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Dear Committee,

RE: HTA Review

Thank you for providing Pfizer Australia with the opportunity to comment on the HTA review.

Pfizer Australia is one of the nation's leading providers of prescription medicines and vaccines. We manufacture medicines and vaccines that millions of Australians use every day to live longer, healthier, and more productive lives. Every day our people work with the sole purpose of ensuring that Australians can access new and innovative medicines that are being used to treat some of the most feared conditions of our time. We are proud of the active role we play in Australia's health system and the wider contribution we make as an innovator, employer, and manufacturer.

Pfizer has a proud history in Australia. We commenced operations here in 1956 with just six colleagues, and, more than 60 years later, we now have more than 1,000 colleagues working at two commercial sites, and a manufacturing facility in Mulgrave, that exports to more than 60 markets worldwide. Pfizer Australia is a member of Medicines Australia (MA), the peak body representing innovative pharmaceutical companies in Australia. Pfizer Australia was involved in the preparation of MA's detailed response to this consultation, and we fully support their recommendations to the Committee.

We are at a critical juncture for the future of the medicines industry in Australia. The collaboration and cooperation between industry and Government to arrest the impact of COVID-19 demonstrates a shared commitment to deliver the best available medicines and vaccines to Australian patients quickly and to take the necessary steps to keep Australians safe and limit the economic impact of the pandemic.

Australia's Long-Term National Health Plan has set the ambitious target of delivering the 'world's best healthcare system'. This review presents an opportunity to achieve this long-term goal with big picture thinking and policy changes that all partners can uphold and improve upon as we work towards reinstating Australia's status as a 'first-wave' launch country.

Prioritisation of Australia as a first wave country for launch of new medicines and vaccines is no longer assured. Ultimately what manufacturers seek is predictability and certainty, and this is not guaranteed in the current reimbursement process and decision criteria for medicines and vaccines in Australia. Eliminating redundancies and improving efficiency in the HTA processes is a start, However, if this occurs without fundamentally reforming evaluation and decision criteria used to determine the way Australians get fast, equitable access to innovative medicines and vaccines, we will have missed an opportunity.

Most importantly this review must place patients front and centre. For too long, patients have had to look through a 'keyhole' when it comes to medicines reimbursement, with limited opportunity to convey the impact breakthrough medicines can have on their lives and a lack of clarity on the weight their voice carries in HTA decision making.

Thank you again for the opportunity to contribute to this consultation. Pfizer Australia is available at any time to provide further information or examples of our experience with the system to the Committee as required.

Yours sincerely,

Anne Harris
Managing Director, Pfizer Australia and New Zealand

HTA Review

Today's challenges:

Many of today's innovative medicines are personalised and treat highly complex conditions, such as cancer and rare diseases. Specialty medicines can provide significant value in some of the hardest-to-treat diseases and may offer a more targeted treatment, meaning they may be more effective or better tolerated than other available options.

Developing new medicines is a risky and expensive enterprise. It can take 10 to 15 years and cost on average $US 2.6 billion to develop one new medicine, including the cost of many failures. Only 12% of new molecular entities that enter clinical trials eventually receive U.S. Food and Drug Administration (FDA) approval.[i] Regulators and reimbursement bodies around the world are grappling with the challenge of assessing and funding patients' fast and equitable access to new medicines. In Australia this is no different.

Australia's medicines landscape continues to change, and our regulatory and reimbursement settings need to keep pace. The House of Representatives Health Committee's Inquiry into approval processes for new drugs and novel medical technologies in Australia received submissions on changes caused by digital health, increasing consumerism and new partnerships in industry and made several recommendations in the 'New Frontiers' Report. [ii] These recommendations focussed on the way rare diseases and highly specialised therapeutics are assessed and valued, including specific recommendations in relation to the Life Savings Drugs Program (LSDP), orphan drugs and a pilot scheme for value-based payments for new antimicrobial drugs. The Committee noted the HTA review should ensure there are 'future pathways for treatments and therapies that do not fit neatly into the current system' and that the review should also:

'*reduce the frequency of HTA resubmissions, streamline interaction between hospitals and HTA bodies, streamline interaction between the TGA, PBAC and MSAC, harmonise Australia's HTA with equivalent overseas bodies, improvement measurement of the PBAC and public data on its performance, increase the use of MAPs to facilitate earlier access, increase the use of real world evidence (RWE), increase flexibility when choosing comparators, introduce a scoping process that includes patients and clinicians and improve broaden access to the independent review process.'* [iii]

The submissions made to that Inquiry from patient groups, clinicians, and voices from across the medicines value chain highlight the reality that our system needs urgent reform.

The HTA review is an opportunity for Government to respond to the recommendations in the New Frontiers report while addressing broader systemic issues in medicines access. The National Medicines Policy (NMP) presents a useful template for the HTA review. Prior to the review, the NMP was more than 20 years old, and there had been significant change in industry since the policy was developed. The consultative approach to developing the NMP meant the policy was updated in line with patient and industry expectations including the vision 'to achieve the world's best health, social and economic outcomes for all Australians through a highly supportive medicines policy environment'.[iv] This review provides an opportunity for the same attention to be given to the reimbursement of medicines and vaccines – to be effective, the review must consider not just reform of the PBAC and Pharmaceutical Benefits Scheme (PBS), but also of the Medical Service Advisory Committee (MSAC) and MBS where appropriate, the National Immunisation Program (NIP), National Blood Authority (NBA) and LSDP.

