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Perspective

Funding therapies for rare diseases: an ethical dilemma with a potential solution

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Abstract. Funding rare disease therapies presents a challenge in Australia where there is a legislative requirement to consider cost-effectiveness. Currently the Life Saving Drugs Programme (LSDP) provides subsidised access to high-cost therapies for rare, life-threatening conditions. However the LSDP is currently under review by the Minsiter for Health and future access to rare disease therapies in uncertain. Internationally there is no gold standard model to evaluate and fund rare disease therapies, and considerable variation exists. However, common features of international systems include the opportunity for early stakeholder engagement, flexibility with evidence requirements, cost-effectiveness criteria and transparency in relation to the decision making framework and outcomes. Australians value equality and equal opportunity in relation to health care. To meet these expectations there is a clear need to maintain a separate fit-for-purpose framework to evaluate and fund rare disease therapies drawing on overseas best practice. This will provide certainty for industry to continue to invest in such treatments, as well as ensuring funding recommendations are reflective of Australian values balanced against the need for financial sustainability.

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Introduction

An estimated 300 million people globally are affected by approximately 7000 rare diseases and disorders.[1] Patients diagnosed with a rare disease face shortened life expectancy, chronic disability and a lack of viable treatment options, which affects them and their families.

In Australia, the need to fund rare disease therapies has conflicted with the legislative requirement to evaluate the cost-effectiveness of new therapies. By their nature, rare disease therapies target smaller markets and prices reflect multiple considerations, including high up-front development costs, difficulties in gathering evidence and commercial objectives. As such, rare disease therapies can be expensive and are often unable to meet cost-effectiveness criteria.

Why fund rare disease therapies?

In this context, the decision to fund rare disease therapies presents an ethical dilemma for decision makers that involves balancing equity considerations and opportunity cost. In essence, the decision to provide funding for rare disease therapies is potentially affected by several conflicting moral arguments, including the pursuit of equality by spending available resources on the greatest good for the greatest number, ensuring equity in access to treatment, the ethical imperative to save individuals regardless of cost and, finally, the responsibility of the medical profession to prioritise the health and well being of patients and to strive to advance knowledge.

There is good evidence that equality and equal opportunity in relation to health care are highly valued attributes of the Australian health system. This is reflected in specific research that shows Australians have a preference towards helping vulnerable members of society, such as the young and those in life threatening situations, regardless of cost.[2] In this context there is a strong community imperative to fund rare disease therapies, which addresses the basic right to health care, the commitment to not abandoning individuals because of the characteristics of their disease and ensuring medicine and science can continue to advance.

The question thus posed is how access to therapies to treat rare disease can be achieved in a manner that addresses equity,

is transparent and ensures the Australian government spends tax payer dollars appropriately.

The Australian situation

Currently, the Pharmaceutical Benefits Advisory Committee (PBAC) is the gatekeeper to providing subsidised access to medicines. Despite flexibility in their funding criteria, historically many rare disease therapies have been rejected by the PBAC for listing on the Pharmaceutical Benefits Scheme (PBS) on cost-effectiveness grounds.[3]

To address this, the Life Saving Drugs Program (LSDP) was established in 1995 with the aim of providing subsidised access to expensive and life-saving drugs for serious and rare medical conditions. Drugs treating rare diseases are only considered for the LSDP once they have been explicitly rejected for funding on the PBS due to cost-effectiveness. Applications are, in turn, assessed on the basis of eight criteria (Box 1).[4]

The LSDP currently funds 12 medicines, which as of April 2015 treated 257 patients at a cost of approximately A$77.5 million.[5] In the context of a growing number of high-cost rare disease therapies, a recent review of the LSDP concluded that the medicines funded were beneficial and safe, but questioned the sustainability of the program.[5]

Through the LSDP, the Government is providing subsidised access to high-cost therapies for rare, life-threatening conditions. However, there are several issues with the LSDP, including the ambiguous nature of the funding criteria and the more recent addition of criterion 4 (see Box 1), which has set an insurmountable hurdle for many rare disease therapies. Only a handful of therapies have been listed on the LSDP in the past several years and questions remain as to whether the LSDP is truly addressing equity issues for rare diseases.

With the Minister for Health considering the future of the LSDP, two scenarios are possible. If the LSDP is retained, there needs to be a thorough consideration as to whether the program is meeting community expectations. Alternatively, if the LSDP is discontinued, there will be a need to create a fit-for-purpose, dedicated framework to evaluate and fund rare disease therapies on the PBS.

