NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

15 August 2014

Feedback on draft RFP for medicines for rare disorders

PHARMAC is pleased to announce the outcome of the consultation on the draft request for proposals for supply of medicines for rare disorders which was the subject of a consultation letter dated 8 July 2014 which can be found on PHARMAC's website at www.pharmac.health.nz/news/consultation-2014-07-08-rare-disorders.

Background

In July 2014 PHARMAC sought public feedback on a draft Request for Proposals (RFP) for medicines for rare disorders. This is a new commercial approach PHARMAC is trialling with the aim of improving access to funded medicines for patients with rare disorders.

We received 23 written submissions to consultation. Ten responses were from suppliers, six from individuals, six from consumer groups, and one from a clinician. Additionally, PHARMAC met with suppliers during the consultation period to discuss the proposal. We received nine Expressions of Interest from suppliers which are considering bidding.

Overview of responses

Overall, people supported PHARMAC trialling this new approach. Most people felt that $5 million per annum of contestable funding over five years was not enough. However, one submitter noted "$5 million seems insufficient but often good ideas start small". Some people thought there was lack of clarity about whether this funding was ongoing or whether there was a risk that funding would cease after five years.

PHARMAC intends that any medicines listed on the Pharmaceutical Schedule as a result of the RFP would continue to be available for people as long as they continue to benefit, as measured by appropriate clinical criteria. PHARMAC has identified up to $5 million per annum that is available for funding rare disorders medicines through the RFP, without placing pressure on its other pharmaceutical funding commitments within the Combined Pharmaceutical Budget (CPB). PHARMAC will be evaluating whether the new approach has achieved its objective before considering whether to run a further RFP in future years.

PHARMAC is not proposing to ring-fence funding for rare disorders. Just as with any new medicine listed on the Pharmaceutical Schedule, any medicine funded as a result of the RFP would become a budget line in our forecast for managing the CPB.

Some people suggested that PHARMAC should use multi-criteria decision analysis to inform its decisions on the RFP proposals, rather than focusing on cost-effectiveness analysis or traditional health technology assessment frameworks. PHARMAC's pharmaceutical funding decisions involve consideration of all of the nine decision criteria[1], of which cost-effectiveness is but one criterion. PHARMAC considers that these current nine criteria provide a suitable basis on which to assess bids

[1] PHARMAC's nine decision criteria can be found at www.pharmac.health.nz/medicines/how-medicines-are-funded/decision-criteria/. The criteria are currently undergoing review.

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received through the RFP process and that using these criteria would be consistent with PHARMAC's Operating Policies and Procedures.

Overall, feedback did not suggest that the proposed prerequisites were inappropriate for the purposes of the RFP. We have made a minor amendment to prerequisite five to better reflect the intent of this prerequisite so that it now reads "The patient's absolute or relative age-specific life expectancy and/or quality of life could be substantially improved as a direct consequence of treatment". We have also clarified the intent of this prerequisite by explaining the meaning of "substantially improved".

Finalised prerequisites and explanatory notes

The updated prerequisites are listed below, followed by an updated description of each of the prerequisites.

Disorder related

1. There is a rare[2] but clinically defined long-term disorder that is identifiable with reasonable diagnostic precision.
2. Epidemiological and other studies provide evidence acceptable to PHARMAC[3] that the disorder causes a significant reduction in either absolute or relative age-specific life expectancy or quality of life, for those suffering from the disorder[4].

Treatment related

3. The medicine is regarded as a proven therapeutic modality for an identifiable patient population[5] i.e. the medicine has been approved by Medsafe or an international regulatory authority[6] for the identified indication.
4. There is evidence acceptable to PHARMAC[3] that the medicine is likely to be clinically effective for the identified patient population[5].
5. The patient's absolute or relative age-specific life expectancy and/or quality of life could be substantially improved as a direct consequence of the treatment[7].

Alternatives related

6. The medicine is not registered for the treatment of another, non-rare disorder, or if it is, the cumulative prevalence across all the indications still falls within the definition of rare[8].
7. There is no suitable comparable[9] alternative treatment on the Pharmaceutical Schedule.
8. There is no suitable[9] funded alternative non-drug therapeutic modality for the rare disorder.

