility to negotiate with government for an adequate budget. Several respondents considered sufficient funds existed to treat people for PNH, and questioned the prioritisation of tax payer funded national spending.

International availability of eculizumab

16. Many respondents found PHARMAC's proposal to decline funding very difficult to accept as eculizumab was thought to be widely available internationally.

Reasons for supporting PHARMAC's proposal

17. Two groups (with women's health interests) and two clinicians supported PHARMAC's proposal to decline funding for eculizumab. This agreement was based on the cost of eculizumab and the effect this would have on the availability of funding for other conditions. Consequently, several of these respondents would support eculizumab being funded if the price could be reduced. Other reasons expressed by these respondents were:

- such funding potentially sets a precedent
- other treatment options for PNH are available

- concerns about the role of pharmaceutical companies in special interest group lobbying.

Summary of questions put to PHARMAC

18. Respondents asked that PHARMAC:

Research & analysis

- Review its method of calculating the exact number of patients that meet the criteria for eculizumab before making a final funding decision and make explicit how it arrived at the figure.
- Look at the policies and processes of countries that fund eculizumab to help it develop a funding model.
- Look at a further round of expert consultation, both nationally and internationally before moving forward with its proposal to decline funding.

Further explanation

- Present the rationale for its figure of the survival improvement for the treatment of PNH with eculizumab.
- Explain why it did not follow its haematology subcommittee's recommendation that eculizumab be listed in the pharmaceutical schedule.
- State whether, if a PNH patient's condition deteriorates, a haematologist would be able to apply for eculizumab under the Named Patient Pharmaceutical Assessment policy using the pre-defined eligibility criteria recommended by the haematology sub-committee.
- State whether it has made a case to the government for additional funding.
- Make clear whether the cost analysis has taken full account of the costs to the public health system of PNH sufferers not receiving eculizumab, and has incorporated the effect of Alexion Pharmaceuticals' global patent on eculizumab expiring.
- Make clear whether it has attempted to seriously negotiate with Alexion Pharmaceuticals, including whether it has indicated the price point at which it would be prepared to buy.

Suggested approaches for funding eculizumab

19. Respondents variously suggested that PHARMAC:

- part subsidise eculizumab
- renegotiate the price of eculizumab with Alexion Pharmaceuticals
- amend the eligibility criteria for eculizumab to make funding the drug more affordable
- set up a separate source of funding for patients with rare conditions who want access to very expensive drugs.

INTRODUCTION

1. This report summarises the feedback from 263 patients, clinicians and others in response to PHARMAC's May 2013 proposal to decline the application from Alexion Pharmaceuticals for funding eculizumab (Soliris) for the treatment of paroxysmal nocturnal haemoglobinuria (PNH).
2. In addition the notes from two meetings PHARMAC held were included in this analysis:
    a. a meeting with PNH patients and their supporters, and
    b. a meeting with a clinician who is treating patients with eculizumab and with the parent of a PNH patient who is receiving eculizumab on a compassionate basis from Alexion Pharmaceuticals.

Background

3. PHARMAC's proposal to decline the funding application is consistent with the clinical advice it received. This advice recommended that the application be declined because although eculizumab is an effective treatment, it is extremely expensive.
4. PHARMAC's cost-utility analysis of the use of eculizumab in patients who have PNH found that eculizumab is not very cost-effective compared with other funding options. The reason PHARMAC is proposing to decline funding is because the price requested by the supplier is extreme and, given the available budget, it appears to be out of reach.

Preparation of this report

5. PHARMAC accepted feedback on its proposal from 21 May to 31 July 2013.
6. During the response period, feedback was received from 263 people, including organisations with an interest in health, people with PNH, clinicians, and others. These responses were entered into a database, using a coding framework developed from the themes presented in the feedback. PHARMAC also held two meetings, as noted above: (1) with PNH patients and their supporters and (2) with a clinician and with a parent of a PNH patient. The notes from these meetings have been included in this analysis.
7. In the analysis, emphasis has been placed on the range of views presented, rather than on the numbers of respondents expressing a particular view. Counting was made difficult because some of the responses represented a single voice, while others represented several or many people. An indication of the level of support for various positions has been given in places to show how widely held particular views were.
8. Quotes have been used to give a sense of the respondents' views. In the interests of privacy, individuals' names have not been supplied with the quotes.

Overview of responses

9. As shown in the table below, the majority of the 263 respondents were individuals, with a small number of responses from clinicians,[1] PNH patients and groups with an interest in health or particular medical conditions. (A list of respondents is provided in Appendix 1.)

[1] This group of respondents comprised 6 haematologists, 1 research nurse, and 1 DHB Primary Care Portfolio Manager.

10. Two hundred and fifty eight respondents (98%) did not support PHARMAC's proposal to decline funding for eculizumab, four respondents supported PHARMAC's proposal, and one was undecided.

11. Two thirds of respondents not supporting PHARMAC's proposal to decline funding provided standard feedback using text provided by the PNH Support Association of New Zealand.

12. Most respondents provided their feedback by email. It was not clear in which country 47% of the 'other individual' respondents lived.

Table 1: Description of respondents providing written feedback

		Clinicians	Groups	Other individuals	PNH patients	Total
Support PHARMAC's proposal		**2**	**2**			**4**
	New Zealand	2	2			4
Maybe support		**1**				**1**
	New Zealand	1				1
Do not support		**5**	**13**	**221**	**19**	**258**
	New Zealand	5	9	89	8	110
	Australia		3	13	7	23
	United Kingdom			10	2	12
	United States		1	4		5
	Canada			1	1	2
	Japan			1		1
	Unknown			103	1	102
Total		**8**	**15**	**221**	**19**	**263**

RESPONDENTS' FEEDBACK

13. This summary of feedback presents respondents' views thematically. As stated, almost all responses received were opposed to PHARMAC's proposal to decline funding eculizumab. The views of those supporting PHARMAC's proposal are noted in discussion of the relevant topics and are also briefly presented together at the end of this report (page 24).

