AstraZeneca

HTA Review Consultation 1
AstraZeneca Submission
5 June 2023

Contents

1. Executive Summary

AstraZeneca (AZ) welcomes the opportunity to provide comments in relation to the five policy questions posed as part of Consultation 1 of the HTA Policy and Methods Review (the Review). AZ notes that this is the first Independent Health Technology Assessment (HTA) Review in 30 years, representing a unique opportunity to modernise the HTA system in Australia.

The benefits of reform will be realised with increased and continuous patient engagement in the HTA process, more opportunity for collaboration between sponsors, evaluators, and committee discussants to fast-track the HTA evaluation and reimbursement, improved funding pathways, formulating more effective HTA methodologies, development of a risk management framework to inform risk sharing policies, and framework for valuing combination therapies.

The HTA Review follows that of the *New Frontier – Delivering better health for all Australians Inquiry into Approval Processes for New Drugs and Novel Medical Technologies in Australia*. AZ strongly supports the prioritisation of consumer engagement and elevating the patient perspective throughout the HTA evaluation process, from the earliest stages through to reimbursement.

AZ believes the issues associated with HTA process flow and associated delays in patients receiving reimbursed access require urgent reform. Previous reforms which have attempted to speed up the HTA process, include parallel Therapeutic Goods Administration /PBAC processing in 2011[1], and early re-entry pathways in 2021. The time to reimbursed access has, however, remained unacceptably longer in Australia compared with to other OECD countries.

Under the current process, innovative medicines that offer high added clinical benefit usually require multiple cycles of evaluation and committee consideration to gain reimbursement agreement. A phenomenon referred to as 'submission churn'. Given that each evaluation cycle is no less than 17 weeks, it stands to reason that reforming the process to eliminate submission churn would greatly improve the time from registration to reimbursement[2].

AZ has summarised the key issues constraining HTA system performance in Table 1, along with features we consider to be working effectively.

[1] Australian Government, Department of Health. Memorandum of Understanding with Medicines Australia. The Pharmaceutical Benefits Scheme.https://www.pbs.gov.au/info/industry/useful-resources/memorandum

[2] Analysis of PBAC submissions for Amgen December 2020 by MAESTr0 Database. Submission 82, Table 5, Attachment 1 of the Amgen Submission to the Parliamentary Inquiry into approval processes for new drugs and novel medical technologies in Australia

Table 1: AZ response to the five HTA policy-related questions

1**. Identify features of HTA policy and methods that are working effectively** • Special Pricing Arrangements (SPAs), indication-based, and confidential pricing • Parallel processing has the potential to significantly reduce time to access • Flexibility with individual recommendations and the opportunity to have pre-submission meetings and post-PBAC meetings for submissions not recommended
2. Identify features of HTA policy and methods that may act as current or future barriers to earliest possible access • Limited engagement between sponsor, patients, evaluator and committee throughout the evaluation process to identify areas of uncertainty, achieve early agreement of key assumptions and strive for reimbursement within one HTA evaluation cycle • A lack of process transparency, co-ordination, and engagement with sponsors during the post-PBAC PBS listing process • A lack of interim funding for medicines of high clinical value • A lack of comprehensive key performance indicators (KPIs) or timeline bound phases in the post PBAC recommendation • PBAC recommendations regarding utilisation assumptions that are not linked to cost-effectiveness, but that inform the financial expenditure estimates • Limited guidance on use of real-world evidence • Inconsistent Guidelines on how to include wider societal benefits of medicines • The reimbursement process for co-dependent technologies is complex • Treatments that require funding from Federal, State and Territory level governments (e.g., COVID treatments and cell and gene therapies) do not have a coordinated funding pathway
3. Identify features of HTA policy and methods that may act as current or future barriers to equitable access. • The LSDP reimbursement pathway includes multiple stages across separate funding assessment processes which delays access to treatments • HTA evidence requirements and methods do not reflect data availability for rare diseases • Eligibility for LSDP funding is limited to medicines that extend life. It does not include medicines that improve quality of life and address or delay progression to disability • Despite the availability of large gene panels, the co-dependent technology pathway requires a submission for each medicine/diagnostic test pairing
4. Identify features of HTA policy and methods that detract from person-centredness • The patient voice in the HTA process is through invitation or voluntary rather than being a required step in the assessment process • Patients receive insufficient feedback when they lodge consumer comments

