Rare Diseases Subcommittee of PTAC

Meeting held 20 June 2014

(minutes for web publishing)

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These Subcommittee minutes were reviewed by PTAC on 4 July 2014.

Record of the

Medicines for Rare Disorders Subcommittee of Pharmacology and Therapeutics Committee (PTAC)

Teleconference held on 20 June 2014

1 Contestable fund for medicines for the treatment of rare disorders

1.1 The Subcommittee considered a noting paper from PHARMAC staff on the planned Request for Proposals (RFP) for accessing a contestable fund for medicines for the treatment of rare disorders.

1.2 The Subcommittee considered whether there was a requirement to have a Subcommittee. Members noted that there were concerns with respect to equity compared with other treatments of less rare diseases depending on the proposed cut-off of the definition of rare disorder.

1.3 Members considered whether there would be a need to seek additional members. Members noted that it would be appropriate to review any proposals with the current membership and if required additional advice could be sought from experts to inform decisions as per current practice for PTAC and its subcommittees.

1.4 The Subcommittee noted it might be appropriate to approach specialists for individual rare disorders to seek an opinion on a relative priority list to help inform discussion. However members noted there might be potential bias in relation to any opinions due to the small size of New Zealand's population and that the individual specialists are also likely be the treatment providers for the patient population considered.

1.5 The Subcommittee considered whether it would be appropriate to include lay members or ethicists to the Subcommittee. Members noted that PTAC has not historically included lay members in its subcommittees, except in the case of Prader-Willi syndrome. The Subcommittee considered that this could be revisited in time alongside other supplementary membership considerations (see 1.3 above).

1.6 Members noted that the evidence of effectiveness of many of the medicines for rare diseases appeared marginal, i.e. the improvements in longevity or quality of life were minimal and clinically of small relevance. However there were some products with established efficacy where the current price meant they were not cost effective relative to other investments typically made by PHARMAC. Members noted that the proposal was a test to see whether competition would improve the cost effectiveness of products, or encourage suppliers to provide evidence for specific patient populations who would benefit most, sufficient to further progress funding decisions.

1.7 The Subcommittee considered that for all pharmaceuticals clinicians consider efficacy and safety when prescribing. Members noted that all bids for funding in response to the RFP should provide evidence of efficacy for the proposed indication and safety for use in the population targeted. Members noted that although greater weight is placed on well-designed randomised controlled trial (RCT) evidence than other data sources, such RCT evidence may not always be available particularly in the rare disorders setting, and reiterated that the Subcommittee could evaluate any evidence provided, as occurs with all funding applications to PHARMAC.

1.8 The Subcommittee noted that many applications to the Named Patient Pharmaceutical Assessment (NPPA) Advisory Panel reasoned that stabilisation would be an acceptable outcome. Members discussed whether it would be desirable to have evidence that the intervention would alter the natural history of a disease. The Subcommittee considered that it would be suitable to wait for proposals before determining the type of evidence required as the type of proposals was currently unknown.

1.9 The Subcommittee noted the information provided by PHARMAC about treatments for rare disorders that PTAC had previously considered and provided funding recommendations on. Members noted that PTAC had recommended for decline nearly all treatments for lysosomal storage disorders, excluding treatments for Gaucher's Disease, presented to date and had recommended declining eculizumab for paroxysmal nocturnal haemoglobinuria. Members noted that in order to consider these products further new information would be required, such as pricing information or clinical data, not previously seen, indicating better efficacy, safety and cost effectiveness.

1.10 Members noted the proposed parameters for bids required evidence acceptable to PHARMAC. The Subcommittee again noted its concerns regarding equity, particularly that if different evidentiary 'thresholds' conceptually for accepting efficacy were applied to medicines for the treatment of high need rare diseases then this could lead to unfair funding decisions across all PHARMAC funding settings.

1.11 The Subcommittee noted PHARMAC's planned timeline and proposed process for the RFP. Members noted that PHARMAC would be releasing an expression of interest at the same time as the draft RFP, and this would be used to identify new medicines for rare diseases that had not been reviewed by PTAC; PHARMAC would work with the suppliers to get full submissions to PTAC at the earliest opportunity, likely November 2014, this would allow the Subcommittee to provide advice, which could feed into the PTAC review.

1.12 The Subcommittee noted that if a product had previously been reviewed by PTAC then questions regarding any proposed clinical criteria, e.g. entry and exit criteria determining eligibility, could be reviewed by the Subcommittee if appropriate, rather than needing a full review by PTAC.