Views of those who oppose PHARMAC's proposal to decline funding

Incorrect or missing information in the consultation document

14. Overall, respondents opposed to PHARMAC's proposal objected to the analysis presented in the consultation document. This objection encompassed both the facts put forward in the consultation document, and the principles underlying the analysis.

15. Many respondents considered that factual errors or misinformation would affect the number and content of responses on the eculizumab consultation. The consultation could therefore not be considered an accurate picture of public opinion on PHARMAC's proposal. A number of respondents asked PHARMAC to withdraw this consultation because of the perceived errors and misleading information in the consultation document.

16. In particular, respondents considered incorrect information had been presented in the consultation document about the number of PNH patients eligible for treatment with eculizumab, and the consequent cost of treating these patients.

Number of eligible PNH patients & the real cost of eculizumab

17. Respondents noted that PHARMAC suggested there are 60-70 PNH patients in New Zealand, and that 12-20 of these patients may qualify for eculizumab if it was available. However, these numbers were disputed by many respondents who commonly suggested that the actual number of PNH patients qualifying for treatment would be 8-10.

18. One group stated that PHARMAC's figures in the consultation document conflicted with advice from the Pharmacology and Therapeutics Advisory Committee (PTAC), which had estimated three patients per million, suggesting up to 13 patients in total.

> *The consultation document exaggerates this by about 55%. The estimate of 13 patients is validated by a pro-rata population-based assessment of number actually treated in Australia, again concluding 13 patients in New Zealand.*

19. Respondents asked that PHARMAC makes explicit how it arrived at the figure used in the consultation document, and review its method of calculating the exact number of patients (at this point in time) that meet the criteria for eculizumab before making a final funding decision.

20. In a meeting with PNH patients and supporters, PHARMAC staff explained that the number of patients mentioned in the consultation document (12-20) had been informed by the supplier's submission to PHARMAC taking into account particular access criteria for treatment and PHARMAC's experience that once a treatment was available, the number of patients was likely to increase.

21. It was noted that a smaller number of PNH patients in New Zealand requiring treatment with eculizumab changes the pharmacoeconomics of funding eculizumab. 'Even if the purchase

price for eculizumab was the quoted $600,000 [per patient] per year, the total cost to PHARMAC would be only $6,000,000 annually; not the $12,000,000 quoted in the Consultation Document.'

22. However, one clinician who supported PHARMAC's proposal noted that funding eculizumab for even a very small number of patients (such as 8-10) 'could have considerable financial implications, with clinical implications for a potentially much greater number of patients deprived of effective treatments because of the finite resources available to fund healthcare in this country.'

23. Most (24) of the respondents querying PHARMAC's information in the consultation document provided or incorporated a standard response stating that they should be able to rely on PHARMAC to provide accurate and reliable information. It was suggested by some respondents that PHARMAC was intentionally misleading the public as to the possible cost of the treatment.

> *You did this back in 2011 when PHARMAC staff reported to the Board that there would be up to 100 affected patients in New Zealand with Pompe disease. That treatment was declined, and it looks as though you intend to decline Soliris, again with dubious data as the basis for a decision. This is not acceptable and you should withdraw this consultation because of the misleading information in it, which is likely to skew responses from the public.*

24. Many of the respondents who queried the number of PNH patients suggested by PHARMAC also questioned the potential cost of eculizumab, considering it would actually be much less than the figure presented in the consultation document ('approximately $12,000,000 per year'). This view was based on the number of patients respondents thought would actually be eligible for eculizumab and the view that the supplier would in fact be open to negotiating a lower cost (a point discussed on page 22).

> *I was very concerned to read in the cost utility analysis document that in its analysis, PHARMAC has assumed a cost of $670k per annum for this treatment. I'm sure you are aware that the list prices of pharmaceuticals are indicative only - I am for instance aware that Australia received discounts off of this list price and that these discounts were substantial. It is of deep concern to me that PHARMAC may have gone public with a proposal that has a life or death impact on patients - and has been the subject of 'recent public interest' (PTAC's words) without being fully transparent about what the costs of the treatment actually are. I look forward to receiving an assurance that this is not the case.*

25. Eight respondents considered it unclear from the consultation document or from the economic outlines provided on the PHARMAC website, that the cost-effective analysis had taken full account of the costs to the public health system of PNH sufferers not receiving eculizumab. Respondents stated that PHARMAC's arguments about cost need to include the total cost of not treating PNH patients; that is, the medical costs and the loss of productivity to society.

26. Several submitters provided details of hospitalisation and treatments for PNH to emphasise the considerable costs. 'The cost of infusions of fresh frozen plasma amongst other treatments must surely be costing more than Soliris.' Additionally these respondents described the loss of productivity and income arising from the illness.

27. During a meeting with PNH patients and supporters, PHARMAC staff stated that cost analysis takes into account savings to hospitals.

Impact of patent expiry

28. Five respondents (two clinicians, one group and two other individuals) suggested that PHARMAC considers the effect of Alexion Pharmaceuticals' global patent on Soliris expiring. The cost was expected by these respondents to drop dramatically as soon as the drug comes off patent in some 10 years' time.

29. Several respondents stated that PHARMAC had not taken the patent expiry into account in its cost modelling. One group cited PHARMAC's 2003 policy document *A Prescription for Pharmacoeconomic Analysis*:

> *It is recommended that in cases where the patent expiry is within 10 years from expected date of pharmaceutical funding, the expected time and price reduction from a likely generic pharmaceutical should be included in the analysis. If the patent expiry is after 10 years from expected date of funding, a conservative proxy should be used for the estimated time until the introduction of a generic pharmaceutical and subsequent price reduction (e.g. 25 years until expiry and 70% price reduction with introduction of generic).*

Length of treatment

30. Two clinicians also noted that treatment of PNH patients with eculizumab has 'opened the door on the pathogenesis and biology of PNH a bit wider. Over time we may well find new therapies emerge such that eculizumab provides a bridge to curing the disease long-term.' That is, treatment with eculizumab may not be a life-long commitment for all PNH patients, with a subsequent reduction in costs.

