Health Technology Assessment Policy and Methods Review – Consultation 1 (https://ohta-consultations.health.gov.au/ohta/hta-review-consultation1/)

Response 911522286

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☐ Include unanswered questions

Introduction

What is your organisation?

(Required)

Vertex Pharmaceuticals

Elements and features that are working effectively

Are there any elements and features of HTA policy and methods in Australia that are working effectively?

Are you able to provide detail of any elements and features of HTA policy and methods that are working effectively? Please use specific details where possible.

Vertex is a leader in the development of new therapies for Cystic Fibrosis (CF), with four CFTR modulator therapies available on Australia's Pharmaceutical Benefits Scheme (PBS). In the last decade, the availability of CFTR modulators has revolutionised treatment for CF patients, significantly improving lung function while reducing pulmonary exacerbations and reliance on physical therapy and other medicines. Evidence is emerging to demonstrate that these clinical benefits translate into meaningful survival benefits for patients [1, 2].

Vertex was established as a legal entity in Australia in 2012. Since this time, Vertex has submitted over 25 HTA submissions to the Pharmaceutical Benefits Advisory Committee (PBAC), leading to subsidised access for four different therapies. This provided approximately 2,900 CF patients with novel disease modifying treatments, allowing them to change the course of their lives.

HTA submissions in Australia follow published guidelines by the PBAC. Vertex has found that the HTA system can be flexible to achieve access - through flexibility in process, in the cost-effectiveness decision making thresholds applied to rare diseases and through the utilisation of unique agreements, including pay-for-performance (PFPs) and managed access programs (MAPs), to improve patient access.

1. Volkova N, Moy K, Evans J et al. Disease progression in patients with cystic fibrosis treated with ivacaftor: Data from national US and UK registries (2020). J Cyst Fibrosis 19(1): 68-79.
2. Bower J, Volkova N, Ahluwalia N et al. Real-world safety and effectiveness of elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis: Interim

results of a long-term registry-based study, J Cyst Fibrosis, https://doi.org/10.1016/j.jcf. 2023.03.002

Are you able to provide details of positive outcomes resulting from Australia's HTA policies and methods? Please use specific examples where possible.

The greatest positive outcome from Australia's HTA policy is enabling subsidised access to four novel disease modifying therapies for CF patients. This includes ivacaftor (Kalydeco®), lumacaftor/ivacaftor (Orkambi®), tezacaftor/ivacaftor and ivacaftor (Symdeko®), and elexacaftor/tezacaftor/ivacaftor and ivacaftor (Trikafta®). Before the introduction of CFTR modulators, CF patients typically had a shorter life expectancy and experienced a range of health complications such as frequent lung infections and poor digestive function [3]. However, with the availability of CFTR modulators, many CF patients have experienced improvements in lung function, reduced hospitalisations, and an overall improvement in quality of life [1,2,4,5,6,7]

1. Volkova N, Moy K, Evans J et al. Disease progression in patients with cystic fibrosis treated with ivacaftor: Data from national US and UK registries (2020). J Cyst Fibrosis 19(1): 68-79.
2. Bower J, Volkova N, Ahluwalia N et al. Real-world safety and effectiveness of elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis: Interim results of a long-term registry-based study, J Cyst Fibrosis, https://doi.org/10.1016/j.jcf. 2023.03.002
3. Balfour-Lynn I & King J. CFTR modulator therapies – Effect on life expectancy in people with cystic fibrosis (2022). Paediatr Respir Rev 42: 3-8
4. Powers C, Yeley J, Teibel H, Crowley E, Brown CD. Quality of life improvement after initiation of elexacaftor-tezacaftor ivacaftor: a real-world study. Pediatr Pulmonol; October, 2020
5. Arooj P, Morrissy, D, Ronan et al. 2019a. Real-world Orkambi cohort CorK study (ROCK) - a prospective twelve months' analysis addressing the effectiveness of CFTR modulation in patients with cystic fibrosis homozygous for F508del CFTR. J. Cyst. Fibrosis. 18, S131–S132
6. Ejiofor L, Mathiesen I, Jensen-Fangel S et al. 2020a. Patients with cystic fibrosis and advanced lung disease benefit from lumacaftor/ivacaftor treatment. Pediatr. Pulmonol. 55, 3364–3370

7. Salvatore D, De Gregorio F, Colangelo C et al.. Real-life effectiveness of lumacaftor/ivacaftor in cystic fibrosis: A single center experience. Ital. J. Pediatr., 24th Congress of the Italian Society of Cystic Fibrosis and the 14th National Congress of Cystic Fibrosis Italian Society. Italy. 45.