HTA Review

Australia's HTA framework has proved a robust model for the consideration of health interventions, and it has delivered great value to Government. However, in Pfizer's experience, Australia's reimbursement system is not keeping pace with comparable overseas markets. The emergence of innovative, targeted therapies has tested the limits of the way Australia approaches HTA and created tension between payers, industry, clinicians and patients. At the heart of these issues is the need for greater transparency, flexibility and consistency in decision making so medicines can be delivered to Australian patients as soon as possible. Previous attempts at reform have led to additional layers of red tape. The result is a system that is complex, rigid and costly.

Pfizer's key recommendations to the HTA review

Policy

- In line with the Strategic Agreement between Medicines Australia and Government, commit to a policy change to:
    a. reduce time to access to new health technologies for Australian patients so that they can access new health technologies as early as possible including an agreed, transparent measure of time to access
    b. maintain the attractiveness of Australia as a 'first wave' launch country
- The Commonwealth invest in the rapid establishment of its own fit-for-purpose pilot fund to combat the threat of antimicrobial resistance
- Commit to new funding arrangements for one-time cell and gene therapy treatments
- The structure of the vaccine approval process is hard-wired to delay access compared to medicines

Methods

- Resolution of the comparator selection issue in line with the intent of the Strategic Agreement between Medicines Australia and Government (2022-2027).
- Lowering the base case discount rate should be introduced as a priority action from the HTA review.
- The assessment of vaccines should be simplified and consider second order effects
- Australia should follow comparable jurisdictions and develop a high-level principles-based framework for accepting and assessing real world evidence
- A transparent national horizon scanning framework must be developed and implemented, including KPIs, to expedite future HTA assessment and service delivery.
- Streamlined HTA pathways and acceptance of broader evidence is needed for rare disease treatments and gene therapies, including those listed on the LSDP.
- A formal framework for the assessment and evaluation and valuation of medicines used in combination, in particular, innovative medicines in the treatment of cancer, must be developed
- Address the perverse incentives caused issues such as by uncertainty in the funding pathways for gene therapies, interchangeability, comparator selection, novel anti-infectives and the use of restricted PBS eligible populations.
- The Enhanced Consumer Engagement Process for patient engagement in HTA must be delivered via genuine co-design and associated principles with clear definitions.

Pfizer's submission

Pfizer Australia has worked collaboratively with industry partners in providing input to this review. Pfizer contributed to the preparation of Medicines Australia's submission which recommends reforms that achieve accelerated patient access as well as methodological changes that can reduce complexity, increase patient involvement and improve efficiency in Australia's HTA system. Pfizer is also a founding member of Australia's first ever Antimicrobial Resistance (AMR) industry alliance AAMRNet and supports their recommendations regarding the urgent challenge of AMR and the need to address the broken market for novel anti-infectives. We are also supportive of the submissions made by the American Chamber of Commerce Health Committee and the Pharmaceutical Research and Manufacturers of America (PhRMA) which shows Australia is behind comparable markets for reimbursement success and timeliness.

Pfizer Australia's submission to the HTA review builds on the themes highlighted in these submissions by providing practical examples of our experience. We argue that Australia, like many other jurisdictions, is at an inflection point. We are on the cusp of a new range of therapies that will require new thinking and adaptability to ensure they are valued appropriately. Consumers are becoming more informed and empowered to take control of their own health, and as a result their expectation of access to the latest interventions will only increase in the years ahead.

Ensuring Australia is keeping pace with these developments will be critical and is certainly within our reach. The collaboration and cooperation between industry and Government to arrest the impact of COVID-19 saw pragmatic decisions made to deliver the best available medicines and vaccines to Australian patients quickly. It is time to extend this approach beyond a pandemic.

Policy reform and a commitment to timely access is needed

The HTA review is an opportunity for reform that reflects the growing complexity of how medicines are developed, whilst stripping back complexity from the way they are assessed and valued. We would like to see common-sense reform of both policy and methods that removes red-tape, promotes efficiency and improves the criteria used to determine the clinical and economic value of new medicines and vaccines. The challenge is not unique to Australia and there is a lot we can learn from other countries to accommodate the next generation of medicines and vaccines in our review processes.

In fact, less than half (44%) of new molecular entities (NMES) registered in Australia between 2016-2021, went on to be reimbursed, compared with 96% in Japan, 84% in Germany, 80% in the UK and 62% in France. For those medicines that are funded in Australia the average time from local regulatory registration to public funding was most recently reported as 466 days[v]. Furthermore, only 12% of new medicines launched globally during the last ten years have launched in Australia within one year of global first launch, compared to 39%, on average, among Australia's peer countries: United States (78%), Germany (44%), United Kingdom (38%), Japan (32%), France (23%) and Canada (21%).[vi] It is clear Australian patients are waiting longer than they should, to access innovative, potentially life-saving medicines.

Changing HTA methods has the potential to remove redundancies and duplication, to simplify the health technology assessment and deliver access faster. But substantive methodological change can only happen if underpinned by an overarching commitment to policies that value innovation and big picture thinking about Australia's approach to new medicines and vaccines.