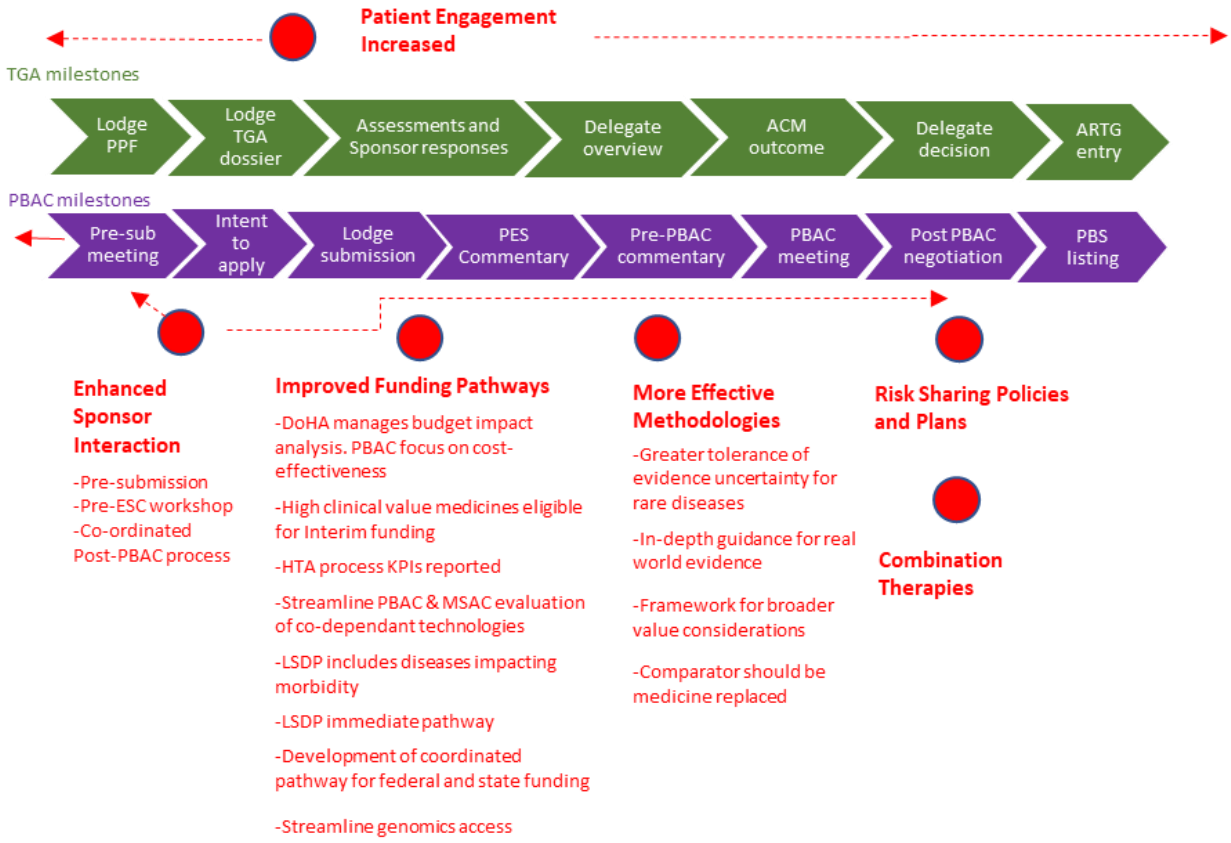
5. Identify features of HTA policy and methods that may be creating perverse incentives

- A lack of effective risk management framework creates a low tolerance for uncertainty
- Product improvements and many second in class therapies which include a benefit for patients are often not introduced into Australia because Lowest Cost Comparator (LCC) pricing policy requires a significant price reduction for PBS listing.
- Combination products (particularly with different sponsors) face reimbursement challenges due the assessment process hindering the valuation of the individual therapies in the combination treatment

AZ's recommendations are outlined in Figure 1. As already noted, improvements sought include increasing patient engagement in the HTA process, improved funding pathways that keep patient access at the forefront of decision-making, and enhanced sponsor collaboration. Specific details of these and other recommendations to address issues associated with each of the five policy questions include:

- **Increased patient engagement across the lifecycle of a medicine,** particularly at early stages of the HTA process.
- **Increased Sponsor engagement during the reimbursement process**, through an expansion in pre-submission meeting scope, mechanism for evaluators to interact with sponsors as part of pre-ESC workshops, and post-PBAC, as part of transparent and co-ordinated post-PBAC listing processes
- **Improved funding pathways**, include the:
    - DoHA manage agreement of assumptions regarding utilisation and financial estimates with the Sponsor, while PBAC remains focused on consideration of cost-effectiveness
    - High value medicines could be made eligible for interim funding in the period between TGA approval and negotiated pricing
    - Ensure HTA processing timeline KPIs are developed and routinely reported
    - Streamline PBAC and MSAC evaluation of co-dependant technologies
    - Expand the criteria on the Life Saving Drug Program (LSDP) for treatments of diseases impacting morbidity
    - Establish a direct pathway for LSDP reimbursement.
    - Establishment of a coordinated pathway and funding program for disease treatments requiring funding from Federal, State and Territory level governments
    - Develop a framework to streamline access to genomic testing.
- **More effective methodologies**, include
    - Greater tolerance of ICER uncertainty for rare diseases
    - In-depth guidance and tools should be developed for the use of RWE in submissions
    - Prepare a framework which includes the scope of considering indirect costs and benefits within the HTA evaluation
    - Comparator should be medicine most likely replaced in clinical practice
- **Risk sharing policies and plans**
- **Combination therapies.** Develop framework for improved valuation

Figure 1: ***HTA methods and policices improvement recommendations.***



2. About AstraZeneca

AstraZeneca is a global biopharmaceutical company employing more than 700 people across Australia and New Zealand. AZ is one of the largest pharmaceutical manufacturers in Australia with a manufacturing site in North Ryde Sydney and is among the largest investors in clinical trials and research in Australia with 96 active trials.

Our therapy areas are focused on: oncology; rare diseases; cardiovascular, renal and metabolism; respiratory and immunology; and vaccines and immune therapies. Through persistent innovation, we have built one of the most diverse portfolios and pipelines in the industry, with the potential to change the practice of medicine and transform the patient experience.

We have a dedicated Diagnostics Division focused on improving the understanding and use of genomics and biomarker testing and breaking down the barriers to accurate and timely diagnosis. Our aim is to support clinical decision-making and enable precision medicines to reach the right patient at the right time.

We are committed to understanding the unique barriers to equitable access for each patient, regardless of type or stage of disease, postcode, or health cover, and working in close collaboration with government, healthcare providers, patient organisations, industry, and partners, to drive equity of access across the healthcare system so no patient is left behind.

3. Response to HTA Review Questions

3.1 Identify features of HTA policy and methods that are working effectively

AZ considers the following elements of the Australia HTA system to be working effectively.

Special Pricing Arrangements (SPAs), indication-based, and confidential pricing
Special Pricing Arrangements are agreed with Sponsors that involve 'published' and 'effective' price components and managed through a rebate arrangement.[3] Some medicines with multiple indications may have indication-specific prices for the relevant patient populations. The confidential pricing arrangement is central to the availability of medicines in Australia.

Parallel processing has the potential to significantly reduce time to access TGA and PBS submissions can be made under the parallel processing arrangement, which enables registration and reimbursement evaluation for major submissions to take place in parallel. Submissions must satisfy criteria[4], such as being a Category 1 or Category 2[5] and must not be a medicine considered a biosimilar. A reduction in re-submission churn will result in the benefits of parallel processing being fully realised.

Flexibility with individual assessments and recommendations; and the opportunity to have pre-submission meetings and post-PBAC not recommended meetings. AZ considers the HTA system should retain its flexibility to account for factors such as healthcare policy objectives and unmet clinical need in addition to cost-effectiveness considerations. Pragmatism and flexibility, along with the ability to have pre-submission and post-PBAC rejection meetings, should be retained in HTA decision making

3.2 Identify features of HTA policy and methods that may act as current or future barriers to earliest possible access

AZ considers the following elements of the current HTA system to be major barriers hindering speed of access.

[3] https://www.pbs.gov.au/pbs/industry/listing/elements/deeds-agreement/b-background
[4] https://www.pbs.gov.au/info/publication/factsheets/shared/tga-pbac-parallel-process
[5] https://www.pbs.gov.au/pbs/industry/listing/procedure-guidance/4-presubmission-requirements/4-1-types-of-submissions

Limited engagement between sponsor, patients, evaluator and committee during the HTA process. Resubmissions into multiple PBAC meeting cycles is the biggest contributor to the patient access gap. AZ believes that by including opportunities in the assessment process for stakeholders to engage 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. By reducing submission churn, much of the inefficiency and resource drain in the current process could also be eliminated. Process efficiency and a reduction in the patient access gap could be further achieved by introducing process transparency, co-ordination, and engagement with sponsors during the post-PBAC PBS listing process. Under the Strategic Agreement, the Federal Government and Medicines Australia have agreed to work together to co-design a trial to facilitate the exchange of information between the sponsor and evaluators during the PBAC submission process.