Current or future barriers to earliest possible access

Elements and features of HTA policy and methods in Australia acting as a current or future barrier to earliest possible access.

After a new treatment is approved for use by regulators, there are a range of challenges
in appraising highly innovative treatments for rare diseases that can have a direct impact
on patient access. These include:
• Standard frameworks applied across both common and rare diseases fail to consider unique attributes of rare disease treatments such as size of the population eligible for treatment, magnitude of innovation, and unmet need.
• Inherent data collection challenges due to the small group of patients available for inclusion in clinical trials and limited comparative data for diseases that
are uncommon by definition, and not always fully understood [8].
• Most value assessment frameworks do not capture wider social and economic benefits (for example returning to work or improving the mental health of an unpaid carer)[9].
• Standard benchmarking tools (such as EQ5D) preferred by HTA bodies fail to fully capture the quality-of-life improvements offered by innovative treatments for rare and genetic conditions {10,11,12] and the availability of such data is often limited in rare disease
• Cost-effectiveness thresholds used by HTA bodies can lack the flexibility to fully reflect the real-world value of innovative medicines for rare diseases [13].
• The approach to handling uncertainty, can lead to delays in access to highly

innovative treatments

Novel medicines and technologies are now extending life beyond what was thought possible even a decade ago. These types of innovations don't fit into the "one-size-fits-all" approach applied to traditional therapies, specifically as methodological approaches can bias against treatments that lead to large gains in survival; this is exacerbated further when these survival gains occur far in the future. This is particularly impactful for rare, chronic, genetic conditions whereby the goal of treatment is to slow or stop disease progression, often from a very young age, and ongoing costs of managing the underlying chronic disease remain.

In Australia, Vertex has entered into innovative agreements including PFPs and MAPs with the Australian Government. Under these agreements, key patient outcome data in CF such as lung function and hospitalisation rates are collected through existing CF registries and shared with the PBAC and the Department of Health.

In order for MAPs to be an effective means of providing funding for new therapies, enabling access for patients while ensuring there is appropriate sharing of risk between the sponsor and Australian Government, the following elements could be considered:
• Prior to recommending a MAP as part of a PBAC recommendation, a feasibility assessment of data collection and analyses required to address outstanding HTA questions should be conducted with the details of the MAP finalized and agreed between the parties.
• The agreement should include sufficient detail on data sources and data analysis methods, particularly for the use of real-world evidence and clear boundaries for meeting/not meeting MAP criteria.
• Evaluation of the available evidence should be conducted in a manner specific to the MAP research question at hand applying the 'most-reasonable' interpretation of data collected within a real-world setting, rather than defaulting to the most-conservative or applying strict HTA methodology.

8. Kempf L et al, Challenges of developing and conducting clinical trials in rare disorders. Am J Med Genet. 2018;176:773–783.
9. Office of Health Economics, White Paper: Are cost-effectiveness

thresholds fit for purpose for real-world decision-making?, February 2020 https://www.ohe.org/publications/are-cost-effectiveness-thresholds-fit-for-purpose
10. Robertson C, et al; PRISM Trial Group. Meaning behind measurement: self-comparisons affect responses to health-related quality of life questionnaires. Qual Life Res. 2009 Mar;18(2):221-30
11. Sinclair VG, Blackburn DS. Adaptive coping with rheumatoid arthritis: the transforming nature of response shift. Chronic Illn. 2008 Sep;4(3):219-30.
12. Schwartz CE, Rapkin BD. Reconsidering the psychometrics of quality of life assessment in light of response shift and appraisal. Health Qual Life Outcomes. 2004;2:16. Published 2004 Mar 23. doi:10.1186/1477-7525-2-16
13. Office of Health Economics, White Paper: Are cost-effectiveness thresholds fit for purpose for real-world decision-making?, February 2020 https://www.ohe.org/publications/are-cost-effectiveness-thresholds-fit-for-purpose

When bringing new highly innovative products to market, funding certainty is essential. Companies need assurance that they will be able to secure the necessary funding to support the development of these highly innovative products. For example, the development of a gene therapy is a long and expensive process, requiring significant investments of time and capital.

Gene therapy is a type of medical treatment that involves introducing or modifying genes within an individual's cells and tissues to cure or treat diseases. This can be done by delivering healthy copies of genes to replace faulty ones or by adding or altering genes to help the body fight off the disease. Gene therapy holds great promise for the treatment of a wide range of genetic disorders, as well as some types of cancer and other diseases.

