HTA Review Consultation 2
AstraZeneca Submission
23 February 2024

1. Summary of AZ Response to the HTA Review Options Paper

The intended outcome of the HTA Review is to greatly improve the efficiency of the HTA process and reduce the time from registration to reimbursement. AstraZeneca (AZ) commends the HTA Review Committee and associated Expert Review Groups for the preparation of a thorough Options Paper based on significant consultation and evidence review.

Although many of the proposed Options have the potential to improve HTA outcomes, they are presented without reference to potential timelines for implementation and several options still require further detail. A limited number of proposed options would negatively impact the assessment of value of innovative medicines (i.e., to generate further savings) from the current position and could ultimately result in a decrease in the efficiency of the HTA process and result in less treatment options for Australian patients.

Correspondingly, options are reviewed by AZ below with reference to their ability to support the intended outcome of the HTA Review, their positive or negative impacts; and where further strengthening or clarification is required. The response then lists detailed comments about the options described.

Options that support the intended outcome

Options proposed by the HTA Review Committee to consolidate evaluation pathways, allow conditional listing, provide mechanisms to accelerate resolution of PBAC objections and promote greater engagement between Sponsors, patients, the PBAC and the Department have the potential to improve HTA process efficiency and reduce the time from registration to reimbursement of new health technologies. The effectiveness of these options to achieve the intended outcome will greatly depend on the details of their implementation and therefore it is critical that ongoing collaboration between all relevant stakeholders continues through to implementation.

Options that do not support the intended outcome.

A number of options proposed by the HTA Review Committee would maintain or create increased barriers to the introduction of new health technologies in Australia. If implemented, these options would undermine the intended outcome of the HTA Review. Options associated with pricing reduction, comparator selection, failure to recognise long term benefits and costs or broader societal perspective of value considerations and the introduction of a disinvestment framework do not support the intended outcome of the Review in their current form.

Most notably, Option 4.1, which proposes that medicines that deliver a similar therapeutic benefit require offers of a lower price as part of a revised cost minimisation approach, would have substantial unintended negative consequences. The implementation of this option would disincentivise reimbursement of treatments with similar effectiveness but different tolerability profiles and limit the choice of treatments available for individualised patient care.

The requirement in the PBAC Guidelines for comparator selection and cost minimisation in most situations where there is no direct head-to-head evidence means Australia already has more restrictive pricing guidance than other similar HTA markets. Any measures to further decrease the attribution of value for follow on medicines will significantly reduce the attractiveness of reimbursement in Australia and likely flow on to a reduced choice of treatments for Australian patients. This reduced attractiveness of reimbursement in Australia will be exacerbated if a lower relative price compared to the existing medicine is a condition of reimbursement of this pathway. i.e., an inferred price reduction could erode the confidentiality of pricing conditions.

In combination with existing price reduction mechanisms, such as statutory anniversary price reductions and price disclosure, the introduction of this additional price reduction mechanism for cost minimisation evaluations would also lead to a larger number of innovative medicines failing to list on the PBS due to unattractive or unsustainable pricing regulations.

The use of the lowest cost comparator by PBAC and the negative impact this approach has had on the time to access was identified by stakeholders in Consultation 1. The Options Paper proposes comparator guidelines be developed for submissions claiming superiority and non-inferiority. Details about the intended principles of comparator selection have not been provided in the Options Paper. Therefore, the principles and subsequent guidelines -as well as the requirement for any changes to existing legislation - must be co-designed with relevant stakeholders to ensure the principles of the National Medicines Policy are no longer undermined by the policy of comparator selection.

Further detail of the positive impacts and unintended consequences of the draft options are discussed in the following sections.

