CONSULTATION

PHARMAC
Pharmaceutical Management Agency

21 May 2013

Proposal to decline a funding application for eculizumab

PHARMAC is seeking feedback on a proposal to decline the application from Alexion Pharmaceuticals for funding eculizumab (Soliris) for the treatment of paroxysmal nocturnal haemoglobinuria.

Background information relevant to the proposal can be found below and on the following pages.

Why is PHARMAC proposing to decline this funding application?

This proposal to decline the funding application is consistent with the clinical advice we have received, which recommended that the application be declined because although it is an effective treatment, it is extremely expensive.

PHARMAC's cost-utility analysis of the use of eculizumab in patients who have PNH shows 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, appears to be out of reach.

There are always more medicine funding applications than the available budget will allow. Even if DHBs had much more money available, at the current price, eculizumab is not cost-effective and would be likely to be at the back of the queue of medicines that could be funded.

PHARMAC's current view is that we cannot justify progressing eculizumab for funding in light of other funding options for DHBs. By way of example, in the 2011/12 financial year, we estimate that $5.5 million was spent on new community medicine investments which benefitted approximately 19,000 patients. A decision to fund eculizumab for 12-20 patients from 2013/14 onwards would potentially mean that 40,000 other patients would be missing out on health gains (from other treatments that could be funded instead).

We recognise that a decline proposal is not what patients with PNH are hoping for, but we are proposing to decline this funding application because we understand that certainty is something that patients with PNH and their families would prefer.

What does a proposal to 'decline' this funding application mean?

PHARMAC has not made a decision about the funding of eculizumab.

Before we do, we are making information available that we have based this proposal on for people to consider and comment on in detail. We want to hear from the community on its views about whether it would be appropriate to decline the funding of eculizumab. We are also interested to hear views as to whether any decision criteria (other than the eight we regularly consider) should be taken into account when deciding this application and, if so, what they should be.

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All consultation responses received for this proposal will be provided to the PHARMAC Board for consideration when it makes a decision on the funding of eculizumab for PNH.

If the PHARMAC Board makes a decision to decline this funding application, it would mean that PHARMAC would not progress eculizumab for funding. However, if such a decision was made, it would not prevent PHARMAC from reconsidering funding for this treatment in the future if (for instance) material new evidence became available or if the price reduced substantially.

Feedback sought

PHARMAC welcomes feedback on this proposal. Your response may include any material which is relevant to the proposal.

Written feedback

To provide feedback, please submit it in writing by **Wednesday, 31 July 2013** to:

Sue Anne Yee	Email: eculizumabfeedback@pharmac.govt.nz
Therapeutic Group Manager	Fax: 04 460 4995
PHARMAC	Post: PO Box 10 254, Wellington 6143

All feedback received before the closing date will be considered by PHARMAC's Board prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the content of their feedback and their identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request.

Consultation meetings

In addition to providing feedback in writing, PHARMAC would welcome requests to discuss this proposal face-to-face with any interested parties. Please forward meeting requests to the email address above.

Information relevant to the Proposal

This section includes a summary of the information PHARMAC has considered when preparing the proposal to decline funding for eculizumab. Information about PHARMAC, how it makes decisions and how a particular patient's individual circumstances can be considered, as well as some material about how such medicines are funded in other countries is set out in the Appendix.

Paroxysmal nocturnal haemoglobinuria and eculizumab

PHARMAC received an application to fund eculizumab (Soliris) for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) from the supplier, Alexion Pharmaceuticals, in November 2011.

PNH is a rare blood disorder which is characterised by the destruction of red blood cells, an increased risk of blood clots, impaired bone marrow function and a risk of developing leukaemia. PNH is a chronic disease which can be life-threatening with approximately 12-20 patients with more severe disease in New Zealand.

Current treatment in New Zealand for PNH aims to relieve symptoms rather than cure the condition, and includes blood transfusion to treat anaemia, immune suppression with steroids to suppress ongoing red blood cell destruction and anticoagulation with warfarin to prevent or treat blood clots. Other than bone marrow transplantation, which is associated with significant risks, there is currently no known cure for PNH.