The international experience

Internationally there is no gold standard model to evaluate and fund rare disease therapies, and considerable variation exists in practice. In the UK, the National Institute for Health and Care Excellence (NICE) recently implemented a multicriteria decision analysis (MCDA) framework to evaluate therapies for ultra-rare diseases.[6] The framework involves balancing criteria, such as the nature of the condition, the effect of the new technology, the cost to the National Health Service (NHS), value for money and impact of the technology beyond direct health benefits.[6]

In Scotland, the Scottish Medicines Consortium (SMC, https://www.scottishmedicines.org.uk/files/PACE/PACE_Overview_Document_V2.pdf; verified 11 January 2017) uses a similar approach to NICE in assessing ultra-rare medicines through the aforementioned MCDA framework. In addition, the Patient And Clinician Engagement (PACE) group is used to help inform decision making,[7] providing a formal stakeholder engagement process. In Ontario, Canada, a similar process to consider evidence from patients or caregivers has been established as part of a framework for Drugs for Rare Diseases (DRD).[8]

At the other end of the spectrum, countries such as Germany and France have less rigorous assessment processes for rare disease therapies, placing greater weight on the lack of treatment options. In particular, Germany will generally grant automatic approval for innovative therapies for which there are no treatment options as long as the budgetary impact is below a threshold of €50 million.[5]

Although there is considerable international variation, common features of international systems include the opportunity for early stakeholder engagement, flexibility with evidence requirements and cost-effectiveness criteria and transparency in relation to the decision making framework and outcomes.

How should we evaluate and fund rare disease therapies?

By building on the lessons of other countries, Australia has the opportunity to create a revised, fit-for-purpose framework to evaluate and fund rare disease therapies that is responsive to community expectations.

Box 1. Criteria for funding on the Life Saving Drugs Program (LSDP)

Source: The Department of Health.[4]

1. There is a rare but clinically definable disease for which the drug is regarded as a proven therapeutic modality (i.e. approved for that indication by the Therapeutic Goods Administration).
2. The disease is identifiable with reasonable diagnostic precision.
3. Epidemiological and other studies provide evidence acceptable to the Pharmaceutical Benefits Advisory Committee (PBAC) that the disease causes a significant reduction in age-specific life expectancy for those suffering from the disease.
4. There is evidence acceptable to the PBAC to predict that a patients lifespan will be substantially extended as a direct consequence of the use of the drug.
5. The drug must be accepted as clinically effective, but rejected for Pharmaceutical Benefits Scheme (PBS) listing because it fails to meet the required cost-effectiveness criteria.
6. There is no alternative drug listed on the PBS or available for public hospital in-patients that can be used as life-saving treatment for the disease. However, the availability of an alternative drug under the LSDP does not disqualify the proposed drug from consideration for the LSDP.
7. There is no alternative non-drug therapeutic modality (e.g. surgery, radiotherapy) that is recognised by medical authorities as a suitable and cost-effective treatment for this condition.
8. The cost of the drug, defined as the cost per dose multiplied by the expected number of doses in a 1-year period for the patient, would constitute an unreasonable financial burden on the patient or his/her guardian.

A suitable framework for evaluating rare disease therapies in Australia should begin with legislative provisions that protect and codify the funding for rare disease therapies. This includes targeting the system to appropriately rare conditions with high clinical need, which ensures patient populations are defined and the financial impact is contained.

Decision-making criteria for a revised framework should be transparent and flexible, with an assessment of benefit that can be derived in the absence of rigorous randomised trials, which are typically unfeasible and unethical for rare diseases. As highlighted above, experience from the LSDP has shown funding approvals, and therefore access to therapies, can be severely affected when evaluation criteria do not align with the nature of the evidence typically available. This sits in contrast with the pragmatic approach adopted in other international systems, which includes holistic and pragmatic criteria that take into account the effect of therapies beyond the patient, to carers, the health system and the community.

To assess the value of rare disease therapies, the Australian system currently uses two tiers, where therapies listed on the PBS are evaluated via cost-effectiveness and therapies listed on the LSDP are explicitly not cost-effective but meet other criteria. We believe a balance can be achieved through a revised, fit-for-purpose framework to evaluate and fund rare disease therapies that is transparent and embraces some consideration of cost-effectiveness. Exemplars can be found in the NICE approach, whereby decision makers assess technical, productive and allocative efficiencies, taking into account the benefit relative to the current treatment, the effect on other resources in the health system and the effect on the budget. For Australia, cost-effectiveness should be considered among other factors with explicit and appropriate weightings that ensure decisions are reflective of community values.

Given the diversity and complexity of rare diseases, the limited number of clinical experts and the methodological limitations of the evidence, stakeholder engagement is fundamental in a revised framework for rare disease therapies. The experience of jurisdictions such as Scotland and Ontario could be used to build an appropriate process to ensure key stakeholders, such as sponsors, patients, clinicians and families, have a mechanism to engage early in the process and in a sustained manner to ensure the uncertainty in funding assessments can be reduced and a holistic assessment of benefit can be made.

Conclusion

The funding of rare disease therapies is founded on strong community support that values equity in such policies. However, the future for new treatments for rare disease is now subject to significant uncertainty with the proposed abolition of the LSDP. We believe there is a need to maintain a separate fit-for-purpose framework to evaluate and fund rare disease therapies drawing on overseas best practice that incorporates community values in decision making. This will provide certainty for industry to continue to invest in such treatments, as well as ensuring funding recommendations are reflective of Australian values balanced against the need for financial sustainability.

Competing interests

Colman Taylor is an employee of Optum, which provides health economics consulting services to industry and government. As part of this work, Colman Taylor has undertaken paid consulting work for manufacturers of rare disease therapies. In particular, Colman Taylor has undertaken paid consulting work in relation to Health Technology Assessment guidelines for rare disease therapies. Neither Colman Taylor nor Optum has received remuneration in relation to the development of this manuscript.

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