1.1 Transparency, communication, and stakeholder involvement.

More avenues are needed to provide opportunities for stakeholders to become involved in the assessment process A high priority in the AZ Consultation 1 Submission was that patient and stakeholder engagement in the HTA process should be improved. More opportunities for stakeholders to become involved in the assessment process with the aim of reaching consensus on modelling structure, assumptions, addressing uncertainty and managing risk during the evaluation process would increase the chance of a positive PBAC recommendation first time, and greatly reduce the patient access gap between registration and PBS listing.

The proposed options associated with developing a stakeholder engagement framework along with strengthening channels for consumer evidence and feedback through publishing plain language summaries and improving the HTA webpage would improve the HTA process. In addition to the options proposed, greater engagement between applicants and the Department of Health is required following a PBAC recommendation to reduce the time to PBS listing. This engagement needs to be embedded in the Pricing offer (PO) and negotiation guidance framework Option which is discussed later in the report.

Equity of access should also be enhanced, and AZ strongly supports the development of a First Nations people's partnership and dedicated resource to prepare submissions.

Greater coordination of state and federal pathways is required. Health technologies, such as cell and gene therapies, that require federal and state implementation currently follow poorly coordinated processes and pricing uncertainty. Centralizing data sharing across government and increasing opportunities for work sharing for jointly funded (State and Federal Government) technologies could accelerate access. It is unclear whether the database would permit appropriate sharing of data among stakeholders outside of federal and state governments. The availability of an experienced case manager to navigate these pathways would greatly assist in shepherding complex technologies to market.

1.2 Funding and assessment pathways.

Streamlining cost-minimisation and proposed early resolution would increase speed to access, however, eligibility for pathway entry could limit impact. The Options Paper noted that some stakeholders felt new medicines that are non-inferior to alternatives do not require a full HTA and could be assessed over a shorter timeframe. AZ concurs with the view that the level of appraisal should be risk calibrated and flexible. This includes new early resolution mechanisms, decoupling the requirement for the TGA Delegate's overview and having appropriately resourced and qualified case managers to expediate the HTA and reimbursement process.

These options will deliver improved efficiency of resource allocation within the process and therefore limitations on these options, such as only allowing medicines that have been approved within 6 months in Europe or the USA, or limiting the number of resubmissions permissible for therapies that deliver a high added therapeutic value, could limit the effectiveness of these options.

Establishing a single, unified HTA pathway for all health technologies including co-dependant technologies, vaccines and life-saving drugs for rare conditions (LSDP) also has the potential to improve process efficiency and reduce the time to patient access. However, it would be preferable if these measures did not increase the timeframe for the evaluation process, and amalgamation must be limited to the HTA process and funding decision-making. Funding programs such as the LSDP must remain separate from the PBS to ensure the continued availability of life-saving medicines. A streamlined pathway for cost-minimisation submissions is a positive option, if not coupled with the requirement to offer a price reduction for technologies of similar therapeutic value. This requirement would greatly reduce the attractiveness of Australia as a market for innovative medicines and limit patient choice of treatments by reducing the number of medicines with similar effectiveness (but different tolerability profile) likely to follow a first to market comparator. Pricing confidentiality also needs to be maintained.

LSDP eligibility is currently too restrictive. LSDP eligibility does not cover innovative medicines that significantly improve quality of life and delay progression to disability. The *Inquiry into New drugs and Novel Medical Technologies* highlighted that there is a need to elevate quality of life or 'life improving' measures in the consideration of funding new medicines for rare diseases.

AZ does not support the development of a disease specific common model. AZ does not support the development of a disease specific common model, which is likely to have an unintended consequence of delaying time from registration to reimbursement by introducing greater complexity and therefore greater uncertainty into HTA decision-making. Enhancing the PICO scoping process would help address modelling uncertainties and define key assumptions to improve HTA efficiency.