Eculizumab is a monoclonal antibody which stops red blood cell destruction, which is characteristic of PNH. Eculizumab is an intravenous infusion administered fortnightly. As with current treatments, eculizumab is not a cure for PNH but it relieves the symptoms associated with PNH (for example anaemia, blood clots and abdominal cramps) and it needs to be used for the rest of the patient's life.

Clinical advice PHARMAC has received about eculizumab

PHARMAC's clinical advisors have considered the eculizumab funding application on a number of occasions:

- February 2012 – by the Pharmacology and Therapeutics Advisory Committee (PTAC)
- August 2012 – by the Haematology Subcommittee
- February 2013 – by PTAC
- March 2013 – by PTAC (with three members of the Haematology Subcommittee in attendance)

In February 2012 PHARMAC's primary clinical advisory committee, PTAC, recommended that the funding application for eculizumab in PNH be declined. The Committee highlighted concerns in regards to the drug's high cost and the uncertainty about its effects on long-term survival of patients. PTAC acknowledged that there was an unmet clinical need for PNH treatments but considered that the effect of treatment with eculizumab is not in proportion with its cost. However, PTAC also recommended that the application be referred to the Haematology Subcommittee of PTAC for consideration.

The Haematology Subcommittee of PTAC reviewed eculizumab at its meeting in August 2012. The Subcommittee recommended that eculizumab be funded with a low priority for patients with PNH who met pre-defined eligibility criteria. The Subcommittee considered that

the available evidence indicated that eculizumab is effective in reducing blood transfusion requirements and thrombosis rates. The Subcommittee also considered that treatment with eculizumab may be associated with a survival benefit although the evidence for this was limited at this time. It considered that there was no clinical reason why eculizumab should not be listed on the Pharmaceutical Schedule, but its low priority recommendation was due to its extremely high cost.

The minutes from the Haematology Subcommittee were reviewed by PTAC at its February 2013 meeting. PTAC deferred making a recommendation for eculizumab at this meeting because the Committee required more time to consider some additional information submitted by the supplier, in February 2013, which it had not previously reviewed.

On 18 March 2013 PTAC convened via teleconference to discuss eculizumab and, at the request of PTAC, available members of the Haematology Subcommittee of PTAC were in attendance. Following extensive review of all the clinical evidence for eculizumab, including new information provided by the supplier, PTAC reached the view that there was evidence that eculizumab reduced blood transfusion requirements, reduced haemolysis, improved haemoglobin levels, reduced blood clots and reduced fatigue and improved quality of life in patients with PNH. PTAC considered that eculizumab would likely prolong survival of patients but considered that the extent of this benefit is uncertain.

However PTAC maintained its previous recommendation to decline the funding application for eculizumab in PNH because, although there is evidence that it could provide clinical benefit, the cost of the pharmaceutical is so high that it was considered unacceptable and unjustifiable when compared to the costs and benefits of other therapies.

Complete texts of PTAC and the Haematology Subcommittee's minutes can be found on PHARMAC's website.

Cost-effectiveness and funding costs

There are an estimated 60–70 patients with PNH in New Zealand and depending on the access criteria, a subgroup of 12-20 patients with more severe disease who might be considered for funded eculizumab treatment. The pharmaceutical cost of eculizumab is estimated to exceed $600,000 per patient per year; therefore, funding eculizumab for PNH in New Zealand would cost approximately $12,000,000 (20 patients) per year. This cost would be likely to increase as more patients meet the access criteria and qualify for treatment each year.

PHARMAC has undertaken a cost-utility analysis for eculizumab in patients with PNH which helps us to assess its cost-effectiveness. We used the same clinical information in our assessment that PTAC and the Haematology Subcommittee of PTAC considered when making their recommendations.

While there is evidence that there are some clinical benefits from eculizumab treatment, even if the treatment restored every patient to full health (which, based on the information we have, it would not), eculizumab would be at least 20 times less cost-effective than the average medicine funded by PHARMAC in the last financial year.

PHARMAC's technology assessment report (TAR) which records its analysis of cost-effectiveness can be found on our website. Some material has been withheld in accordance with the withholding grounds set out in the Official Information Act 1982.

Appendix

PHARMAC

PHARMAC (the Pharmaceutical Management Agency) is the Crown entity responsible for deciding which medicines are funded in the community by District Health Boards (DHBs) and, from 1 July 2013, in DHB hospitals. PHARMAC manages the Combined Pharmaceutical Budget (which is set by Government) and must ensure spending on pharmaceuticals used in the community and cancer medicines in hospitals is within the annual agreed budget.