The current process to evaluate and fund gene therapies in Australia requires reform in order to provide a clear pathway to reimbursement for these products. Based on precedents to date, Vertex notes:
• Gene therapies have been evaluated by either the PBAC or the Medical Services Advisory Committee (MSAC) – more clarity on how the evaluation pathway is selected would be helpful.
• Gene therapies are typically funded under the National Health Reform

Agreement (NHRA) framework with the process constantly evolving – clarity on future direction would be useful.
• Funding under the NHRA adds considerable delays to access because of the need to reach agreements at both the Federal and State level which often involve complex risk-share arrangements.
• The Independent Hospital and Aged Care Pricing Authority (IHACPA) may develop a new DRG funding model for gene therapies – more clarity on this pathway would also be helpful.

All these factors underpin an uncertain environment to launch innovative therapies. This lack of certainty may delay investment decisions and ultimately patient access.

Regulatory incentives for rare disease medicines have been instrumental in encouraging the development and availability of treatments for rare diseases, which otherwise may not have been developed. There is broad recognition amongst policymakers, experts, academics and patient groups that value assessment frameworks need to be adapted to address the unique attributes of innovative rare disease medicines and support the timely introduction of innovative, precision medicines for rare diseases.

There are already several examples where European countries have implemented different methods for rare disease treatments, including adaptable pathways which allow for patient and clinical engagement and flexibilities in methods of value assessment.

Vertex supports continued development and reform of value assessment approaches
to ensure they are robust, flexible and involve all relevant stakeholders in capturing the full value of new innovative therapies for rare disease treatments, taking into account their unique attributes. Vertex proposes that value assessment frameworks for innovative rare disease treatments should be based on the following three principles:

1. A balanced set of perspectives
All relevant stakeholders, including patients, carers and medical experts should be able

to participate in a clear and transparent process that represents a meaningful contribution to HTA considerations. This should include:
• Medical experts in the specific rare disease under review should be involved
in assessing the value of new treatments. This should include involvement in both submitting evidence, deliberations and decision-making.
• Patients and carers have unique expertise and insights, which should be at the centre of value assessment and given sufficient weight. As our understanding of rare diseases continues to grow and knowledge gaps are filled, patients and carers play a key role.

2. A comprehensive evaluation of benefits
• Broader perspective and benefit: Assessments should allow for the consideration
of additional value elements to capture the wider benefits of new therapies, such as level of innovation, population size, disease severity, unmet need, patient/caregiver perspective, and societal/economic benefit associated with treatment (multiple criteria).
• Thresholds: Existing cost-effectiveness thresholds, developed for common conditions (for example, cardiovascular disease) and often established long before innovation
in rare diseases existed, should not be the central decision-making criteria to determine access. Where an explicit threshold is in place, it should be higher for rare and severe conditions than that applied to common diseases, and potentially tailored to the individual disease. This would better reflect the real-world value of innovation and encourage continued investment in research and development for rare and severe conditions.
• Innovation: Assessments should consider the level of therapeutic innovation
as a measure of value and spur of further medical breakthroughs. Investing in research and development in rare diseases is a high cost and high risk pursuit, particularly for first in class treatments. While the level of risk can be considerably greater in rare diseases, the cost of development is comparable to disease states with much larger patient populations. It is important that policies and processes maintain appropriate incentives for research and development to bring transformative medicines for serious diseases to the people who need them.

3. A pragmatic and flexible approach to assessment of the available evidence and appropriate economic evaluation

The assessment of the robustness of evidence must take account of the challenges
of conducting research in populations with rare diseases. Therefore, value assessment frameworks should allow for:

- The use of all sources of evidence, including Real World Evidence (RWE) where for valid reasons, there is no or limited country specific data and direct comparative data;
- Allow for the use of alternative methods (e.g. treatment-specific quality of life instruments, QALY weighting, etc.) to value and measure quality of life in rare diseases.
- Use of data best suited to measuring health impact (e.g. surrogate endpoints).
- To address the challenges which are particularly acute for life-long therapies that substantially extend life and whereby outcomes accrue over a long period, economic evaluations should:

i. Better recognise future health gains and value them appropriately;
ii. Reward medicines that prolong life rather than penalise them due to ongoing direct medical costs;
iii. Consider likely price reductions resulting from patent expiry in their cost effectiveness modelling (dynamic pricing).