Considering the eculizumab patient group as a whole

31. One respondent queried whether, as eculizumab made its presence felt in the treatment of other rare diseases, PHARMAC would consider each disease treated with eculizumab separately for funding purposes, or consider the patient group as a whole.

Effect of funding eculizumab on others

32. Related to the cost of eculizumab cited in the consultation document, several submitters commented on the figures provided by PHARMAC about how funding eculizumab would affect funding available for others.

33. These respondents were concerned that PHARMAC was not sufficiently recognising the extreme nature of eculizumab in which the cost is considerable but so is the benefit to the individual patient. Respondents considered that PHARMAC's approach to funding decisions means that a life saving, highly specialised treatment for a rare disease is evaluated alongside medicines that either don't offer live saving benefits, or have benefits that are less tangible. One patient commented:

> *I don't want to trivialise the health concerns of others… - but it concerns me that a treatment that I need in order to stay alive is being evaluated using the same decision criteria as things like statins, paracetamol, ritalin and at the ridiculous end of the scale, flavoured condoms. This situation is not equitable.*

34. Another submitter considered PHARMAC's statement that funding eculizumab would deprive 40,000 other patients of treatments 'a gross exaggeration.' This opinion was due to the number of PNH sufferers that would receive eculizumab being no more than eight, savings that could be made elsewhere, and PHARMAC possibly succeeding with making a case to the government for additional funding.

35. Additionally, 10 submitters noted that people have PNH through no fault of their own – in contrast to people with conditions acquired through lifestyle choices.

Efficacy of eculizumab in treating PNH

36. Sixteen respondents commented on the efficacy of eculizumab in treating PNH, including a clinician who supported PHARMAC's proposal to decline funding. Respondents agreed that eculizumab was extremely effective in reducing haemolysis, transfusion requirements and some of the complications of this disease as well as greatly improving quality of life for sufferers. Eculizumab was described as dramatically reducing disease symptoms, allowing patients to return to full, active and productive lives. Respondents noted that PHARMAC's analysis had concluded that eculizumab is an effective treatment for PNH, although some considered PHARMAC's statement about efficacy in the consultation document to inadequately reflect how effective eculizumab is in treating PNH.

37. In a meeting with a clinician and with a parent of a PNH patient, PHARMAC staff reiterated that clinical advice has indicated that eculizumab is an effective treatment. The barrier it faces is that it is very cost-ineffective. Its high cost means that even if it was 100% effective, the cost-utility analysis result would be at least $600,000 per quality-adjusted life year.

38. Fifteen respondents (clinicians, groups, PNH patients and others) and meeting attendees discussed the quality of life those with PNH have - with and without eculizumab. These responses emphasised the significant impact of eculizumab in enhancing patients' daily lives (as well as their survival prospects) and ability to contribute to society.

39. Respondents (including clinicians) described the very prompt and dramatic reduction in symptoms from PNH, and the resulting improvement in quality of life.

> *Soliris has changed my life dramatically both personally and professionally. My outlook and quality of life has improved and I am living life like any other normal person. I have more energy to do all the things I have dreamt about. I am more focused at work and have taken leading roles which I never thought would be possible. I no longer worry about the many complications I may suffer from PNH, instead I am living my life without any barriers and fear of what could possibly happen. …. I no longer have blood transfusions and am working full time and contributing to the country.*

40. Thirty-eight respondents and meeting attendees noted they were related to or acquainted with a PNH sufferer. Several of these described in some depth the experiences of PNH sufferers before and after treatment with Soliris.

Understatement of the survival gain

41. Respondents also considered that PHARMAC had understated the survival improvement for the treatment of PNH with eculizumab.

42. One PNH patient stated that PHARMAC's figure of five years differed 'significantly from the advice I've received over the years from the health professionals involved in my treatment - and I am keen to understand the rationale for them. '

43. During the meeting with PNH patients and their supporters, PHARMAC staff explained that the survival gain used in the consultation document is an estimation from clinical trial data that takes into account the uncertainty about the evidence. When making these assumptions, PHARMAC always tests its assumptions through sensitivity analysis with different ranges. These ranges are noted when considering proposals so, in the case of eculizumab, the focus is not only on the '5-year' number.

44. While respondents had slightly differing opinions on the extent to which eculizumab reduced the risk of dying from complications of PNH, most respondents commenting on survival gain stated their views that clinical studies prove eculizumab gives PNH sufferers 'normal' life expectancy or extends the life of PNH patients by an average of 32.5 years.

45. Two clinicians noted that as eculizumab has been shown to be a highly effective therapy in PNH patients, no placebo-controlled study of eculizumab treatment in PNH patients will ever be conducted. This meant data must come from historical comparative studies involving selected cohorts of eculizumab-treated PNH patients. Such studies suggest eculizumab treatment 'will result in prolongation of survival in PNH patients by in excess of 20 years.'

46. One group (which supported PHARMAC's proposal to decline funding) could not find any new evidence aligning with the PNH Support Association NZ's claims that eculizumab 'is a life-saving treatment,' nor that it 'returns life expectancy to expected norms.'

Lack of other treatment

47. Five respondents, including a clinician, pointed out that apart from eculizumab there is currently no other treatment for PNH besides trying to manage the symptoms. Several respondents referred to bone marrow transplant, which not all patients were able to have and 'which can be fatal' as the only option without eculizumab.