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[2] Rare is defined as an identifiable and measurable patient population with a prevalence of 1:50,000 or less.
[3] On the basis of advice from PTAC and / or the RAD Subcommittee of PTAC.
[4] As measured by absolute or proportional QALY loss.
[5] The definition of the patient population must be clinically meaningful (not arbitrary) and must treat patients with the same clinical circumstances equally.
[6] Regulators that are recognised by Medsafe for the purposes of an abbreviated approval process, as listed on page 38 of - http://www.medsafe.govt.nz/regulatory/Guideline/Full%20-%20NZ%20Regulatory%20Guidelines%20for%20Medicines.pdf
[7] As measured by absolute or proportional QALY gain.
[8] Bidders would be required to reveal their overseas approved indications and their phase three development programme.
[9] Suitable is defined as a treatment that provides a comparable health outcome to the medicine under consideration, for the patient population under consideration.

Explanation of prerequisites

Prerequisites one and six – rarity

There is no universally-accepted definition of what 'rarity' is. A condition may be considered rare in one part of the world, or in a particular group of people, but be considered common elsewhere.

For the purpose of this RFP PHARMAC intends to define a rare disorder as one that affects one person for every 50,000 people in the general population. This definition would mean there are currently up to 90 people across the whole of New Zealand that have each rare disorder.

The prevalence definition would apply to ongoing conditions - a condition lasting longer than 12 months.

Suppliers might wish to seek to limit the total number of patients eligible for funding to a number which offers a sufficient return on investment, taking into account the fixed funding available. We therefore propose that suppliers would be able to identify a sub-set of people with the disorder who would be eligible for funding, as long as the sub-set is distinct and clinically meaningful, and the total number of people with the disorder still meets the 1:50,000 prevalence criterion.

Prerequisite 2 – disease severity

Under the fund, not only must the disorder be rare but it must cause a significant reduction in either absolute or relative age-specific life expectancy or quality of life, for those suffering from the disorder.

We will measure severity by any reduction in a person's Quality Adjusted Life Years (QALYs) that is due to the disorder. Changes in QALYs measure how much the disorder shortens a person's life expectancy (loss of quantity of life) and how much it reduces the quality of life. Further information on the QALY measure is available in past PHARMAC annual reviews[10].

Prerequisite 3 – registration

The bid must be for a medicine to treat the rare disorder. This can include medicines integrated within a medical device (eg, as a delivery mechanism) but only funding proposals for products classified as medicines will be considered).

The treatment must be a proven therapeutic modality; it should not include experimental medicines or those still in trials. To this end, we will only consider bids for medicines that have been registered by Medsafe or an international regulator recognised by Medsafe. This will provide an appropriate level of assurance of the product's quality, safety and efficacy. It is our expectation that, prior to being listed on the Pharmaceutical Schedule, medicines funded via the contestable fund would need to be registered by Medsafe or have been submitted for registration with Medsafe. If we receive a bid for an unregistered product, we have the option to initiate a Pharmaceutical Schedule listing application outside of the contestable fund process.

You can find a list of international regulators recognised by Medsafe on page 38 of Medsafe's Regulatory Guidelines for Medicines at http://www.medsafe.govt.nz/regulatory/Guideline/Full%20%20NZ%20Regulatory%20Guidelines%20for%20Medicines.pdf.

[10] PHARMAC Annual Review 2010/11. Wellington: PHARMAC, 2011. http://www.pharmac.health.nz/assets/annual-review-2011.pdf (pages 12-13, article by Prof Anthony Harris)

Prerequisites 4 and 5 – effectiveness

There needs to be evidence "acceptable to PHARMAC" that the medicine is effective. We need to reach a threshold of confidence, and it may not be possible for us to determine whether this threshold is reached for completely new medicines that have not already been assessed by the Pharmacology and Therapeutics Advisory Committee (PTAC) (whether they are registered or not) within the time we have available for the RFP.

We will also have the option to initiate a Schedule listing application for any medicines that we are unable to fully consider within the RFP timelines.

Suppliers seeking funding will need to demonstrate that the medicine could significantly affect the natural history of the disorder it treats. We will need evidence that the medicine is likely to be clinically effective and would result in a significant extension in life expectancy or quality of life compared with currently funded treatments. For the avoidance of doubt the requirement that the treatment provide 'substantial improvement' does not mean an absolute gain in health status is needed. Stabilisation or substantially slowing the natural progression of the disorder would be a desirable outcome alongside other possible outcomes. PHARMAC will seek clinical advice as to the likely benefit, based on the evidence provided.