In the 2012/13 year, the combined pharmaceutical budget is $783.6 million.

Eculizumab would not be funded from the combined pharmaceutical budget, as it is administered to patients in a hospital setting. However, from 1 July 2013 PHARMAC takes over responsibility for determining the list of pharmaceuticals that will be funded in DHB hospitals and we are working towards taking over responsibility for managing a budget for spending on hospital pharmaceuticals.

PHARMAC's funding process

PHARMAC's evaluation of pharmaceutical funding applications falls into three broad assessment areas: clinical, economic and commercial.

Clinical assessment

Our main clinical advice comes from the Pharmacology and Therapeutics Advisory Committee (PTAC). In addition, there is a network of Subcommittees of PTAC providing specialised advice on a range of medical areas. Overall, PTAC and the Subcommittees provide PHARMAC with a resource of over 160 practising clinicians to call upon for advice.

The clinical committees provide recommendations to PHARMAC based on PHARMAC's nine decision criteria (see below) – they are not the decision-makers.

See our website, specifically http://www.pharmac.health.nz/about/committees/ptac and http://www.pharmac.health.nz/about/committees/ptac/ptac-subcommittees for more information.

Economic assessment

Economic assessment looks at the benefits and costs of proposals.

Most funding applications would result in spending more money for additional health gains for New Zealanders. PHARMAC uses a method called cost-utility analysis to compare potential funding options on a more-or-less equal basis, and as one factor (see decision criteria information below) that is considered when ranking all the potential investments we have in order of priority. Cost-utility analysis includes consideration of:

- The medicine's effects on quality of life (e.g. ability to work/perform usual activities, pain/anxiety, mobility) as well as its effects on the duration of life;
- current available treatments that are used;
- short and long-term effects of treatments;
- pharmaceutical cost of the proposed treatment and current treatments;

- changes to other health sector costs (e.g. hospitalisations, doctor visits); and
- the risk and uncertainties of the evidence available.

Assuming that any impacts of other decision criteria we take into account when ranking potential investments are identical, the more cost-effective an intervention is the more likely it is to be funded.

Commercial Assessment

We enter into direct negotiations with companies where they are the only suppliers of a pharmaceutical (because the medicine is patented or for some other reason) as is the case with eculizumab. Where there is more than one potential supplier, we encourage price competition through the use of competitive processes such as tendering for supply (asking for quotes), and reference pricing (applying the same subsidy to all medicines with same or similar effects). PHARMAC does not "regulate" prices by requiring that pharmaceutical companies supply at a particular price, rather we negotiate subsidies on a 'willing buyer-willing seller' basis.

Commercial assessment means establishing whether funding proposals from pharmaceutical companies represent good value. There are many aspects to this, such as using economic assessment, comparing prices for existing subsidised medicines in the same therapeutic group and with the prices that other countries are paying.

Consultation

Before we make a medicine funding decision or make a change to our policies, we want to be sure that we have considered all the possible reasons for and against a decision, and any likely implications. Consultation is a way of drawing out these issues.

More detail on PHARMAC's decision-making processes can be found at: http://www.pharmac.health.nz/medicines/how-medicines-are-funded

What are PHARMAC's decision criteria?

When deciding which medicines to fund, PHARMAC pursues its statutory objective of securing the "*best health outcomes … from pharmaceutical treatment … within the amount of funding provided*." Given PHARMAC is managing taxpayer funding, PHARMAC's decisions need to represent good value for money for the benefit of all New Zealanders.

PHARMAC uses the criteria set out below, where applicable and giving such weight to each criterion as PHARMAC considers appropriate, to make decisions about proposed amendments to the Pharmaceutical Schedule:

1. The health needs of all eligible people;
2. The particular health needs of Māori and Pacific peoples;
3. The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;
4. The clinical benefits and risks of pharmaceuticals;
5. The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health & disability support services;
6. The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Schedule;

7. The direct cost to health service users;
8. The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere; *and*
9. Such other criteria as PHARMAC thinks fit. PHARMAC will carry out appropriate consultation when it intends to take any such "other criteria" into account.