> *Blood transfusions, warfarin to try to prevent blood clots and a listening ear is all we can do. The amount of blood transfusions required increases as does the frequency of hospital visits from pain, especially abdominal, from clotting episodes and renal impairment*

48. However another clinician (supportive of PHARMAC's decision) noted that while treatment options (other than eculizumab) for PNH are limited, there are some beneficial therapeutic strategies for some patients. [2]

The haematology subcommittee's recommendation

49. Two clinicians questioned why PHARMAC was not following its haematology subcommittee's recommendation that eculizumab be listed in the pharmaceutical schedule (with certain eligibility criteria and the possibility of an advisory panel to administer the criteria).

50. Related to this point, one respondent asked whether, if a PNH patient's condition deteriorated, their haematologist would be able to apply for eculizumab under the named patient pharmaceutical assessment policy using the pre-defined eligibility criteria recommended by the haematology sub-committee.

[2] This respondent noted that:

a. Although the subject of some debate, in my experience corticosteroids have some activity and can be effective in some patients, both in the acute setting, and in lower doses longer term. While not as reliably effective as, and potentially more toxic than eculizumab, this class of drugs is a reasonable option in some clinical circumstances, in my opinion.

b. Transfusion therapy, although not ideal, allows many patients to lead a relatively normal life. There are numerous patients with other haematological disorders who are transfusion-dependent and who are unable to access drugs considerably cheaper than eculizumab (erythropoietin, azacytidine. lenalidomide. etc) that have the potential to reduce their transfusion requirements, improve their quality of life and extend their survival.

c. Allogeneic transplantation is the only curative strategy for this disease. Although there are risks with this therapy, it has been used successfully in this condition in New Zealand and the safety of this form of treatment for other conditions is improving. Patient selection is critical and the outcomes are particularly good in PNH patients transplanted for haemolysis without complicating thrombosis or aplastic anaemia (deLatour et al. *Haematologica*, 2012;97:l666- 73). Although this form of therapy is also expensive, the average cost of an allogeneic stem cell transplant is a fraction of the annual cost of eculizumab therapy for one patient.

Equity of access to treatment

Overview

51. Another major theme in responses from those opposed to PHARMAC's proposal was the right of those with PNH to have equity of access to treatment. Approximately a fifth of respondents opposing PHARMAC's proposal cited the rights of all to receive quality care and treatment. These responses focused on:

    - basic human rights as expressed by the United Nations and in New Zealand law
    - the obligations of District Health Boards (DHBs) under the New Zealand Public Health and Disability Act 2000, and on PHARMAC as DHBs' purchasing agent
    - a general social responsibility to provide equity of access to people requiring treatment.

52. Twenty-two of these responses provided standard statements citing the agreement between DHBs and PHARMAC about how funding decisions are made. Further, several respondents stated that there was no indication in the consultation document that human rights and legal obligations had been addressed by PHARMAC.

Human rights

53. Many respondents stated that New Zealand was part of the United Nations and took pride in the country's human rights record. These respondents considered that New Zealanders would agree that citizens have a right to life. Hence, PHARMAC has a moral obligation to ensure that everyone has access to life sustaining treatment when such treatments are available, with no clinical population being abandoned.

54. Further, in all decisions, PHARMAC must act consistently with the human rights framework that exists in New Zealand, including acting equitably and incorporating community values to give practical effect to the right to life and the right to health.

55. PHARMAC's proposal to decline funding for eculizumab was considered to breach the Human Rights Act 1993 which states, among other things, that it is unlawful to deny, or treat a person less favourably, on any of the prohibited grounds of discrimination. PHARMAC's proposal would also be in breach of the Universal Declaration of Human Rights and the International Covenant on Economic, Social and Cultural Rights, to which agreements New Zealand is a signatory.

The New Zealand Public Health and Disability Act 2000

56. In addition, respondents stated that PHARMAC's proposal to decline funding is in contradiction of a stated objective of the New Zealand Public Health and Disability Act 2000; that is, ensuring the best care and support of those in need of services. It was also considered by respondents to be contrary to the agreement between DHBs and PHARMAC about how funding decisions are made. This agreement has goals of 'equity of access, reducing inequalities and improving health outcomes for individuals and communities, which should guide the relationship and decision making.'

57. Further, some respondents considered PHARMAC must as an agent of the DHBs place greater emphasis on:

    - the purposes of the New Zealand Public Health and Disability Act 2000
    - the objectives of DHBs
    - the Health Minister's expectations (specifically about access to specialised medicines), and

- PHARMAC's memorandum of understanding with DHBs, and policy and decision criteria guidance in the health sector.

58. More specifically, District Health Boards have a duty to address issues of rights, equity, fairness and community values. PHARMAC is acting as their purchasing agent and should use the same decision criteria and priorities that DHBs have – and not place so much emphasis on costs, cost-effectiveness and alternative use of the money. Respondents stated that the consultation document does not address any of these factors.

59. It was noted by one PNH patient that PHARMAC's proposal did not adhere to the government's medicines strategy which states that 'New Zealanders in similar need of medicines have an equitable opportunity to access equivalent medicines. Medicines and other resources are allocated in a manner that reduces inequality of outcomes'. Further there was no mention of the medicines strategy in any of the material relating to PHARMAC's proposal to decline funding eculizumab.

60. Some respondents contested PHARMAC's interpretation of several key phrases in its legislative brief, including the meaning of 'best health outcomes' and 'reasonably achievable'. These respondents' alternative perspectives would, they believe, lead to a different decision on funding eculizumab.

> *We expect PHARMAC would argue that they are delivering their legislative objective which is 'to obtain the best health outcomes that are reasonably achievable within the budget'. It's all down to interpretation of course. Our family's interpretation is that PHARMAC have fallen short. Given we don't see anywhere, the words 'excluding those people with rare diseases', we assumed all New Zealanders' needs would be debated fairly and honestly.*

General social responsibility & equity of access

61. In addition to citing specific legislation and health sector guidelines, many respondents considered PHARMAC has a social responsibility or moral obligation to help improve the quality of people's lives and where possible to improve their life expectancy.