1.3 Methods for HTA for Australian Government Subsidy (technical methods)

Adding a PICO scoping phase for PBAC submissions would improve HTA evaluation efficiency. Gaining agreement on the appropriate PICO elements prior to HTA submission could accelerate the HTA process for some health technologies. The advice currently provided during pre-submission meetings by the Department is often not guided or endorsed by decision-makers, and time constraints limit the depth of discussion. Whilst pre-submission meetings are somewhat helpful, they could improve the chance of a submission successfully meeting the evaluation requirements of the PBAC by including more relevant stakeholders such as the evaluator, the ESC and PBAC discussants, as well as, when relevant, consumers with lived experience and clinicians.

Clinical evaluation methods require updating and a comprehensive approach is needed for genomic technologies. AZ is aligned with the overarching principles for adopting clinical methods in Australian HTA outlined in the Options Paper. The proposed options to update methods associated with nonrandomised and observational evidence, surrogate endpoints, control group creation, treatment switching and having a list of curated methods are all reasonable, if utilised to determine the most likely treatment effect.

However, the lack of an effective risk sharing framework in Australia often results in a conservative approach to managing data uncertainty. This approach can undervalue medical innovation and disincentivises the rapid introduction of new health technologies to Australia. Therefore, to achieve the intended outcomes of the Review, robust clinical evaluation methods and broad utilisation of data sources to support evidence of clinical effectiveness must be accompanied by an effective framework for managing the risk of uncertainty.

AZ is also a proponent for funded access to comprehensive screening and genomic testing for a broader range of cancers beyond the most common cancers. This includes investment in broad and routine screening for more cancer types and increased access to genomic testing through a coordinated national approach similar to the National genomic Test Directory in the UK (operated by the NHS) - as discussed

at the recent Senate Inquiry into equitable access to diagnosis and treatment for individuals with rare and less common cancers. Such an approach could facilitate a de-coupling of the HTA evaluation of medicine and test to increase efficiency in the HTA evaluation process.

The HTA comparator should be the therapy most likely to be replaced. Selection of the appropriate comparator is a key issue for ensuring rapid access to medicines, as its cost and effectiveness are used to benchmark the cost and effectiveness of innovative medicines and those of therapeutic equivalence. The relevant Expert Paper included a review of 29 HTA methods guidelines and reported that 86% recommended the comparator be "the standard of care for local practices". Similarly, the first PBAC Guidelines defined the comparator to be the *most likely medicine(s) to be replaced in clinical practice.* The "lowest cost comparator" is now often used in the HTA evaluation process.[1]

Choosing the lowest cost comparator, rather than the medicine most likely to be replaced, results in reduced pricing for innovative medicines and limited incentives for product commercialisation. The Options Paper proposes guidance is required about comparator selection, however further details about the principles that determine the appropriate selection of comparator are required in the Options Paper.

Focussing on health sector impacts and employing low discount rates undervalues the societal benefits from innovations in health technology. The omission of second order effects, social benefits, broader impacts of disability and carer cost and benefit considerations in economic evaluation underestimates the societal value of health innovation. These components of value should be included when relevant in Australian economic analysis. An HTA Review Expert Paper included a survey of discount rates for 19 countries and found they ranged from 1.5% to 5%. No justification was outlined in the Expert or Options Papers as to why the Australian discount rate is at the highest bound of this range. A high discount rate devalues longer term benefits delivered by innovative medicines. Benefits such as prevention of illness and long-term disease morbidity are undervalued with a higher discount rate. Rather than a recommendation for further analysis, the Options Paper should include a recommendation that the base case discount rate for benefits and costs is reduced from 5% to 1.5%.

Value for money guidelines for rare diseases should be developed that reflect uncertainties of the evidence base. Medicines that follow the LSDP pathway are evaluated by a separate evaluation committee for rare disease. The pathway is used for medicines that are clinically effective but not sufficiently cost effectiveness to be listed on the PBS.[2]

The Options Paper proposes a new consolidated pathway for LSDP medicines to streamline access, and that medicines could be assessed using value-for-money considerations. It is unclear what methods may be used. Cost-effectiveness of treatments for rare diseases can be highly uncertain because of rare

[1] HTA Comparators" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[2] https://www.health.gov.au/our-work/life-saving-drugs-program/about-the-lsdp

disease natural history data gaps, limited availability of comparator efficacy data, and small patient populations which limit the statistical analyses of clinical studies. Assessing value for money of rare disease treatments needs to account for these limitations and acknowledge the increased costs of developing, manufacturing and supplying medicines in very small quantities.