Additionally, more flexibility in the process for evaluation of submissions to the PBAC may improve the ability to make timely, well-informed decisions that benefit both patients and the broader healthcare system, and could consist of:

1. Providing the ability to address questions from the evaluators during the evaluation process in relation to clinical data or analyses presented to avoid misinterpretation since once documented, these can be difficult to alter and, in some cases, may lead to submission deferrals or rejection.
2. Providing for a flexible and responsive HTA process that can accommodate new and emerging data and evidence about medicines. This may include the ability to supplement reimbursement dossiers with new data as it becomes available to ensure PBAC has all available data to assist in its decision making.
3. Allowing for economic models to be adapted over time as new evidence becomes available, which may require the assumptions and data inputs

originally applied in the model to be updated.
4. Having the opportunity, as is the case in other countries, for face-to-face discussions with the Department of Health and Ageing (and/or PBAC) to finalize the financial estimates related to PBS listing of the medicine after a positive recommendation is provided by PBAC. This would avoid the need for resubmissions to PBAC with subsequent delays to patient access.

Current or future barriers to equitable access

Elements and features of HTA policy and methods in Australia that are acting as a current or future barrier to equitable access.

When evaluating rare diseases, the PBAC applies the same process to applications treating a small number of patients (e.g. 5 patients) as it does to applications treating a larger number of patients (e.g. 5,000 patients). Currently, there is a specific pathway in place for ultra-rare conditions through the Life Saving Drugs Program (LSDP). However, for rare conditions that do not meet the LSDP criteria, there is little flexibility in the process. As a result, Sponsors may be discouraged from seeking reimbursement for treatments for rare conditions in Australia with resultant challenges for patients who may have limited treatment options available to them.

Introducing more flexibility in the criteria used to assess treatments for rare diseases, and encouraging sponsors to submit applications for treatments that benefit small patient populations may improve the HTA process for rare diseases.

Refer also to comments in previous section

Elements and features that detract from person centredness

Elements and features of HTA policy and methods in Australia that may be detracting from person-centeredness.

Traditional HTA methods focusing on clinical and economic outcomes, with limited consideration of the patient voice and lived experience may lead to an incomplete conclusion regarding the value and impact of new therapies. For example, CF patients are prone to lung infections, which can cause significant lung damage and contribute to disease progression. The effectiveness of new treatments is often based on traditional clinical endpoints, such as reduction in bacterial load or improvement in lung function measured by spirometry. However, these measures may not fully capture the patient's experience of living with the disease.

A person with lived experience of CF may provide valuable insights into the practical aspects of managing lung infections, such as the frequency and severity of symptoms, the impact on work and family life, and the burden of treatment. For example, a CF patient may provide feedback on the tolerability and side effects of a new antibiotic, the ease of administration, or the impact on their ability to play sport or participate in social activities.

The Australian HTA system could aim to better and more consistently incorporate carer quality of life (QoL) into appraisals and decision-making. Vertex's experience with CF suggests that the traditional utility measures such as the EQ-5D which are used to incorporate QoL into economic evaluations, may not sufficiently capture the impact of new treatments on families and carers. Guidance should be provided on how carer quality of life can be incorporated into HTA submissions and contributed by members of the disease community during the evaluation. In addition, a clear plan for further research in this area needs to be set out.

Additionally, the present system places an excessive burden on patients and caregivers who are already suffering from an immense disease burden. A lack

of understanding of the complex HTA system and time constraints inhibit patients and their families from providing submissions to the PBAC. In addition, the make-up of the PBAC includes only limited representation from people with lived experience, which undermines decision making.

Actively seeking targeted input from people with lived experience and their caregivers rather than relying on people to submit comments via a portal may improve the quality of information used for decision making. This approach should be centered on identifying gaps within HTA submissions while also affording individuals with lived experiences an opportunity to be heard.

Incorporating the perspectives and experiences of individuals with lived experience and their caregivers is crucial for achieving person-centeredness in HTA decision-making. Patients and their families possess unique insights into the lived reality of the disease, its impact on their quality of life, and the effectiveness of treatments. As such, they are in a prime position to inform decisions about which treatments are most appropriate and valuable for patients. The current composition of the PBAC does not reflect this reality, with only two consumer representatives compared to the number of clinical experts and health economists. To truly prioritise person-centeredness in HTA decision-making, the PBAC should strive to improve this ratio and place more emphasis on the perspectives of those who have experienced the disease firsthand. This will ensure that decisions are based on a comprehensive understanding of the patient experience and the needs of those living with the disease.