> *The rights of these patients are paramount in order that they may have access to life restoring and life saving treatment. These patients have a fundamental human right to achieve the goals, to work, to study and be contributing members to their families, and community. To deny them this basic right is inhuman and unethical.*

62. One clinician noted that in a country where a single DHB spends $63 million on treatment of alcohol related harm, it is inappropriate to withhold treatment from a small group of patients with very severe disease who have a significant chance of dying from it.

63. Focusing specifically on cost in relation to basic human rights, these respondents stated that:

- Cost must not be a factor in deciding whether to provide New Zealand citizens a proven, life saving treatment that they deserve. The issue of cost should be handled after the right to receive this life saving treatment is delivered to these citizens by their government.
- Rare disease patients have as much right to health services as those with chronic disease. The cost is but a drop in the bucket compared to what is spent on cholesterol lowering drugs.

64. One respondent also commented that people who have worked and paid taxes, when in need of medical treatment, are told that their tax dollars go to support other people and not them.

65. Additionally it was pointed out that PHARMAC funded drugs such as paracetamol and statins that people could afford to buy themselves, whereas eculizumab was unaffordable for individuals.

Role of ethics in decision making

66. Many respondents considered there was no 'ethical fairness' in discriminating against someone with a rare disease and yet offering equally or more expensive treatments to groups of people with more common diseases.

> *Much of the New Zealand health budget is spent on preventable diseases and yet people born with congenital, genetic conditions and other rare diseases are largely ignored. This inequity needs to be addressed immediately.*

67. Respondents stated that the role of ethics in decision making had not been addressed at all in this consultation (and had been poorly addressed by PHARMAC over many years). 'Appropriate and proper decision-making in health requires that these issues are more robustly addressed in a way that is consistent with the widely accepted role of ethics in healthcare in New Zealand.'

68. One respondent stated that PHARMAC had developed its internal culture in response to perceptions of amoral commercial interests, and it was time for PHARMAC to evaluate what it has become as a consequence.

> *PHARMAC's actions, in proposing to decline funding for a treatment for which there is little or no debate over with regard to efficacy, on the basis of a cost which has not yet been determined through good faith negotiation, is immoral.*

69. PHARMAC was asked by many submitters to see the value that funding eculizumab will have on PNH sufferers and their families – rather than focusing solely on the cost.

Consumer engagement

70. One group and an attendee at a meeting with PHARMAC suggested that PHARMAC had not adequately engaged with consumers with this particular proposal ('and in general PHARMAC's consumer engagement falls far short of a standard expected across all areas of life in New Zealand').

Special decision criteria required

71. Related to the equity of access to treatment issues presented above, most respondents opposed to PHARMAC's proposal considered that PHARMAC should have special decision criteria for particularly high cost pharmaceuticals or treatment for rare diseases.

72. One hundred and fifty seven respondents provided standard feedback in support of the PNH Support Association of New Zealand's proposition that PHARMAC establish fair assessment criteria, based on expert advice from the international haematological community, to assess patient need for Soliris.

73. Respondents providing more detailed feedback also made a number of other points:

- Patients suffering from rare diseases were considered to be doubly disadvantaged by 1) the higher cost of new treatments, and 2) the higher cost of a very small 'market' for that medicine.
- In addition, (as previously noted) in the case of PNH where a highly effective treatment is available, no randomised trial of sufficient size is ever likely to be done.

Hence, trying to get a strong case for funding eculizumab based on a compelling cost utility analysis is very difficult.

- Consequently, there should be an additional layer of decision-making for rare diseases that do not fit the standard cost effectiveness threshold for large populations.
- Such an additional layer was stated to exist in Australia, Scotland and other countries, 'because they have decided that is a fair way to deal with the disadvantage people with a rare disease face.'

74. In standard statements put forward by respondents, it was noted that the Ombudsman considered that the decision criteria under the exceptional circumstances scheme ought to be clearly differentiated from those under the pharmaceutical schedule. 'This opinion demonstrates the inappropriateness of considering medicines for individuals or tiny populations under the same criteria used for large populations.'

75. Similarly one group noted that PHARMAC appears to consider that the issue of high cost medicines was dealt with by the McCormack and Hansen study some years ago; however, this study does not address the point that if and when medications for rare conditions are placed in competition with drugs for more common conditions, they are 'always doomed to fail.'

76. PHARMAC was considered poorly equipped to handle rare diseases and their speciality medicines – 'if specialized medicines do not fit your business model you need a new model.' One respondent stated that the wider health system in New Zealand has recognised the importance of very expensive treatment through its high cost treatment pool for high cost surgery – 'yet for some reason PHARMAC is yet to substantively address this issue.'

77. Respondents were concerned that some conditions could be treated because enough people suffer from them to allow bulk buying to be possible, while others born with a rare condition are considered to have lives that are expendable due to the cost of medications that cannot be bought in sufficient quantity to obtain discounts. This approach was considered both grossly unfair and overly simplistic.

78. More generally, several respondents argued that PHARMAC needed to be flexible in assessing medicines, taking into account the cohort of patient numbers, the variability of disease progression and other factors as a matter of urgency.

> *Presently we are entering an era of personalised, genetic therapies and PHARMAC and the government need to recognise this and quickly develop more flexible and empathetic processes of assessment to provide a more fair and equitable program to those who need it.*

79. Using standard responses provided by the PNH Support Association of New Zealand, 60% of respondents (including two groups, six NPH patients and 149 other individuals) stated that PHARMAC 'must amend its operating policies and procedures to acknowledge the right of rare disease patients to access life restoring and life saving treatments as in the specific example of the Soliris treatment.'

80. One group considered that even within the current operational policies and procedures PHARMAC had failed to adequately address several important decision criteria.