Recommendation 1: Increased engagement between sponsor, patients, evaluator and committee discussant throughout submission evaluation to achieve a PBS listing within one cycle, and with DoHA post-PBAC to identify and address process bottlenecks. Specifically, this includes:

- **Expansion in pre-submission meeting scope**. Pre-submission meetings are conducted between sponsors and the DoHA, around 12 weeks prior to lodgement and can last up to an hour. The advice is not endorsed, and time constraints limit the depth of discussion. AZ believe pre-submission meetings are very helpful but could be improved by including more relevant stakeholders such as the evaluator, the ESC and PBAC discussants, as well as a patients and clinicians. Agreed minutes of the discussion of patient-perspective disease impact, PICO elements, evidence requirements, modelling structure and assumptions, and other relevant considerations could guide ongoing engagement as the HTA process progresses. DoHA officers could take on a coordinator role, managing engagement and triaging the submission through the process in the most efficient and timely manner.

- **Introduce pre-ESC workshops**. The collaboration between evaluation stakeholders described above for pre-submission meetings could be continued following the first evaluator's commentary of the submission in a pre-ESC workshop. AZ support inclusion of an additional pre-ESC workshop in the HTA process which involves Sponsors, evaluators, and other stakeholders to resolve issues identified in the evaluator's commentary. Clinical experts could be engaged to validate assumptions and methods as required.

- **Greater transparency and interaction with the sponsor should be introduced to the post-PBAC PBS listing process.** The PBS restriction, utilisation estimates, risk sharing agreements and pricing activities should be co-ordinated by a process manager and the sponsor should be engaged throughout the process for efficient and timely completion of listing processes.

Interim funding is not available for medicines of high added clinical value. Given the large time delays to reimbursement in Australia relative to other OECD countries, medicines of high added clinical value cannot be rapidly accessed by patients following TGA approval.

Recommendation 2: Medicines of high added clinical value could be made eligible for interim funding during the period between TGA approval and PBS listing. The methodology for interim pricing agreement, dispute resolution require consideration. Such consideration involves evaluation of managed access programs performance across the world.

There are no comprehensive key performance indicators (KPIs) or time-bound phases against which to measure the time to reimbursement. The government does not systematically measure access from registration to PBS listing, there appears to be limited consensus as to how to measure time to access.

Recommendation 3: Ensure HTA processing timeline KPIs are developed and routinely reported. AZ supports the development of a framework to measure time to access. The approach should involve a selected number of simple and transparent indicators that can be readily verified. The reporting of agreed KPIs for HTA process timelines should be legislated and time to access targets should be agreed.

PBAC recommendations regarding utilisation assumptions that are not linked to cost-effectiveness, but that inform the financial expenditure estimates. AZ firmly aligns with MA[6] in that it is necessary to achieve a separation between PBAC consideration of cost-effectiveness and DoHA consideration of budget impact and RSA negotiations. The Pharmaceutical Benefits Pricing Authority (PBPA) used to play a major role in financial negotiations, but since it was abolished in 2014, PBAC recommendations regarding assumptions of utilisation and financial estimates that are not related to cost-effectiveness are a significant cause of patient access delay.

Recommendation 4: PBAC should remain focused on cost-effectiveness. **DoHA should manage agreement of assumptions regarding utilisation and financial estimates in collaboration with the sponsor.** AZ believes that the PBAC should make its recommendations based on cost effectiveness and associated health benefits for Australians. The scope of the PBAC should not include consideration of utilisation estimates that are not directly linked to cost-effectiveness, budget impact or opportunity cost. The agreement of assumptions of utilisation and financial estimates should be managed by the DoHA in consultation with the sponsor.

Limited guidance on use of real-world evidence. Observational studies, registries, MBS and PBS claims data, chart reviews, and electronic health records can be used as real-world evidence (RWE)[7]

[6] "Funding Innovative Medicines" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[7] "Real world evidence" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

to support clinical effectiveness, economic modelling, and budget impact analyses. These data may be used in economic modelling and budget impact analyses. PBAC prefers high level evidence[8] (e.g., RCT data) in evaluating effectiveness claims and current PBAC guidelines do not provide detailed guidance on how RWE can be used in economic analyses.

Recommendation 5: In-depth guidance and tools should be developed for the use of RWE in submissions AZ aligns with MA[9] that there is a need for comprehensive guidance on how RWE should be used in the Australian HTA process for economic analysis. The infrastructure required to support the collection and curation of RWE in Australia needs further investment.