Prerequisites 7 and 8 – alternative treatments

We will exclude medicines for which there is already a comparable treatment funded. Before a medicine is excluded on the basis of prerequisites 7 and 8, the safety and efficacy of the alternative funded treatment must be comparable to the medicine for which we have received a bid, in terms of either absolute or relative age-specific life expectancy or quality of life. For example, this would mean that best supportive care typically will not be considered to be a comparable alternative treatment.

Feedback received

PHARMAC appreciates all of the feedback that it has received and acknowledges the time people took to respond. All consultation responses received were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposal. The following issues were raised in relation to specific aspects of the proposal:

Feedback received	Response
1. What do you think of the proposed rarity definition?	
Overall, people were comfortable with the proposed 1:50,000 rarity definition. Many acknowledged there is global variation in the definition of “rare” and considered our proposed definition aligns more closely with “ultra-rare” or “ultra-orphan” and suggested we adopt this term. People also felt there should be some flexibility as it was often difficult to determine true prevalence. People were less clear about the rationale for pre-requisite 6: “the medicine is not registered for the treatment of another, non-rare disorder, or if it is, the cumulative prevalence of all indications still falls within the definition of rare”. Some people considered this unnecessary as each individual indication should be considered separately for funding. One person noted that rarity should be disease specific not drug specific.	As people noted, there is no international consensus on what constitutes rarity; PHARMAC is comfortable that the proposed definition is fit for purpose. The rarity definition proposed as prerequisite 1 will be adopted for the RFP. Prerequisite 6 intends to provide PHARMAC with greater certainty that the medicine in question will remain targeted to rare disorders and that the risk of pressure on the overall pharmaceutical budget is minimised. Further, in circumstances where a supplier has a potentially large population able to benefit from treatment, the argument that the treatment should be considered differently is less strong due to the ability to recoup research and development costs from a larger patient population.
2. Do you think that the RFP should be limited to medicines that treat disorders that cause a significant reduction in either life expectancy or quality of life? Why or why not?	
People broadly supported limiting the RFP in this way. However, many noted a lack of clarity or context for the meaning of “significant”. People tended to link this with prerequisite 5, which addresses the benefit to the person as a direct consequence of the treatment. As such, people expressed a view that stabilisation of disease progression was a desirable outcome. There was some concern at the level of evidence that would be considered “acceptable” to PHARMAC.	Prerequisite 2 attempts to identify the severity of the disorder to ensure the RFP gives prominence to those rare disorders causing serious deterioration in health status. Prerequisite 2 does not consider the impact that a treatment has on the natural course of the disorder. PHARMAC will retain prerequisite 2 for the RFP. PHARMAC considers all evidence provided for all applications, regardless of level of evidence or quality. Level and quality of evidence contribute to the assessment of clinical benefits and risks (with consequent effects on cost-effectiveness assessment), where clinical benefits are but the fourth criterion of PHARMAC’s current nine decision criteria.
3. Do you think that prerequisite 3, which limits eligible bids to those that have either been approved Medsafe or an international regulator recognised by Medsafe, is appropriate? Why or why not?	
All respondents agreed prerequisite 3 was appropriate but one person also noted that evidence of safety and efficacy should be independent where possible.	PHARMAC will retain prerequisite 3 for the RFP.