> *PHARMAC's narrow perspective on technical assessment and budget management, to the exclusion of patient rights and interests from their decision processes, and outcomes that effectively discriminate against patients with rare diseases, is not a reasonable outcome by any measure.*

81. One group in favour of PHARMAC's proposal noted their support for PHARMAC's funding process, and the three assessment areas that PHARMAC uses to make decisions about the

funding of pharmaceuticals. This group would, though, support the setting up of a separate source of funding for patients with rare conditions who want access to very expensive drugs.

International funding of eculizumab

82. Twenty-eight respondents noted in their feedback that other countries (ranging in number but generally put at between 30-40 internationally) fund eculizumab. Eculizumab was specifically stated to be currently available to patients with PNH in Australia, many countries in Europe, the United Kingdom, Japan, the United States, Canada, Turkey and Brazil.

83. One group suggested that PHARMAC had misinformed the community about eculizumab funding decisions in Canada and Scotland,[3] thus misleading people about funding decisions made in other jurisdictions.

84. Respondents considered that as eculizumab was widely available internationally, PHARMAC's proposal was very difficult to understand: other 'cash strapped' nations were meeting the funding challenge, and 'putting a higher value on their citizens' lives than New Zealand.'

85. It was suggested by these respondents that PHARMAC look at the policies and processes of countries that fund eculizumab to help it develop a funding model.

86. It was also suggested by two clinicians that PHARMAC should look at a further round of expert consultation, both nationally and internationally, before moving forward with its proposal to decline funding for eculizumab. These clinicians stated that PHARMAC had not consulted with either New Zealand or international haematologists who have experience in treating PNH patients with eculizumab, and therefore does not appreciate the dramatic benefits of eculizumab treatment.

87. During a meeting with a clinician and with the parent of a PNH patient, PHARMAC staff stated that they had sought advice from haematologists who have experience with eculizumab, including advice from international specialists. For example, PHARMAC staff had met with Professor Peter Hillmen (the lead investigator for a pivotal eculizumab clinical study) and Professor Hillmen had submitted information to PTAC and the haematology subcommittee for their review. This current consultation for eculizumab is also a mechanism for PHARMAC to obtain advice from clinicians.

88. One parent of a PNH patient noted that other countries have met the challenge of funding eculizumab by developing strict criteria to limit patients' eligibility. In Quebec the policy was to wait until the patient had severe complications, then allow it.[4] Brazil, 'with a huge

[3] With reference to the PTAC recommendations about cost and cost-effectiveness in the consultation document. See the PTAC minutes of August 2012 [para 3.11] relating to the drug's high cost and poor cost-effectiveness: 'The Subcommittee noted that this is the reason why the Canadian Agency for Drugs and Technologies in Health (CADTH) and Scottish Medicines Consortium did not recommend it for use within their jurisdictions.'

[4] One respondent stated that the following eligibility criteria were used in Australia and Canada:
The diagnosis of PNH must have been established by flow cytometry. (The proportion of circulating cells of each type which are GPI-deficient and hence of the PNH clone is quantitated by flow cytometry.) To be eligible for subsidised treatment, patients must have a PNH granulocyte clone size equal to or greater than 10% and a raised LDH (value at least 1.5 times the upper limit of normal for the reporting laboratory). PNH Patients with a clone size greater than 10% also require at least one of the following criteria to be eligible for treatment with eculizumab:
a) Thrombosis: This is a thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy.
b) Transfusions: Evidence that the patient has been transfused with at least four units of red blood cells in the last twelve months
c) Anaemia: Chronic or recurrent anaemia where causes other than haemolysis have been excluded and demonstrated by more than one measure of less than or equal to 70g/L or by more than one measure of less than or equal to 100 g/L with concurrent symptoms of anaemia.
d) Pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than

population in need of many services across the board and a very tight budget' reportedly allows appeals, and funds the most severe cases. These examples were considered by submitters to be better than a 'no exceptions' rule.

89. Some submitters considered that the smaller population (and wealth) of New Zealand was offset by the correspondingly lower number of individuals with PNH. Several respondents questioned whether PHARMAC was arguing that New Zealand was fiscally the same as 'under-developed' African countries.

90. Many of the respondents making international comparisons stated that PNH patients were effectively obliged to emigrate or remain away from New Zealand.

> *The fact that Soliris treatment is not funded in New Zealand is perhaps the most significant factor in my decision whether to commence this recommended treatment. I always intended to return to New Zealand to live. Should Soliris continue not to be funded in New Zealand, I will be prevented from returning to my homeland.*

91. However one clinician in support of PHARMAC's proposal suggested that although eculizumab has been funded in other countries, New Zealand must make its own decision about this in relation to the health needs of the population and the resources available. 'Funding decisions made in other developed countries should not automatically be adopted here, in my opinion.'

Prioritisation of spending

92. Outside of PHARMAC's area of responsibility, eight respondents questioned the prioritisation of tax payer funded national spending in New Zealand.

93. One of these respondents considered it should be the job of the public to decide how important they think life saving medicine is compared to other priorities.

> *The public should be able to decide whether to spend more on life saving medicine or to put interest on student loans, or to raise taxes, or to stop wasting money on a pointless military that could defeat no one. Why should these decisions be the domain of a few bureaucrats with a defeatist attitude? Bottom line is that if there is treatment that is life saving and we do not try it then we as a nation need to re-evaluate our priorities. The notion that we just can't afford it doesn't wash.*

94. Another respondent queried PHARMAC's decision in light of the government giving '$67 million to the production of the Hobbit.'

95. During a meeting PHARMAC held with PNH patients and their supporters, one attendee questioned whose job it was to lobby government for more money for pharmaceuticals. PHARMAC staff replied that PHARMAC's role is to implement government policy and advise the government on funding options. PHARMAC cannot publicly lobby government but can provide recommendations.