It is time for a policy approach that values innovation *and* commits to expediting the time between the registration of medicines, and them being reimbursed. There is no greater incentive to develop novel medicines and medical technologies than predictability and certainty in terms of how studies will be established, how products will be assessed for their safety and efficacy and how their value to the community will be determined.

The benefit of this certainty is that innovative medicines and vaccines made available in Australia, have the potential to generate a significant return on investment in the overall health system and economy as they allow Australians to live longer, healthier, more productive lives. Clear, transparent, agreed goals can provide the same level of certainty for patients, clinicians and stakeholders with a vested interest in timely access to medicines. As recommended in the New Frontiers report, application processing times and positive recommendation rates should be benchmarked against other nations with advanced HTA and published annually.

Consideration of the funding envelope for new medicines

Consideration must also be given to the funding for innovative medicines and vaccines, ensuring that the PBS envelope and other related budgets can accommodate new technologies and meet the shared objectives of the Strategic Agreement. While PBS funding is not explicitly in scope for the HTA review, reform to HTA policy and methods and the funding for new and innovative medicines in the PBS budget should be considered together because they are both required to achieve accelerated patient access. When reviewing Government expenditure on the PBS since the start of the century it is evident that savings measures, combined with the growth in rebates paid by companies have curtailed growth in the PBS. In fact, the PBS has been gradually falling as a share of GDP once rebates are considered, and today the PBS represents a smaller share of Commonwealth health expenditure than it did in 2000.[vii] Future budgets will need provisions for real growth of the PBS over time. With Australia's ageing population and the convergence of mobile technology and data with healthcare, new and innovative medicines and vaccines need to be seen as an investment in the health of Australians, and in turn, the health of our economy.

The broken market dynamic restricting the development of novel anti-infectives requires a new policy approach

Research and development of new innovative antibiotics is critical to addressing AMR, though current structures don't adequately value research and development. Despite the importance of new antimicrobials to allow our health system to stay ahead of AMR, the market is not structured to incentivise research and development in this space. In order to preserve their effectiveness for as long as possible, use is restricted through antimicrobial stewardship. This means, a company produces a new anti-microbial, has it approved by the Therapeutic Goods Administration (TGA), and then the health system does not prescribe it so it can remain effective in the most complex cases. The company which invested significantly in the research and development of that drug might see no return as their highly effective drug is held back in case of emergency. [viii]

A recently released study on the burden of AMR attributed 1.27 million deaths globally to bacterial AMR[ix] and this figure is expected to worsen. AMR is on track to claim 10 million lives per year globally and put at risk a cumulative US$100 trillion of economic output if no action is taken by 2050.[x] In Australia, the estimated annual impact of AMR on the economy by 2050 will be between A$142 billion and A$283 billion.[xi] Australia is also vulnerable to shortages due to geographic isolation and the high costs and difficult logistics in international drug supply chains. This becomes critical when lifesaving novel anti-infectives are impacted.

Pfizer example: Pfizer has an important medicine, linezolid (Zyvox) which is indicated for:

1) the treatment of microbiologically proven, multi-resistant methicillin-resistant Staphylococcus species (MRSS) infection in patients where no other antimicrobial agents can be used; and

2) treatment of microbiologically proven Vancomycin-Resistant Enterococcus species (VRE) infection.

In 2013, the PBAC rejected this medicine, expressing concern about the lack of effective means to monitor emergence and trends of antimicrobial resistance, despite wide acknowledgement in all healthcare sectors of the importance of these data. PBAC also considered that the framework of the PBS did not easily accommodate new antibiotics intended for use against resistant microorganisms and considered that it may be appropriate to explore whether a suitable policy construct could be identified which would recognise both the value of development of new antibiotics and the risks of emerging resistance to antimicrobial agents. This problem persists.

Many countries have recognised these issues and the consequences of not having new antimicrobials and are pursuing new models for assessing the value of novel antimicrobials taking account of the broader value they bring to society. In the UK, the Government has partnered with industry to pilot a reimbursement model that will de-link the revenue of an antimicrobial from the volume sold, and base it instead on the antimicrobial's value to the NHS and wider public health. This pilot will also help to reduce the financial uncertainty in antimicrobial research and increase incentives to develop novel anti-biotics. The model, if expanded globally, has the potential to generate a pull incentive that would overcome the market failure of antibiotics.[xii] Other countries including the US and Sweden are also progressing new models for assessment of novel anti-infectives.

Pfizer is a member of the Australian Antimicrobial Resistance Network (AAMRNet) and we support their submission to this consultation which provides a comprehensive background and rationale for why a novel reimbursement approach is required. AAMRNet recommends the Australian Government invest in the rapid establishment of its own fit-for-purpose fund, taking learnings from the UK pilot.