The current PBAC and MSAC guidelines are inconsistent in advice on inclusion of wider societal benefits of medical innovation. Both PBAC and MSAC guidelines require use "of a health care system perspective to inform the base-case analysis, and describe any alternative perspectives provided as supplementary analyses". The healthcare perspective excludes wider indirect benefits and costs to the patient, their carer, tax revenue, social welfare impacts, National Disability Insurance Scheme (NDIS) impacts, as well as benefits valued by patients and productivity gains.[10]

Although both guidelines include some information on "non health outcomes" to be included in the supplementary analysis, there is inconsistency in the level of guidance on which non health outcomes can be included and how to assess their validity. For example, MSAC guidelines (Section 5) provide detailed guidance on assessing the "value in knowing" from investigative technology (defined as, "any consequence for the wellbeing of a patient beyond the changes in the health outcomes attributed to changes in the health care provided").[11] Such a novel element of value is not captured as part of the tradition Quality Adjusted Life Year (QALY) calculation but clearly important to MSAC's consideration.

PBAC guidelines suggest a few "non-health outcomes" that could be presented in a supplementary analysis but provides limited guidance (PBAC guideline Appendix 6). Such a limited consideration of value beyond the healthcare perspective can hinder assessment of the full benefit for a range of medicines such as rare diseases, where the availability of evidence is limited; chronic diseases that impair a person's workforce participation; and vaccines which, as demonstrated during the pandemic, can deliver both individual and societal benefits well beyond the clinic.

[8] Ghijben P, Gu Y, Lancsar E, Zavarsek S. Revealed and Stated Preferences of Decision Makers for Priority Setting in Health Technology Assessment: A Systematic Review. Pharmacoeconomics. 2018 Mar;36(3):323-340. doi: 10.1007/s40273-017-0586-1. PMID: 2912463

[9] "Real world evidence" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[10] Value of medicines" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[11] Lakdawalla DN, Doshi JA, Garrison LP Jr, Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. Value Health. 2018 Feb;21(2):131-139. doi: 10.1016/j.jval.2017.12.007. PMID: 29477390

Recommendation 6: Prepare a framework for including indirect costs and benefits within HTA evaluation. AZ proposes a comprehensive review of important elements of value that are not currently captured as part of PBS cost-effectiveness analysis, and their acceptability should be included in both the PBAC and MSAC guidelines. This review should conclude with the development of agreed criteria and methods for situations where indirect benefits should be included in the HTA assessment process.

The reimbursement process for co-dependent technologies is complex. Currently, PBS listing of medicines that are a co-dependent technology (e.g. precision medicines that target a biomarker identified with a diagnostic test) need a positive MSAC recommendation of the diagnostic test, prior to a positive PBAC recommendation for the medicine. Submissions require review by multiple committees whose meeting schedules are not co-ordinated. This process results in delays due to duplication of assessment across multiple committees, differences in meeting timing, limited communication between the committees and duplication in information requirements.

Recommendation 7: Streamline the PBAC and MSAC evaluation of co-dependent technologies. This could be achieved by PBAC assuming the role of MSAC for co-dependant submissions (establishment of a co-dependant sub-committee) or establishing a new committee for the consideration of MBS and PBS listing of co-dependent technologies. Current MSAC/PBAC coordination could be improved by increased MSAC Secretariat resourcing, improved meeting timing and coordination.

Treatments which require funding from Federal, State and Territory level governments do not have a coordinated pathway. Cell and gene therapies and COVID-19 treatments require multiple levels of government funding to support uptake. For example, gene therapies follow differing HTA pathways depending on whether treatments are provided in inpatient or outpatient settings. There have been multiple studies and reviews which have analysed the inefficiencies in the system and the cost impact because of lack of coordination for treatments involving complex pathways. The Halton Review[12] of COVID-19 Vaccine and Treatment Purchasing and Procurement calls for a clear policy framework.

A National Health Reform Agreement Long Term Reforms Roadmap has been endorsed by all Australian Health Ministers at the Health Ministers' Meeting on 17 September 2021.[13] The case for change noted "The Commonwealth, states and territories acknowledge that, within the constraints of limited budgets, robust and transparent prioritisation of spending on health technologies is critical for coordinated, equitable and efficient service delivery".

[12] https://www.health.gov.au/resources/publications/review-of-covid-19-vaccine-and-treatment-purchasing-and-procurement-summary-and-recommendations

[13] https://federalfinancialrelations.gov.au/sites/federalfinancialrelations.gov.au/files/2021-10/NHRA-longterm-reforms-roadmap.PDF

Recommendation 8: Establish a coordinated pathway and funding program for disease treatments requiring funding from Federal, State and Territory level governments. AZ proposes the development of a coordinated pathway and funding program within the DoHA. This includes establishing DoHA officers who specialise in cooperation across multi-jurisdictional pathways, who could be made available during pre-submission meetings, and at other points of the HTA process to help shepherd complex submissions and ensure timely access. They would work with sponsors to facilitate meetings with the relevant state authorities to coordinate funding mechanisms.