Reprioritising or increasing the pharmaceutical budget

96. Several respondents suggested that if PHARMAC's budget was not adequate, then it was PHARMAC's responsibility to address the issue. This could be done by applying to the

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PNH have been excluded.
e) Renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60mL/min/1.73m2, where causes other than PNH have been excluded.
f) Smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalisation and/or narcotic analgesia, where causes other than PNH have been excluded.

government to increase the pharmaceutical budget. Another respondent considered that sufficient pharmaceutical funding existed to treat people for PNH. 'Why not borrow from some of the drugs aimed more at the baby boomers, who own two homes already, and spend their lives on cruise ships?'

Suggested approaches for funding eculizumab

Negotiation with Alexion Pharmaceuticals

97. Approximately two-thirds of respondents asked that PHARMAC renegotiate with Alexion Pharmaceuticals. Most of these respondents were individuals using standard feedback provided by the PNH Support Association of New Zealand that included the statements:

> *PHARMAC must return to the negotiating table with the supplier of the Soliris treatment. PHARMAC must negotiate in good faith toward funding Soliris for a minimum of eight New Zealand PNH patients.*

98. Many respondents expressing this view considered that PHARMAC's responsibility is to facilitate access to viable therapies in as cost effective manner as possible. In relation to eculizumab it was up to PHARMAC to negotiate the most advantageous deal to supply the treatment, and not to 'deny New Zealanders life' because it could not negotiate a solution. PHARMAC must return to negotiations to find a solution – 'the precise expertise upon which PHARMAC has built its international reputation.'

99. All respondents that suggested PHARMAC renegotiate with Alexion Pharmaceuticals were of the view that Alexion would be prepared to enter negotiations with PHARMAC and to lower the price of eculizumab.

100. One clinician stated that the supplier had indicated that they would be able to provide a 50-80% discount via confidential rebate. Relating to PHARMAC's expressed concern that 'costs would be likely to increase as more patients meet the access criteria….', the same respondent stated that Alexion Pharmaceuticals 'are comfortable with entering into a risk-sharing proposal, if there are concerns about potential patient numbers increasing.'

> *Indeed, they have already done that in several other countries where eculizumab is available, and would be quite happy to do that for New Zealand. … PHARMAC might be pleasantly surprised by the level of co-operation and goodwill they receive.*

101. Respondents queried whether PHARMAC had seriously attempted to negotiate with Alexion Pharmaceuticals, and indicated to Alexion the price point at which they would be prepared to buy.

102. During a meeting between PHARMAC and a clinician and a parent of a PNH patient, PHARMAC staff noted that PHARMAC had repeatedly stated to the supplier that they need to provide the best pricing possible as this is very relevant to PTAC and the haematology subcommittee. PHARMAC had also made it clear to the supplier that they could put in a submission to this consultation, which could be an updated commercial proposal. The pricing in the consultation document is in fact the net price. PHARMAC would be interested in discussing the provision of discounts with the supplier.

103. One respondent noted that PHARMAC has stated that the drug idursulfase is supported (through the named patient pharmaceutical assessment) at a cost of $419,000 per year, and questioned whether this indicated the price point below which PHARMAC would (re)consider funding eculizumab.

Effect of decision on the pharmaceutical industry

104. One respondent commented that one of the many benefits of funding eculizumab is that it encourages the pharmaceutical industry to invest in and develop new therapies.

> *There are considerable financial risks involved in funding research and development of new treatments and therapies for rare diseases. The pharmaceutical industry cannot be expected to continually fund and support research into rare diseases when the government will not fund effective treatments using very shaky ethical grounds as their reason for refusal.*

105. However, two groups supportive of PHARMAC's proposal expressed concern at the role of the pharmaceutical industry in funding special interest groups to lobby for particular drug treatments.

The eligibility criteria for eculizumab

106. In addition to the wider points about funding eculizumab described above, several respondents suggested amending the eligibility criteria for eculizumab to make funding the drug more affordable.

107. Respondents suggested:

- Getting PNH experts' advice on how to prioritize 'who shall live' - which patients' lives are most likely to be saved is the most reasonable approach. 'Even that sounds harsh but is more acceptable than saving no one.'
- Covering some patients on a case by case basis – 'the larger the clone the greater the risk. History of a clot (often life threatening) greatly increases the odds of another clot, then death. Since not all high risk patients would get Soliris, some will die.'
- Providing eculizumab only for those with the most advanced symptoms and high risk of blood clotting in particular.

108. One clinician noted that PHARMAC's proposed symptomatic criteria (severe abdominal pain, fatigue, shortness of breath) are subjective, relatively non-specific and with considerable variability in interpretation. This respondent considered it hard to justify spending over half a million dollars per year to improve fatigue in a single person, which appeared to be possible under the proposed criteria (noting the highly variable clinical severity of PNH). This clinician stated it may be appropriate to consider a different threshold for funding a small number of the most severely affected patients rather than just adopting the 'arguably quite liberal criteria' used in some countries for such expensive therapy. As a compromise it may be appropriate to explore different thresholds for funding eculizumab for a very small number of patients with the most severe clinical manifestations of PNH.

109. Another clinician suggested making changes to the Australian access criteria for use in New Zealand:

- Increase the clone size from 10% to 20%. Clone size must be assessed formally, using standardized criteria, preferably in a single laboratory in New Zealand.
- Increase the red blood cell transfusion requirement to more than six units of blood in 12 months, rather than four units.
- These slightly more restrictive criteria would reduce the number of New Zealand patients that would be potentially eligible for eculizumab treatment, perhaps bringing the patient number down from 10 patients to around eight patients.