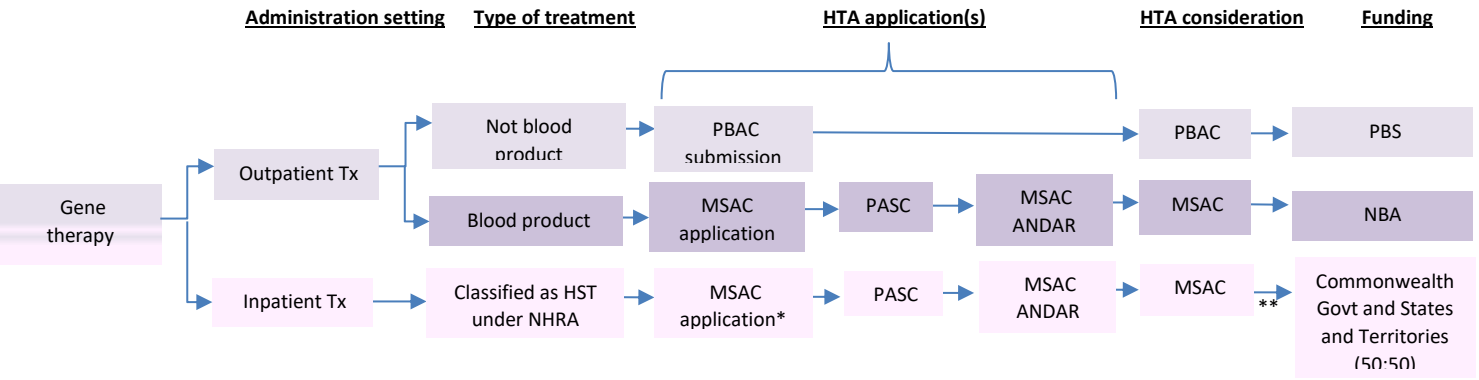
Gene and cell therapies with potentially lifelong impact need special pathways

Complex and unpredictable reimbursement frameworks complicate patient access to potentially curative gene therapies. Under the current HTA frameworks, gene therapies, which offer the promise of one-off treatments for curative and/or life-long or prolonged benefits, face complex and uncertain funding pathways which fail to consider all the benefits of these treatments.

Current HTA criteria also fail to acknowledge the broader benefits of gene therapies. Current HTA methods may not fully capture decreased burden on the patient resulting from potentially one-time or short treatment regimen, value of hope and spillover effects on carers and family. Current HTA and evidence generation methods and criteria must evolve to fully recognise the potential of gene therapies and facilitate patient access, as current methods are ill-suited to capturing the life-long health gains that can flow from these potentially curative therapies.[xiii]

There are a number of reimbursement and funding pathways for gene-therapies. Australia's funding models distinguish between drugs administered in hospitals which are accessed via state run public hospitals and drugs administered to outpatients which are dispensed in pharmacies. In Australia, gene therapies that will be administered to outpatients are considered by the Pharmaceutical Benefits Advisory Committee (PBAC) and listed on the PBS. Gene therapies that are blood-related products will be considered by MSAC and funded by the NBA. Gene therapies that are administered to inpatients and classified as highly specialised therapies (HST) will be considered by MSAC and funded by Commonwealth Government and State and Territory (50:50). The MSAC path

involves an MSAC application which goes to PICO Advisory Sub-Committee (PASC) and then submission of an Applicant-Developed Assessment Report (ANDAR). Following the MSAC application a committee which includes the Chair of the PBAC, Chair of MSAC and a representative of the States meet and agree which pathway should be followed, PBAC or MSAC. This means that the company may have been working toward an MSAC ANDAR and at a very late stage, are advised to instead make a submission to PBAC. This can result in additional work to convert the ANDAR to a PBAC submission and delays in access for patients. The various pathways and funding models are not fit for purpose if the goal is to provide fast, equitable access to all Australian patients regardless of postcode.



Gene therapy pathways

**Consideration by Committee of Chairs to determine pathway*
***Negotiation and contracting with States and Territories*
ADAR, Applicant-Developed Assessment Report; Govt., Government; HST, Highly Specialised Therapy; MSAC, Medical Services Advisory Committee; NBA, National Blood Authority; NHRA, National Health Reform Agreement; PBAC, Pharmaceutical Benefits Advisory Committee; PBS, Pharmaceutical Benefits Scheme; PASC, PICO Advisory Subcommittee; Tx, treatment

The figure above highlights the uncertainty and delay inherent to review of products that will or may be administered to inpatients. An unintended and potentially devastating consequence of the complexity of this system is that by the time the treatment becomes available, the patient may no longer be eligible due to increased age, progress of disease and exposure to neutralising antibodies. This phenomenon can cause lifelong disease and disability for patients who miss the eligibility window as well as significant frustration for patients and their families.

Gene therapies will have significant budgetary implications and will require new funding models. While treatments for chronic conditions are paid per prescription and costs are dispersed over time, gene-therapies are one-off, high-cost interventions. This challenge will be exacerbated by the existing cohort of patients waiting for breakthrough gene-therapies who will seek access as soon as possible. The first year of access is likely to see a significant spike in costs before the curve normalises with access aligning with new diagnoses.

The structure of the vaccine review and approval process for access is hard-wired to be slower compared to medicines

In Australia, vaccines reimbursement follows a lengthy, multi-step journey which includes two unique steps which are additional to the PBS reimbursement of medicines. While the intent behind these additional steps may be benign, the structure delays access to vaccines and creates additional costs and complexity. This structural barrier to timely access for vaccines conflicts directly with the goals of the HTA review to reduce time to access and to provide new health technologies as early as possible.[xiv]