How much might funding eculizumab cost?

A full adult dose of eculizumab would cost more than $600,000 per patient per year and treatment is likely to continue long-term. With 12-20 patients in New Zealand likely to need treatment for PNH, it would cost $7.2m - $12m per year to fund. This makes it the most costly per-patient pharmaceutical PHARMAC has ever considered.

How much does PHARMAC usually spend on new investments each year?

Typically $10 million would fund nearly all investments PHARMAC would make in community and cancer medicines in any financial year, either through listing new medicines or widening patients' access to existing medicines. For example, 23 new investments made in 2011/12 cost $5.5 million, benefiting 19,000 new patients in that year. Medicines benefited patients with conditions such as osteoporosis, rheumatoid arthritis and other auto-immune disorders, asthma, heart failure, cystic fibrosis and whooping cough.

Does PHARMAC make a distinction between drugs based on price?

PHARMAC uses the same process to assess medicines, regardless of their cost. It uses the nine decision criteria (see above), which ensure that we take into account factors like the benefit to patients, the availability of other treatments, cost, and cost-effectiveness. The decision criteria are used for both Pharmaceutical Schedule listings (for populations of patients), and assessments through the Named Patient Pharmaceutical Assessment policy (NPPA, for individual patients).

PHARMAC doesn't necessarily expect the highest level of clinical evidence for every drug it assesses (i.e. randomised clinical trials). We recognise that in some cases, for instance where very small numbers of patients are affected by a condition, it will not be practical to demonstrate benefit in such a robust way. PHARMAC has, and does, rely on expectations of benefit from weaker sources of information in this context.

The NPPA policy has funded some very expensive treatments for individuals, even in circumstances where the evidence of benefit was weak, but there was a reasonable expectation of good gains. While we afford such circumstances plenty of leeway on the evidential requirement, we do still expect that the benefit is commensurate with the cost of treatment, to maintain a fair allocation of resources.

What do other countries do?

Some countries run `orphan' or high-cost drugs programmes. For example, eculizumab is funded through the Life Saving Drugs Program in Australia. The UK's National Institute for Health and Care Excellence consulted on an orphan drugs policy in 2006, but this has not been implemented. Some treatments for rare conditions are funded in the UK through the National Health Service's Specialised Services programme.

In New Zealand, medicines are funded either through DHB hospitals, the Pharmaceutical Schedule or through NPPA. The high cost of a medicine is not necessarily a barrier to funding, provided that the expected benefits are reasonably proportional to the cost, and compared with other medicines. In New Zealand, the NPPA policy (through the Unusual Clinical Circumstances pathway) takes into account the individual patient's clinical circumstances, and applies a consistent decision-making framework, regardless of the cost of the treatment.

Highest-cost drugs funded by PHARMAC

Below is a table of the highest cost per year pharmaceuticals funded by PHARMAC, which includes patients funded through the Pharmaceutical Schedule and named patient policies:

Medicine	**Medical condition**	**Funding mechanism**	**Cost per Patient**
Idursulfase	Hunter's Disease	NPPA	$419,000
Imiglucerase	Gaucher's Disease	Schedule	$154,000
Total parenteral nutrition (TPN)	Nutritional deficiency	Schedule	$151,000
Octreotide LAR (somatostatin analogue)	Hormonal deficiency	Schedule	$130,000
Sunitinib	Kidney cancer	Schedule	$111,000
Dasatinib	Chronic myeloid leukaemia	Schedule	$100,000
Iloprost	Pulmonary arterial hypertension	Schedule	$100,000

The NPPA Policy

The Named Patient Pharmaceutical Assessment (NPPA) policy (launched in March 2012) provides a mechanism for considering funding for medicines needed by individual patients, but which aren't funded (or haven't been considered for funding) via the Pharmaceutical Schedule.

PHARMAC received 1,105 NPPA applications in the policy's first year of operation. By comparison, the policy it replaced (Exceptional Circumstances) received 898 initial applications. Of the 1,105 NPPA applications received, 693 were approved.

Details of the NPPA policy, including questions and answers for clinicians and patients, and a list of the decisions made, can be found on the PHARMAC website: http://www.pharmac.health.nz/tools-resources/forms/named-patient-pharmaceutical-assessment-nppa-forms.