3.3 Identify features of HTA policy and methods that may act as current or future barriers to equitable access

MA[14] noted that Japan, Germany, the UK and France have developed specific processes to overcome the challenges of patient access to orphan drugs. These include the lack of need for cost-effectiveness analysis in HTA and flexible thresholds for funding. The 2020 National Strategic Action Plan for Rare Diseases[15] calls for the best possible health and wellbeing outcomes for Australians living with a rare disease. AZ believes there are several barriers in the HTA system which need to be addressed to achieve this vision.

The LSDP reimbursement pathway includes multiple stages across separate funding assessment processes which delays access to treatments. The Life Saving Drugs Program (LSDP) pathway is complicated and slow as medicines are considered by the LSDP following rejection by PBAC. The *Inquiry into New drugs and Novel Medical Technologies* recommended that the assessment process for the LSDP be streamlined and delays in access to treatments be reduced by ensuring that a sponsor only need to lodge one HTA application for a single pathway.

It was recommended that sponsors be provided with an immediate pathway to the LSDP Expert Panel or a pathway by adjusting the Pharmaceutical Benefits Scheme section 100 program, with specific criteria, as with other section 100 programs. AZ supports the formation of an immediate pathway to the LSDP or providing a pathway by adjusting the Pharmaceutical Benefits Scheme section 100 program, with specific criteria, as with other section 100 programs

Recommendation 9: Establish a direct pathway for reimbursement via the LSDP

HTA evidence requirements and methods do not reflect data availability for rare diseases. The cost-effectiveness of treatments for rare diseases can be highly uncertain because of rare disease natural history data gaps, limited availability of comparator efficacy data, and small patient populations which limit the statistical analyses of clinical studies.

[14] "HTA and rare diseases" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[15] https://www.health.gov.au/resources/publications/national-strategic-action-plan-for-rare-diseases

Recommendation 10: Reduce the emphasis on cost-effectiveness to support reimbursement recommendations for rare diseases. AZ believe that the burden of proof should be lower for rare disease treatments, with a greater acceptance of an uncertain ICER within the HTA process. As recommended by MA[16], there should be less emphasis on cost-effectiveness to support reimbursement recommendations for rare diseases given the degree of uncertainty around the ICER. Rare disease evaluation should involve more acceptance of RWE and registry data.

LSDP eligibility does not cover innovative medicines that improve quality of life and address or delay progression to disability, in addition to those that extend life. Treatments for rare diseases that cause significant chronic disability but are not life-threatening are not eligible for funding through the LDSP. The costs of treatment for these rare diseases are generally high, due to the small group of patients in which the research and development (R&D) costs can be recovered. The cost, coupled with limited evidence and the exclusion of indirect costs and benefits, tends to lead to ICER's above PBAC acceptable cost effectiveness thresholds, resulting in limited availability of reimbursed medicines for rare disabling diseases in Australia.

Recommendation 11: **Expand the LSDP eligibility criteria to include treatments that improve life, not just those that extend life**. The *Inquiry into New drugs and Novel Medical Technologies* highlighted that there is a need to elevate quality of life or 'life improving' measures (such as reduction in significant disability, slowed disease progression or stabilisation of condition) in the consideration of funding new medicines for rare diseases. AZ supports this recommendation.

Despite the availability of large gene panels, the co-dependent technology pathway requires a submission for each medicine/diagnostic test pairing. Co-dependant submissions that require a demonstration of cost-effectiveness for an individual medicine/diagnostic test pairing and on individual indications is a lengthy and overly complex process that is not feasible for the predicted increase in use of these technologies in the near future. The Australian Institute of Digital Health (AIDH) and InGeNA 2022 Federal Election Statement[17] included estimates from Deloitte that the genomics and precision health sector is expected to contribute $3.77 billion to Australia's GDP. Therefore, AZ supports the solutions discussed in the InGeNA Whitepaper: '*Realising the full potential of genomics to personalise healthcare'*.[18]

[16] HTA and rare diseases" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[18] https://ingena.org.au/patient-access/

There are more than seven thousand rare diseases and approximately two million Australians are estimated to be living with a rare disease.[19] [20]Diagnostic testing is not readily available for many of these diseases in Australia and small patient populations result in limited incentives for diagnostic development and commercialisation. Without access to comprehensive genomic sequencing, patients may have to undertake multiple tests prior to accurate diagnosis, or their treatment may be delayed by the requirement for diagnostic testing.