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The approval of vaccines for funded access starts with initial clinical consideration by the Australian Technical Advisory Group on Immunisation (ATAGI). Then the Pharmaceutical Benefits Advisory Committee (PBAC), undertakes formal health technology assessment. If a positive PBAC recommendation is received, approved vaccines must finally participate in a tender process which is used to procure vaccines for the NIP. If TGA review for registration is also included, companies seeking to have a vaccine listed on the NIP now need to go through four evaluation processes: TGA, ATAGI, PBAC and NIP tendering which is time consuming, complex, and costly. TGA, ATAGI and PBAC processes are all cost recovered, meaning the evaluation of an innovative vaccine costs the sponsor approximately double that of a medicine, if recommended first time by PBAC.[xv] A recent report analysing the time to PBS and NIP listing for medicines and vaccines, respectively, noted that vaccines take on average an extra two years to navigate approval and procurement compared with the PBS processes required for medicines.[xvi]

Having compared Australia's vaccines access pathways to those of comparable countries (Austria, Canada, France, Germany, Japan, Switzerland and UK), only France and Australia have a two-step process (National Immunisation Technical Group [NITAG] and Health Technology Assessment Body [HTAB]). In the other countries, the vaccine is not considered by an HTAB and the NITAG makes the recommendation including a determination of cost-effectiveness, except for Austria which does not consider cost-effectiveness. The issues and international comparisons detailed here highlight the urgent need to streamline approval, HTA evaluation and procurement of vaccines in line with the time it takes to provide access to new medicines and most importantly, to achieve the shared goals of timely access for Australian patients and ensuring our assessment processes keep pace with rapid health technology advances.

Terms of reference 1: Elements and features that are working effectively

Pfizer welcomes reforms that have occurred over a number of years to address some of the challenges facing registration and reimbursement. Since the last review of HTA in Australia in 2009 there have been reviews and policy developments aimed at alleviating pressure on Australia's regulatory and reimbursement processes including the Sansom regulatory review of medicines and medical products in 2013 and PBS reform amendments to the National Health Act in 2017. The previous Strategic Agreement between Medicines Australia and the Commonwealth also delivered streamlined pathways and opportunities for early re-entry and resolution to PBAC assessment and in 2020, the introduction of a PBS new medicines funding guarantee within the Federal Budget and a commitment to the removal of the cost-offset policy for the listing of new medicines was well received by industry and patients.[xvii] In addition, Pfizer would like to recognise the following changes that have had a positive impact on medicines access.

TGA international work sharing

The TGA has increased international collaboration through the adoption of international guidelines and international work sharing initiatives such as ACCESS and Project Orbis; demonstrating a willingness to expedite Australia's regulatory assessment, where appropriate.[xviii] The signing of an international cooperative HTA agreement between the National Institute for Health and Care Excellence (NICE), the Canadian Agency for Drugs and Technology in Health (CADTH), Scotland and Wales present further opportunities for collaboration and to progress shared priorities for HTA reform. The issues needing to be addressed through the Australian HTA review are not unique, and these new partnerships can work to benefit Australian patients.

Rapid HTA assessment of COVID antivirals

In response to the urgency of the COVID-19 pandemic, the Pharmaceutical Benefits Advisory Committee (PBAC) expedited consideration of the Pharmaceutical Benefits Scheme (PBS) listing of COVID-19 antivirals for use in treating patients with mild to moderate COVID-19 who are at risk of developing severe disease requiring hospitalisation. The expedited consideration recognised the urgent public health need related to the prevention, management, or treatment of SARS-CoV-2 infections. This response demonstrated, where there is a pressing need, that pragmatic, common sense decisions can be made to expedite patient access. Pfizer is hopeful that through the HTA review, reforms will occur to institute similar rapid approaches, to ensure medicines and vaccines are made available to patients at the earliest possible opportunity.

Parallel processing

While it is not clear that the reduction in time to reimbursement of new medicines can be attributed entirely to parallel processing of TGA and PBAC submissions, it has undoubtedly contributed to faster access for Australian patients. There is an opportunity to build on this success by extending parallel processing to more PBAC submission types and removing the requirement to provide the TGA Delegate's overview to the PBAC before a recommendation can be made.

Value of additional therapeutic options

Unlike some other countries, Australia recognises the importance of including additional treatments in a therapeutic armamentarium. The same value is attributed to later entrants into a therapeutic class as the first treatment. This allows companies to bring these products to market which allows clinician choice and expanded therapeutic options to optimise treatment for individual patients.

Special pricing arrangements and confidential pricing

The capacity within the Australian reimbursement system to have published and effective prices is a key feature that helps retain access to medicines in Australia, while also providing price signals for markets that use Australia as a reference-price. Without this flexibility, it is likely fewer medicines would be registered, launched, and reimbursed in Australia. While effective for the purpose of ensuring Australian access in the international context, confidential pricing and special pricing arrangements including rebates are a 'band aid' solution to Australia's current unwillingness to pay comparable prices for innovative therapies. Until our HTA system values timely and equitable access to novel and innovative medicines at a level commensurate with the wealth of our nation, the ability to secure confidential pricing arrangements is essential for providing access for Australian patients.

Terms of reference 2: Current or future challenges to earliest possible access

Comparator selection: Comparator price erosion and application of the lowest cost comparator

The Pharmaceutical Benefits Advisory Committee (PBAC) makes recommendations about which medicines should be listed on the PBS. The current PBAC guidelines outline how an applicant should distinguish their intervention from the clinical comparator. The Guidelines indicate that most comparators will be one of the following:

- A current PBS listed medicine. If the proposed medicine is likely to replace listed PBS medicines, the relevant comparator would be a medicine prescribed on the PBS to treat that target population.
- Standard medical management. If the proposed medicine is for a target population for which there are no currently listed PBS medicines, or the proposed medicine will be used in addition to – rather than replace – a medicine, the comparator would usually be standard medical management. Standard medical management would need to be clearly defined and could include a non-PBS-listed medicine, a surgical procedure, best supportive care or conservative management. In the absence of a PBS-listed medicine, standard medical management may be to use a medicine that is not PBS listed. In this circumstance, this medicine may be the appropriate comparator.