110. It was similarly suggested by another clinician that if using clearly defined but restrictive New Zealand access criteria, PHARMAC must look at ways of identifying the most severely affected

patients. Using the Australian criteria in New Zealand there would be 12 patients who would be eligible. If the criteria were stricter, for example, 60% clone and a history of thrombosis, this would reduce the number to six – ensuring the most severely affected patients are treated. 'This approach does carry the risk that the first episode of thrombosis may be fatal but it will at least allow the most severely affected patients to be treated.'

Other suggestions for funding eculizumab

111. It was also suggested that PHARMAC consider:

- introducing a part funding model where perhaps families, a DHB, government department or non-governmental organisation shared the cost
- matching the number of PNH patients that receive eculizumab free of cost on compassionate grounds from the manufacturer.

112. As noted previously, one of the groups in favour of PHARMAC's proposal to decline funding would support the setting up of a separate source of funding for patients with rare conditions who want access to very expensive drugs.

113. During the meeting between PHARMAC and PNH patients and their supporters, an attendee asked what needed to be done to get eculizumab funded. PHARMAC staff explained that the drug supplier could present PHARMAC with a new proposal. Even if a decision is made to decline the funding, this will not prevent PHARMAC from reconsidering funding eculizumab if the supplier presents a new commercial proposal or new clinical evidence arises.

Views of those who support PHARMAC's proposal to decline funding

114. The views of those who support PHARMAC's proposal to decline funding for eculizumab have been noted where relevant above. This section of the report draws these views together.

Cost

115. Two groups (with women's health interests) and two clinicians supported PHARMAC's proposal to decline funding for eculizumab. This agreement was based on the cost of eculizumab and the effect this would have on the availability of funding for other conditions. Consequently, several of these respondents - and one additional clinician - would support eculizumab being funded if the price could be reduced.

> *Although I do not have any information about the actual price that might be achievable through negotiation, unless this were to be a small fraction of the suggested price of over $500,000 per patient per year, it is my opinion that much greater health benefits could be achieved for the New Zealand population by spending this money on other initiatives.*

116. The clinician who possibly supported PHARMAC's decision agreed that it was difficult to see how, at the list price, eculizumab represents value for money. However this agreement was dependent on whether PHARMAC had negotiated with the supplier. ('If the price could be brought down to perhaps $300,000 per year per patient I would endorse its listing given there are probably only about 10 patients that really need it.'). This view was based on two current cost benchmarks: imatinib ('and its kin') for chronic myelogenous leukemia and treatment of haemophilia.

The former set the bar at $60-80k per year per patient for a life-transforming therapy but, arguably, one that had an existing therapy in the form of allogeneic bone marrow transplant. Haemophilia, although outside your funding remit, has a wide range of cost / patient but a severe (as in severely deficient factor 8) adult would usually consume approximately $150-200k of F8 in prophylaxis and this might double if the joints are bad. Patients with inhibitors cost far more than this. One could argue, therefore, that the current standard for life-transforming therapies is an ongoing cost of $100-200k per patient per year. If one factors in the novelty and small numbers (which affects the returns to the supplier as well as your costs), I believe that a price of <$300k per patient per year would be reasonable in this case.

117. As previously noted another clinician who supported PHARMAC's proposal because of the expense of eculizumab suggested it may be appropriate to consider a different threshold for funding a small number of the most severely affected patients.

Setting a funding precedent

118. One clinical respondent stated that although funding eculizumab for PNH would represent a small proportion of the pharmaceutical budget because of the rarity of the disease, such funding potentially sets a precedent.

> *Other companies seeking funding for rare disease treatments are likely to view the price achieved as a benchmark … Collectively, funding expensive rare disease treatments could have enormous financial implications if the cost of treating each disease is similar to that of using eculizumab for PNH.*

Efficacy of eculizumab & other treatments

119. Three of the four respondents supporting PHARMAC's proposal commented on the efficacy of eculizumab.

120. Respondents acknowledged that eculizumab provided some treatment benefits over current treatment options; and also that length of survival rates are extended for some (but not all) patients treated with this drug. However, one group could not find any new evidence that supports the PNH Support Association of New Zealand's claims that eculizumab returns life expectancy to expected norms.

> *Of the various trials using Soliris for PNH treatments as listed on the ClinicalTrials.gov website that have been notified as being completed there are no new postings of study results. We continue to emphasise that, without the opportunity for independent scientific peer-review critique of all the findings, reliance on the evidence provided by the drug company of efficacy, safety, and long term benefit must be treated with caution. We note key authors named on the published papers publicly available to date have all declared a conflict-of-interest association with Alexion Pharmaceuticals.*

121. Consequently this group continued to endorse the current decision criteria used by PHARMAC, and agreed that budgetary impact is a valid and significant matter to consider alongside other criteria. This group did not find the equity and fairness claims for this particular patient group outweighed those of any other claimant group seeking access to new drugs.

122. One group's support for PHARMAC's proposal was also based on the fact that funding of eculizumab would be needed long term for those who need treatment, and that there are currently other treatments available and being used in New Zealand for PNH.

123. As previously described, one clinician noted that while other treatment options for PNH are limited, there are some beneficial therapeutic strategies for some patients.

Role of the pharmaceutical industry

124. Two women's health interest groups expressed concerns about the growing potential for pharmaceutical companies to 'educate' patient groups and the public about treatment options to 'fix a problem' through a particular drug, and then claim to have brought an informed public alongside them.

125. Such practices included drug companies' establishing or helping patient support groups, and providing funding for such groups to lobby publicly for a particular drug.

> *This unacceptable use of vulnerable people to publicly pressure governments and health agencies to fund expensive or over-priced new drugs must be exposed and rebutted wherever and whenever it occurs. Alexion Pharmaceuticals' funding for PNH patient support groups is widely recognised and the funding it has given to the New Zealand PNH support group is a matter of public record.*

126. Eculizumab was seen by one of these groups as an extreme example of the pharmaceutical industry charging exorbitant prices for niche drugs and then 'vigorously' marketing these to the public.