1.13 The Subcommittee noted that there could be evolving problems defining a rare disease. Members noted that historically, rare diseases were identified by genetic testing of individuals; however the development of potentially effective treatments (incentivising lower thresholds for testing for and then identifying their diseases), alongside the rapid increase in the scope and uptake of patient genomics and associated large decreases in unit costs of testing, will mean that numbers of diseases which might meet the criteria of a rare disease will continue to grow.

1.14 The Subcommittee considered the quantification of rarity for the purposes of the proposed commercial transaction. Members noted international quantification of rarity used in some other health funding settings. Members noted that there was no clinical rationale for the use of any particular prevalence maxima; however the prevalence rates used appeared to be accepted internationally. Members considered that a prevalence of 1:50,000 would be acceptable quantification of rarity to use for the purposes of this contestable fund. A Member noted that it could be possible to consider additional dimensions other than rarity which would allow a sliding scale for access to the contestable fund, i.e. that the 1:50,000 prevalence would not necessarily have to be an absolute threshold. Members noted that a further discussion paper would be provided by the member for later discussion.

1.15 The Subcommittee noted that it would be difficult to determine if suppliers were attempting to use genotyping as a means to determine rarity. Members noted that the proposed criteria require the patient population to be clinically meaningful and this would require that patients with similar clinical circumstances would be treated similarly. Members noted that PHARMAC proposed to aggregate the prevalence number of patients with indications a treatment could be used for and if this summed to more than 1:50,000 people then the treatment could be excluded, but a supplier could make a bid that targeted funding to subpopulations within the 1:50,000 person limit if the proposed subgrouping(s) was (were) clinically meaningful.

1.16 The Subcommittee noted the proposed eight parameters and prerequisites for the draft RFP. Members noted that an earlier proposed parameter 9, a $5 million per annum cap, had been removed subsequent to the release of the discussion document. Members also noted that the prerequisites were intended to define clinical inputs to the RFP and not commercial inputs. Members noted that considerations with commercial issues would be included in the RFP document itself.

1.17 The Subcommittee considered that proposed prerequisite 7 could be made clearer with the insertion of the word “comparable”, although members noted the additional information in the footnotes did specify what would be required.

1.18 The Subcommittee considered that the eight proposed prerequisites appeared to be appropriate and would allow the Subcommittee to evaluate any proposals and provide advice.

1.19 The Subcommittee noted that for evaluation purposes the Subcommittee would require all relevant evidence, preferably peer-reviewed journal articles, PTAC and Subcommittee papers and minutes and a cost utility analysis. At least 1 hour of meeting time should be set aside for analysis and discussion of data provided per pharmaceutical being considered.

1.20 The Subcommittee noted PHARMAC’s analysis of the potential impacts of consideration of bids to the RFP on NPPA applications. Members noted PHARMAC’s view that bids would not constitute an application to PHARMAC for consideration of Schedule funding (and therefore make the related products ineligible for progression under the NPPA Policy). Members noted that it might be appropriate for the Subcommittee to recommend, for bids that are unsuccessful via the RFP process, that PHARMAC progress a Schedule funding application for such products to ensure the NPPA Panel was able to refer to such advice should there be future NPPA applications for the product.

1.21 The Subcommittee noted that if products were funded as a result of the commercial process then it might be necessary to have a panel to assess applications as to whether a patient would meet any entry and exit criteria.

1.22 The Subcommittee **recommended** the following eight prerequisites for the draft RFP as follows:

Disorder related:

1. There is a rare[1] but clinically defined long-term disorder that is identifiable with reasonable diagnostic precision.
2. Epidemiological and other studies provide evidence acceptable to PHARMAC[2] 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[3].

Treatment related:

3. The medicine is regarded as a proven therapeutic modality for an identifiable patient population[4] i.e. the medicine has been approved by Medsafe or an international regulatory authority[5] for the identified indication.
4. There is evidence acceptable to PHARMAC[2] that the medicine is likely to be clinically effective for the identified patient population[4].
5. The patient's absolute or relative age-specific life expectancy or quality of life could be substantially improved as a direct consequence of the treatment[6].

Alternatives related:

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

[1] Rare is defined as an identifiable and measurable patient population with a prevalence of 1:50,000 or less.
[2] On the basis of advice from PTAC and / or the RAD Subcommittee of PTAC.
[3] As measured by absolute or proportional QALY loss.
[4] The definition of the patient population must be clinically meaningful (not arbitrary) and must treat patients with the same clinical circumstances equally.
[5] 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
[2] On the basis of advice from PTAC and / or the RAD Subcommittee of PTAC.
[6] As measured by absolute or proportional QALY gain.
[7] Bidders would be required to reveal their overseas approved indications and their phase three development program.
[8] Suitable is defined as a treatment that provides a comparable health outcome to the medicine under consideration, for the patient population under consideration