Where there is more than one comparator, the main comparator should be the therapy that prescribers would most likely replace with the proposed medicine.

Comparator Price Erosion

In therapy areas where little-to-no innovation has occurred for a long period of time, the appropriate clinical comparator may be very old. These medicines are commonly in the F2 formulary, having reached the end of patent life and been subject to price reductions to reflect the discounting occurring in the market among competitor brands. A new therapy seeking listing on the PBS is required to demonstrate incremental gains in health outcomes compared to the relevant comparator which is typically treatment with a medicine already listed on the PBS which may have been subject to significant reductions in price. Demonstrating cost-effectiveness of a new medicine compared to an old comparator medicine is particularly challenging when the price of the latter has been eroded significantly and does not reasonably value innovation. Therapeutic areas and new medicines that have faced difficulty include new cancer medicines where the comparator is a substantially older chemotherapy and novel antibiotics. The consequence is that patients are missing out.

Today's innovative medicines are increasingly targeted and personalised to treat highly complex conditions, such as cancer and rare diseases. These medicines can provide great value in some of the hardest-to-treat diseases,

meaning they may be more effective than other available options. They are developed at significant risk and cost to the innovator. Comparing these medicines to older existing medicines that are less complex and developed decades earlier – even at their previous on patent price – may not represent a fair value for the innovation.

The solution lies in allowing new, innovative medicines to be valued appropriately for innovation in today's market. Otherwise, comparator price erosion will place a ceiling on the value of an innovation, providing little incentive for manufacturers to bring these treatments to market in Australia. One possible solution is the application of shadow pricing to allow F1-like price for F2 medicines that have undergone significant price reduction and this should be re-considered in this review.

Lowest Cost Comparator

The National Health Act 1953 (the Act) requires that, for the purpose of deciding whether to recommend to the Minister that a medicine be listed on the PBS, the PBAC should consider the cost effectiveness of that medicine compared to that of alternative therapies. In addition, according to the Act, where a drug is substantially more costly than an alternative or alternatives, the PBAC cannot recommend that the drug be PBS listed unless the committee is satisfied that the drug provides a significant improvement in efficacy or reduction of toxicity over an existing therapy or therapies.

Reference to the lowest cost comparator (or "least costly comparator") means that, where a new medicine has not been demonstrated to have a significant improvement over existing therapies, the price of that new medicine is determined by comparison to the cheapest clinical alternative, rather than the therapy most used in clinical practice. This means a new medicine will be priced in comparison to the cheapest in class rather than the most used which fails to value innovation and fails to recognise the expertise of prescribers where the most prescribed therapy represents Australian therapeutic practice. This practice jeopardises the integrity of HTA in Australia.

Use of the lowest cost comparator by the PBAC has become increasingly common in the past five years. To date, its greatest impact has been on the biological disease-modifying antirheumatic drugs (bDMARD) class. There are a number of reasons for this:

- The bDMARD medicines, used to treat conditions such as rheumatoid arthritis, psoriasis and ulcerative colitis have represented a significant proportion of PBS spending for many years.
- The move of infliximab to F2 in late 2015, due to the launch of the first biosimilar, triggered the use of lowest cost comparator for new bDMARD listings.
- The class includes a long series of launches over many years, with innovative products such as tocilizumab subcutaneous formulation still entering the market in F1 even when products such as infliximab and etanercept had moved to F2, with their prices dropping substantially due to competition.

Pfizer example: When HTA doesn't adequately recognise incremental innovation a product that shows incremental improvements may be PBS-listed on the basis of cost comparison with the original product. An example is pneumococcal vaccination, where 13-valent pneumococcal conjugate vaccine and 10-valent pneumococcal conjugate vaccine were listed on the basis of cost-minimisation at the same price as 7-valent pneumococcal conjugate vaccine, despite providing coverage with six and three additional serotypes respectively. More recently, the 15-valent pneumococcal conjugate vaccine was recommended on the basis of cost-minimisation at the same price as 13-valent for both adult and paediatric NIP populations and 20-valent pneumococcal vaccine received a recommendation on the basis of cost-minimisation for adult NIP populations. This situation means that the addition of further serotypes which have the potential to significantly reduce the incidence of invasive pneumococcal disease and sequelae as well as mortality yet this is not appropriately valued.

The valuation of pneumococcal vaccination is a prime example of Australia's unwillingness to pay for innovative medicines and vaccines. Early indications are that the 20-valent pneumococcal vaccine to be launched in 2024-2025 will be priced at the value of 7-valent pneumococcal vaccine which was listed on the NIP more than twenty years ago.