1.4 Health Technology Funding and purchasing approaches and managing uncertainty.

As highlighted in the introduction, the HTA Committee proposed Option that Sponsors would be required to offer or incentivise lower prices for health technologies that provide similar efficacy or safety will likely lead to fewer medicines listed on the PBS. The Options Paper notes that 'there may be clinical areas where patient response to treatment is heterogeneous and for clinical reasons having a range of treatment options is necessary for achieving overall optimal outcomes for patients.' Reducing the price for products of similar therapeutic value will reduce commercial incentives to seek reimbursement and limit the available range of treatments.

A pricing offer (PO) and negotiation guidance framework is required. The HTA Committee noted that the amount of time required after a PBAC recommendation to negotiate pricing and PBS listing arrangements is inefficient. A post-PBAC pricing and listing process framework with target timeframes for commencing and finalising each step is required. Improved transparency of progress through the process and engagement between Sponsors and the Department is also needed.

Independence of the HTA evaluation through separation between the PBAC's consideration of cost-effectiveness from the Government's consideration of budget impact and expenditure cap negotiations will improve efficiency, reduce the number of resubmissions and reduce the time that patients wait for PBS access to new medicines.

PBAC recommendations regarding assumptions of utilisation should be limited to advice on the relationship between utilisation and cost-effectiveness, rather than estimates of uptake among cost-effective populations. Also, subsequent adjustments to the financial estimates that do not relate to pricing and budget impact negotiations are a significant cause of resubmission and PBS listing delay. The framework should reflect this requirement for independence in the process of cost-effectiveness evaluation.

The process of post-listing re-assessment of health technologies needs to match the level of rigour and analysis employed at listing. Disinvestment considerations are currently reflected in post-market review arrangements, along with statutory price reductions and reference pricing. Any developments in a program that provides disinvestment advice to Government should incorporate greater rigour, or at least match - the efforts, stakeholder engagement, evidence requirements and HTA methods employed to support recommendations of PBS listing. This includes following high level evidence principles outlined in the clinical evaluation section of the Options Paper,

such as favouring RCTs. Criteria for disinvestment decisions need to be explicit, stakeholders must be consulted with enough time to provide relevant information or data analyses during disinvestment considerations and the reasons for disinvestment decisions must be clearly communicated to all relevant stakeholders. The framework needs to differentiate between treatments that are listed conditionally and those that follow standard entry pathways.

Revising managed entry arrangements in Australia has the potential to accelerate access to medicines of high unmet clinical need and value. Managed entry arrangements in several countries such as the UK have proven to successfully manage HTA uncertainty without delaying access to innovative medicines that provide a high added therapeutic value. AZ supports the establishment of a working group to formulate an appropriate managed entry model in Australia. To ensure the optimal uptake of managed entry programs, risks to Government and Sponsors must be balanced and the process for program exit must be clear. The source of data used to confirm treatment effectiveness also requires development.

1.5 Futureproofing our systems and processes

The future proofing Options outlined in the Options Paper address many issues associated with Australia taking a more proactive approach to identifying therapies that address unmet clinical need and future health system readiness. In the case of environmental considerations in HTAs, inclusion of an environmental lens is a positive development, however, additional analysis requirements should be calibrated so they do not slow the time to access. Reviews of the HTA system should occur more frequently and it is imperative an agreed set of KPIs are developed so improvement can be objectively assessed. AZ agree further workforce capacity development is required. International workshare arrangements could help improve efficiencies although more detail is required as to how the program could be implemented.