Recommendation 12: **Develop a framework to streamline access to genomic testing**

3.4 Identify features of HTA policy and methods that detract from person-centredness

The patient voice in the HTA process is through invitation or voluntary rather than being a required step in the assessment process and patients receive insufficient feedback when they lodge consumer comments. Currently, consumers can provide commentary about medicines on a PBAC agenda, consumer hearings provide the opportunity for invited consumers to have direct communication with PBAC about medicines seeking reimbursement, stakeholder meetings are convened for medicines treating high burden diseases that have not been recommended, and there is consumer representation on PBAC.[21] [22]

Patient and clinician input to PBAC and MSAC decision making could be improved. AZ believes that patient participation is provided far too late in the HTA decision process and participation rates remain low. Recent evidence suggests that two thirds of all PBAC submissions (between 2014-19) did not receive a single consumer comment.[23] Additionally, patients receive insufficient feedback when they lodge consumer comments.

[19] https://www.health.gov.au/topics/chronic-conditions/what-were-doing-about-chronic-conditions/what-were-doing-about-rare-diseases

[20] Jackson A, Geatches L, The McKell Institute 2021 Progress Update: Funding Rare Disease Therapies in Australia - Ensuring Equitable Access to Healthcare for all Australians, The McKell Institute. https://mckellinstitute.org.au/wp-content/uploads/2022/02/McKell-Funding-Rare-Disease-Therapies-in-Aus-2021.pdf

[21] "Consumer engagement" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[22] https://www.pbs.gov.au/pbs/industry/listing/procedure-guidance/6-consideration-submissions/6-7-consumer-input

[23] Tjeuw E, Wonder MJ. Analysis of consumer comments into PBAC decision-making (2014-9). Int J Technol Assess Health Care. 2022 Feb 4;38(1):e18. doi: 10.1017/S0266462321001744. PMID: 35115073

Recommendation 13: The patient voice should be central to medicine reimbursement considerations. Establish opportunities throughout the reimbursement process of a medicine for sponsors, evaluators, and committees to seek the patient perspective, with a focus on early engagement. Specific opportunities include:

- **Horizon scanning.** Horizon Scanning reviews could be conducted between the Commonwealth and industry, including individual companies, to effectively identify and document future therapeutic area products and technologies, to gather valuable patient insights, identify gaps in knowledge and data in a collaborative and independent manner. This process could be used to identify early system assessment pathways for new and emerging co-dependent technologies including companion diagnostics.

- **Invite Patients to Early Access Forums**. AZ sees a future where patients are engaged and informed in a collaborative, consultative forum including clinicians, patients and caregivers, industry, and the DoHA earlier in the life cycle of the access pathway – formalised prior to the TGA submission. This requires early notification and awareness, the exchange of plain language information directly with patients, carers, and other stakeholders to assist with identifying areas in the submission that would benefit from enhanced understanding of the disease and benefit of the therapy with consumers.

- **PBAC Patient Engagement Touchpoints**. Patient involvement would continue in the pre-submission meeting and pre-ESC workshop processes, with consumers included in formal hearings to address patient issues or assumptions where this is warranted to frame the PBAC's decision making, without extending overall access timelines. Consumers should continue to share their views via consumer commentary via flexible, accessible options.

- **Guidance and education** around expectations of patient involvement in the HTA process needs to be addressed, with the Consumer Evidence and Engagement Unit working with the PBAC to provide clear guidelines for HCOs on the types of information that is valued and the standard of evidence that can support evaluation, so that patients can meaningfully participate.

- **Post PBAC Outcomes**: Improved feedback mechanisms and providing greater clarity and transparency for patients, carers, and other stakeholders to ensure the value of lived experience is evident and communicated in decision-making are required

3.5 Identify features of HTA policy and methods that may be creating perverse incentives

AZ considers the following features of HTA policy and methods are creating perverse incentives:

A lack of effective risk management framework creates a low tolerance for uncertainty. Uncertainty is the reason most often cited by the PBAC when a submission is not recommended. The requirement to resubmit through the HTA process again delays patient access to new treatments. An analysis conducted by Commercial Eyes[24] indicated there were 62 rejected Major Category 1 and 2 submissions between March 2021 and March 2022, of which uncertainty in the ICER or magnitude of clinical benefit was noted in 37 (60%) of the rejections.