While the lowest cost comparator issue has had the greatest impact on bDMARD listings, it is also now being applied in other therapeutic areas, including precision oncology. Lorlatinib which was recommended at the December 2021 PBAC meeting for first-line treatment of an ultra-rare form of lung cancer (advanced ALK-positive non-small cell lung cancer (NSCLC)) saw a PBAC recommendation made on the basis of cost-minimisation against the least costly alternative therapy, with the alternative therapies cited including alectinib and brigatinib (agreed clinical comparators for the submission) in addition to ceritinib. Importantly, ceritinib was not required to be included as a clinical comparator for the submission and reported minimal and declining utilisation (1% all services for anaplastic lymphoma kinase (ALK) inhibitor therapies through the PBS), reflecting current treatment practice and the evolving international oncology treatment guidelines (National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO)) for first-line ALK-positive NSCLC.
According to Clause 6.6 of the current Strategic Agreement 2022-27, the Commonwealth and Medicines Australia acknowledge that when the PBAC exercises its function under sections 101(3A) and 101(3B) of the Act:

- *it is for the PBAC to determine whether a particular therapy is 'an alternative therapy,' and*
- *the PBAC can determine, including after taking into account matters put to it, whether a particular therapy is an alternative therapy, regardless of whether it is the lowest cost comparator.*

Pfizer recommends resolution of the comparator selection issue in line with the intent of the Strategic Agreement between Medicines Australia and Government (2022-2027). This could include establishing a clinical and pricing comparator ahead of a PBAC submission (the medicine which will likely be replaced in clinical practice) and consistent use of comparator for both clinical comparison and pricing purposes to reflect current Australian therapeutic practices.

The current base case discount rate (5%) is out of step with comparable countries and undervalues medicines and vaccines with benefits delivered over a long period of time

Pfizer Australia provided numerous submissions to the review of the base discount rate in the PBAC guidelines. In these submissions we recommended that the discount rate should be reduced to 1.5%. In their report to government, the Centre of Health Economics Research and Evaluation (CHERE) highlighted the current base case discount rate of 5% is higher than several comparable international jurisdictions (including the UK and Canada) and over the last 30 years international discount rates have been trending downwards.

Using 5% as the base case rate means that Australia systematically undervalues vaccines, medicines and other novel treatments that have up-front costs and longer-term health benefits, relative to comparable overseas markets. If we do not move to reduce the base discount rate, we risk hindering access to many breakthrough therapies that could have lasting impact on the lives of Australian patients.

The CHERE report cites the submission from O'Mahoney et al, which states that if the discount rate and effective willingness-to-pay threshold are reduced, then the proportion of treatments yielding benefits further into the future is likely to increase, displacing healthcare interventions whose benefits accrue over shorter time horizons.

Reform of the base case discount rate is overdue and is essential if Australia is to support innovation and recognise the benefits that vaccines, medicines and emerging novel therapies can bring to our people, society and economy. A discount rate in line with international best practice (such as Canada which uses a rate of 1.5%) would contribute to achieving the shared goals of reducing time to access for Australian patients and maintaining the attractiveness of Australia as a first-launch country for innovative medicines. This is a key reason why the Strategic Agreement[xix] envisioned that any change to the discount rate recommended by the Pharmaceutical Benefits Advisory Committee (PBAC) should have been incorporated into PBAC guidelines by July 2022.[xx] It is disappointing that this reform has been delayed and should be introduced as a priority action from the HTA review.

Reassessing the value of vaccines to include second-order effects

Vaccines are uniquely valuable as they provide protection against infectious diseases which often have limited treatment options and cause significant morbidity in otherwise healthy populations, and can also provide benefits to unvaccinated individuals through reduced infection risk (i.e. herd immunity).

The Australian access environment for innovative vaccines is increasingly challenging and threatens the shared goal of the HTA review to maintain Australia's attractiveness as a first launch country. Australia must revisit the criteria for attribution of value to vaccines to ensure that the vaccines of the future can be made available to Australians in an equitable, timely manner.

The PBAC utilises well-established HTA principles, among other factors, in determining the value of vaccines to the community, however these are not always fit for purpose. These principles can disadvantage vaccines compared to medicines, in some of the following ways:

- the high discount rate of 5% applied to future costs and benefits for all interventions means vaccines appear less cost-effective given it often takes time for the benefits of vaccines to accumulate i.e. in contrast to medicines, all costs are paid at the time of vaccination, but the health benefits accrue over decades;
- the narrow assessment scope which usually looks at the benefits/costs relevant to the individual and the healthcare system rather than the broader benefits to the community (for example, vaccination that prevents illness that causes long term disability not only impacts the individual but also their family and community who become carers); and
- the low cost-effectiveness threshold applied to preventive interventions like vaccines (compared to therapeutic medicines) means lesser value is being placed on the population health benefits which can be achieved through vaccination.

Australia's constrained approach to vaccines leads to public underinvestment in prevention. The short budget cycle creates a perverse incentive to favour treatment over prevention. With a change in approach, a virtuous cycle could be created in which Government invests in health promotion through vaccines which incentivises vaccine

research and development which in turn will mean more innovative vaccines will become available. Vaccines are one of the most effective ways to reduce the global infectious disease burden and support the control and prevention efforts against antibiotic resistance. Their health, economic, and societal value should be considered appropriately.