4. Do you think prerequisites 4 and 5, relating to the effectiveness of the medicine, are appropriate? Why or why not?

Most people observed there is difficulty obtaining high quality data demonstrating the clinical effectiveness of treatments for rare-disorders due to the small population size. Suppliers in particular were concerned about data quality and also felt it was unclear what an “acceptable” level of evidence meant. Many suggested that modelling or extrapolation data should be acceptable. Consumer groups and individual submitters also noted some concerns at the PTAC Rare Disorders Subcommittee’s perspective on evidentiary thresholds and felt this could disadvantage some groups. Further, a number of this group of submitters felt that cost-effectiveness would be difficult to demonstrate for this type of treatment. One submitter also felt that independent rather than manufacturer provided evidence would be preferable where possible. This person also noted that the QALY was probably the best determinant of treatment effectiveness available for PHARMAC to use. People felt that prerequisite 5, that age-specific life-expectancy or quality of life be substantially improved with treatment, was unreasonable for these groups of people. For many people, stabilising their condition would be an exceptional health outcome whereas a substantial improvement is not realistic.	PHARMAC acknowledges there are challenges collecting evidence for treatments for rare disorders. During the consultation period we sought expressions of interest and met with suppliers, which enabled us to discuss with potential bidders the sorts of evidence and information we would require to inform a bid. The clinical advice we receive from PTAC or its subcommittee will be an important input into our assessment, but it is important to distinguish advice from decision-making. PTAC is able to provide advice, which PHARMAC can use as part of its decision making process. A key reason for trialling this contestable approach is to attempt to improve cost-effectiveness of these medicines through a competitive process. PHARMAC will retain prerequisite 4 for the RFP. Prerequisite 5 was not intended to suggest a mutually exclusive scenario whereby a medicine could **either** improve quality of life **or** life-expectancy but not both. The most highly desirable outcome of treatment would be for both to occur. Noting stakeholder concerns about the feasibility of achieving a substantial improvement, PHARMAC’s view is that a substantial improvement could represent stabilisation or substantially slowing the natural progression of the disorder, alongside other possible outcomes. PHARMAC would seek clinical advice as to the likely benefit, based on the evidence provided. We have amended prerequisite 5 as follows for greater clarity: The patient’s absolute or relative age-specific life expectancy **and/or** quality of life could be substantially improved as a direct consequence of treatment. We have also clarified that stabilisation of a patient’s condition may be a desired outcome of treatment.

5. Do you think prerequisites 7 and 8, relating to the availability of suitable alternatives are appropriate? Why or why not?	
People generally supported these prerequisites although some submitters felt it wasn't clear how they would be interpreted. Many people were pleased that PHARMAC had explicitly stated that this would not include best supportive care. Submitters felt it was important that the suitability of existing treatments was taken into account (eg, if the alternative treatment was an organ transplant, PHARMAC should consider the risks associated with this).	PHARMAC will consider the suitability of the alternative treatments when assessing these prerequisites. The comparator(s) used in PHARMAC analyses can be medicines, devices or services, and need to be both funded in New Zealand and: 1. the funded treatment that most prescribers or clinicians use in New Zealand clinical practice; and/or 2. the treatment given to the largest number of patients (if this differs from the treatment most prescribers or clinicians use). PHARMAC will retain prerequisites 7 and 8 for the RFP.
6. Do you consider it appropriate to state in the RFP that the existence of proposals is not confidential? Do you consider it appropriate for PHARMAC to secure the ability to make the name of the suppliers submitting proposals public?	
Not everyone answered this question, however most were supportive of the proposed approach. All suppliers responded and all except one were comfortable with this information being released. One submitter noted some concern that confidential commercial arrangements following the decision-making process could be breached, given the size of the fund has been disclosed.	PHARMAC will retain this provision in the RFP. We will ensure that communications following any decisions are well-managed so that any confidential commercial arrangements are not undermined.

7. Named Patient Pharmaceutical Assessment (NPPA) implications

Those that responded to this part of the consultation were generally comfortable. There was some lack of clarity about whether all items for rare disorders would be considered via this new mechanism or whether NPPA would remain a legitimate avenue for some. Reassurance was sought that the NPPA process would also not be compromised.	NPPA is an important mechanism for PHARMAC to fulfil its statutory function to provide for subsidies in exceptional circumstances to pharmaceuticals not listed in the Pharmaceutical Schedule. As such, NPPA will remain an option to access treatments for rare disorders, providing the prerequisites of the NPPA policy are met. Bids received through the RFP will not prevent a medicine from subsequently being considered through NPPA, unless the treatment has already been considered by PTAC and prioritised or declined by PHARMAC (in this case the NPPA prerequisites would already not be met). If a medicine was listed in the Schedule as a result of the RFP, a NPPA application might be considered provided the patient was not part of the group that was assessed when the decision to fund the treatment was made **and** all other NPPA prerequisites were met. We will carefully assess any impacts on the NPPA policy as a result of this RFP.

More information

If you have any questions you can email PHARMAC at enquiry@pharmac.govt.nz or call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.