Perverse incentives

Elements or features of HTA policy and methods in Australia that are causing or could cause unintended consequence or perverse incentives.

The PBAC tends to adopt a highly conservative stance on uncertainty. This can lead to delays to patient access, since multiple submissions are often required to resolve issues surrounding the interpretation of clinical data and

its application in the economic evaluation.

Another area that leads to unnecessary delays is misalignment on the number of patients to be treated when a medicine is PBS listed. Where financial caps on expenditure are applied, under-estimating the total number of patients to be treated places all, and sometimes unacceptable, risk on to the sponsor of the product. Vertex maintains that financial caps should be set at a level equivalent to the known number of patients eligible for treatment when applied in a setting where the number of patients can be readily quantified and treatment of all patients is deemed cost-effective, with no risk of leakage in populations with unknown cost-effectiveness.

Another factor that may have unintended consequences is the choice of comparator during the HTA evaluation. Currently the PBAC may choose the cheapest therapeutic alternative rather than the treatment that the new medicine is most likely to replace in clinical practice which may fail to recognise and value innovation.

By addressing measures to encourage interactions with evaluators and face-to-face discussions, reducing the reliance on modelling parameters and defining the comparator by utilisation rather than cost, the HTA process will incentivise submission and facilitate access to better serve the needs of patients, Sponsors, and the broader healthcare system.

Areas for further investigation or analysis

Noting the overall scope of the analysis from the HTA expert will be in line with the ToR and agreed by the Reference Committee, are there any HTA or reimbursement models, or elements thereof, utilised in other countries that you believe should be considered for potential adoption in Australia, or that it

would be good for the Reference Committee to understand?

Country / Jurisdiction:

England/NICE

Details of: Which elements of the HTA policy, method, mechanism for suggested for consideration; Any outcomes that the suggestion is achieving that should be considered; Any unintended consequences that the suggestion is having or may have if adapted in Australia

While no system is perfect, there are several ways other HTA countries incorporate broader value and impact. While all systems include patient involvement on decision making committees, NICE in England, has established Citizen Councils, which are groups of people who use health and care services, carers, and members of the public, who are selected to represent a diverse range of perspectives and experiences. Citizen Councils meet regularly to provide feedback and input on NICE's work and decision-making processes. NICE has also established patient expert groups for specific health conditions or areas of work, which are made up of people with personal experience of the condition or area.

Additionally, NICE recognizes inequalities in access and is running efforts to improve equality considerations through their guidance development process.

Country / Jurisdiction:

Scotland/SMC

Details of: Which elements of the HTA policy, method, mechanism for suggested for consideration; Any outcomes that the suggestion is achieving that should be considered; Any unintended consequences that the suggestion is having or may have if adapted in Australia

The Scottish authority, SMC, encourages patient groups to submit evidence on the impact of new medicines on patients' lives. Patient groups can provide information on the benefits and risks of new medicines and how they affect patients' quality of life. This information is taken into account when making recommendations. SMC also involves patients and the public in its review processes, including the development of review protocols and the

dissemination of findings. Additionally, the SMC has adopted a process that gives patient groups and clinicians a stronger voice in the evaluation of end-of-life medicines and medicines to treat rare conditions. Sponsors are able to request that SMC convenes a Patient and Clinician Engagement (PACE) meeting.

Country / Jurisdiction:

Canada/CADTH

Details of: Which elements of the HTA policy, method, mechanism for suggested for consideration; Any outcomes that the suggestion is achieving that should be considered; Any unintended consequences that the suggestion is having or may have if adapted in Australia

CADTH, in Canada, conducts patient engagement activities, such as focus groups, surveys, and interviews, to gather input from patients and the public on its work. Both SMC and CADTH involve patients in a horizon scanning process, which identifies new and emerging drugs and health technologies that may have an impact on patients' lives. This helps to ensure that the needs and preferences of patients are taken into account when considering new treatments.

Currently there is no perfect system that embeds patient lived experience and undertakes a comprehensive assessment of value and impact. The HTA review in Australia is an opportunity to build a world leading system that incorporates lived experience in an end-to-end fashion and values what truly matters to patients.

Other details of importance to the HTA Policy and Methods Review not covered above + document / attachment upload point.

Noting the objectives of the review set out in the Terms of Reference, is there any other information relevant to the Review not provided above that you would like to add?