MA noted that PBAC usually manages uncertainty by using highly conservative estimates rather than most likely estimates. This includes time horizons of economic evaluations being truncated, artificial waning of effectiveness, a reliance on single conservative clinical outcome measures (e.g., Overall Survival) and multivariate sensitivity analyses undertaken using unreasonable parameters to assess the degree of uncertainty.[25] Without an effective framework to manage risk, it is challenging for the PBAC to balance the risk of listing a medicine that is not cost effective, with the risk of delayed access to a medicine that is cost effective. Furthermore, financial uncertainty managed with overly conservative estimates of utilisation and expenditure that inform RSAs are challenging to negotiate and often delay access.

Recommendation 14: Develop a risk sharing framework that identifies risks associated with key uncertainties and formulates effective risk management plans (RMP). AZ supports the development of a framework and policies for identifying the risks associated with key uncertainties and formulation of associated risk management plans (RMP) that manage these risks. Risk management planning should articulate parameters such as cost-effective populations, market increasing potential for the new product, impacts of a new entrant, and accommodate renegotiation of caps.

Managed Access Programs (MAP) may be part of RMPs, or alternatively the ability to renegotiate Deeds of Agreement within the 5-year period to redefine utilisation estimates as more evidence becomes available. This was stipulated in the recent vosoritide PBAC approval as the ability to re-evaluate the CER as evidence becomes available (Vosoritide PSD 2022).[26] The need for, and potential development of RMPs, would be part of discussions during early and ongoing engagement between Sponsors and PBAC.

[24] Managing uncertainty" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta

[25] "Managing uncertainty" https://www.medicinesaustralia.com.au/policy/health-technology-assessment-hta/

[26] https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2022-07/Vosoritide-Voxzogo-PSD-july-2022

Product improvements and many second in class therapies which include a benefit to the patient are often not introduced into Australia because Lowest Cost Comparator (LCC) pricing requires they take a significant discount for PBS listing. The comparator is the benchmark used to estimate the comparative efficacy, safety, and cost-effectiveness of a novel medicine in HTA. The first PBAC Guidelines defined the comparator to be the *most likely medicine(s) to be replaced in clinical practice,* although more recently the "lowest cost comparator" is being used in the HTA evaluation process.[27]

Recommendation 15: **The comparator used as a benchmark should be the medicine which is the most likely to be replaced by the new medicine**. AZ agrees with MA[28] that if the use of lowest cost comparator and reference pricing policy continues, it will hinder the launch of innovative medicines in Australia. AZ advocates that the comparator used in HTA assessments should be the medicine most likely to be replaced in clinical practice.

Combination products (particularly with different sponsors) face reimbursement challenges due the assessment process hindering the valuation of the individual therapies in the combination treatment. Some treatments when used in combination, can result in greater efficacy than when used alone or in sequence. The use of combination therapies is becoming more prevalent, particularly for diseases such as multiple myeloma, lymphoma and lung cancer.[29] Reimbursement is complex when medicines are supplied by different sponsors, are under patent protection and used in more than one indication. Sponsors may wish to negotiate the prices of component medicines within the combination treatment; however, this is prohibited under the *Australian Competition and Consumer Act*.

The *Inquiry into New drugs and Novel Medical Technologies* identified the need to improve how combination treatments are assessed and funded in Australia. It called on the Australian government to review how it assesses combination treatments, particularly those including components from different sponsors. The Bellberry Forum[30], and subsequent publication[31], explored policy challenges and proposed several recommendations to assist in reimbursement.

Recommendation 16: Develop a combinations therapy reimbursement framework that would enable pricing negotiation between multiple sponsors of a combination treatment regimen.

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

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

[29] Danko et al, Challenges in the value assessment, pricing and funding of targeted combination therapies in oncology, Health Policy 2019

[30] Latimer et al, Challenges in valuing and paying for combination regimens in oncology. Report of an international workshop convened by Bellberry in Sydney Australia November 2019 (provided as attachment).

[31] Towse et al, Why we need a new Outcomes-based Value Attribution Framework for Combination Regimens in Oncology, Office of Health Economics 2020. Accesses at: https://www.ohe.org/publications/why-we-need-new-outcomes-based-value-attribution-framework-combination-regimens

4. Conclusion

Thank you to the Committee for the opportunity to provide input into the Review's first consultation.

AZ is grateful for the opportunity to provide comments in relation to the five policy questions posed as part of Consultation 1 of the Review. It is AZs hope that this first consultation identifies key barriers to improve speed of access and equity, and that progress is made towards maintaining the attractiveness of Australia as a first-launch country.

It is essential that we work together constructively and pragmatically to advance new medical interventions for the benefit of the Australian people and society. As such, AZ remains committed to working with government and across the healthcare industry towards improving the HTA process and methods. If we can be of further assistance to the Review, or if any additional information is required, please contact:

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5. References

References have been included as footnotes throughout the submission.