Consistent, predictable, and transparent use of real-world evidence

Real world evidence (RWE) provides evidence of the usage and potential benefits or risks of a medicine in routine medical practice. Common sources include electronic health records (EHRs), hospital episode data, claims data (PBS and MBS), patient registry data (product and disease), chart reviews, clinical audits, and observational cohort studies. RWE complements evidence from clinical trials to provide a more complete picture of treatment effectiveness and safety within a real-world patient population. RWE represents an increasingly relevant option for evidence generation where traditional trials may be unethical or subject to design and logistical challenges). High quality evidence may be generated where there are clear frameworks that detail the data elements, characteristics, and the internal validation approach used.

Utilisation of RWE in patient access decisions can support claims of efficacy and/or safety in reimbursement applications, regulatory approvals or monitor outcomes in the post-marketing setting, in addition to clinical trial data. It is often used in situations where the data is scarce or where randomised clinical trials are not feasible or ethical (e.g., rare diseases and paediatric populations).[xxi] The effective use of RWE in the reimbursement setting can allow all available evidence to be considered in decision-making and potentially lead to faster patient access to treatments.

Pfizer supports the RWE4Decisions Initiative which aims for stakeholders to agree what real world data can be collected for highly innovative technologies to generate RWE that informs decisions by healthcare systems, clinicians and patients. [xxii]

We are also supportive of the Medicines Australia position on RWE which calls for:

1. **a high-level principles-based framework for accepting and assessing RWE:** The TGA has updated guidance on the use of RWE to reflect FDA and European Medicines Authority (EMA) guidance documents. There is a pressing need for the PBAC and MSAC to follow suit and develop a single guidance for the use of RWE. This could be based on the UK NICE Framework Guidance and outline when and where RWE is appropriate to use, how to demonstrate its relevance and develop standards for data integrity. Both the UK and Canada have frameworks for the incorporation of RWE into HTA.
2. **Develop standards for the utilisation of RWE for post marketing monitoring in reimbursement:** Agencies around the world are grappling with how to develop a framework for real world evidence. NICE (UK) and CADTH (Canada) are two jurisdictions Australia could learn from. Further, NICE (UK), Finnish Medicines Agency, FIMEA (FI), the Belgian Health Care Knowledge Centre, KCE (BE), are also core members in the HTA steering group of the RWE4Decisions Initiative which aims to bring stakeholders together to agree what RWE could be collected for highly innovative therapies to inform decisions by healthcare systems (HTA/payers), clinicians and patients.[xxiii]
3. **Enhance system infrastructure to centralise linked health data and provide appropriate access to stakeholders, including industry:** Greater use of RWE in HTA can be expected to require investment in Australia's digital health capabilities. Evidence generation requires increased collaboration and public/private partnerships among industry, healthcare organisations and other stakeholders to develop high quality data

and/or research networks that allow for the integration and interoperability of data from medical records, administrative claims data, registries, patient data, and individuals' non-health data and broader environmental data. However, it is critical that there should be appropriate data governance in place to ensure patient and clinician motivation and trust in such a collaborative model. Comparable countries provide examples of how to improve the utility of healthcare data. Denmark, Sweden and the US Sentinel System[xxiv] have established linked data infrastructure across the healthcare system. NICE has made substantial investments in linking data across NHS-funded services.

Establish a nationally coordinated horizon scanning process to prepare for disruptive therapies

Under clause 6.2 of the Strategic Agreement, the Commonwealth and Medicines Australia have a shared ambition to promote greater understanding and insight into the new medicines, vaccines and new and emerging technologies coming through development pipelines.[xxv] Horizon scanning for innovative medicines is vital to address the challenges caused by the lack of proactive planning and implementation for new technologies and treatments. Without nationally coordinated horizon scanning, there is a risk of lengthy delays in introducing new treatments that fall outside the scope of the current assessment system. Emerging therapies, such as gene therapies, often possess unique characteristics that require novel evaluation approaches. In addition, these therapies can pose other challenges to the healthcare system, such as the need for complex clinical delivery protocols and potential strain on health budgets due to their high-value nature as one-time treatments with lifelong benefits.

By conducting horizon scanning, governments, patient groups, and industry can work together to anticipate the arrival of these transformative treatments and adequately prepare for enabling rapid, equitable access, including establishing appropriate regulatory frameworks and evaluation methodologies and new funding models where needed.

Pfizer example: Pfizer participated in the Medicines Australia 'Medicines of Tomorrow' forum, discussing our experience preparing for the arrival of a potential new treatment for Duchenne's Muscular Dystrophy (DMD). Gene therapies are complex treatments that require end-to-end solutions for both funding and service delivery. No two gene therapies are the same. There are different therapies for different conditions all of which will need very different processes and systems in place.

Patients with DMD receive complex multidisciplinary care at neuromuscular centres located in children's hospitals in major cities, involving large teams of medical, nursing and allied health specialists. Appropriate and effective infrastructure and care pathways must be designed in advance, ready for implementation should the DMD clinical trial program be successful, and registration and funding be achieved.

An understanding of the public hospital impacts must be developed such as the systems and criteria for site selection, cold-chain delivery, storage, preparation, administration, and post-infusion care. In essence, all stakeholders – Commonwealth and state/territory governments, clinicians, patient groups and manufacturers will need to work together and successfully coordinate planning, if we are to have a smooth implementation of gene therapy for DMD without undue delays.

Every delay means a patient's eligibility window is likely to be closing, either because their disease has progressed, or they have grown beyond the age eligibility criterion. A nationally established horizon scanning process will ensure steps can be taken to prepare for the arrival of novel therapies, especially in cases where treatment is time sensitive.

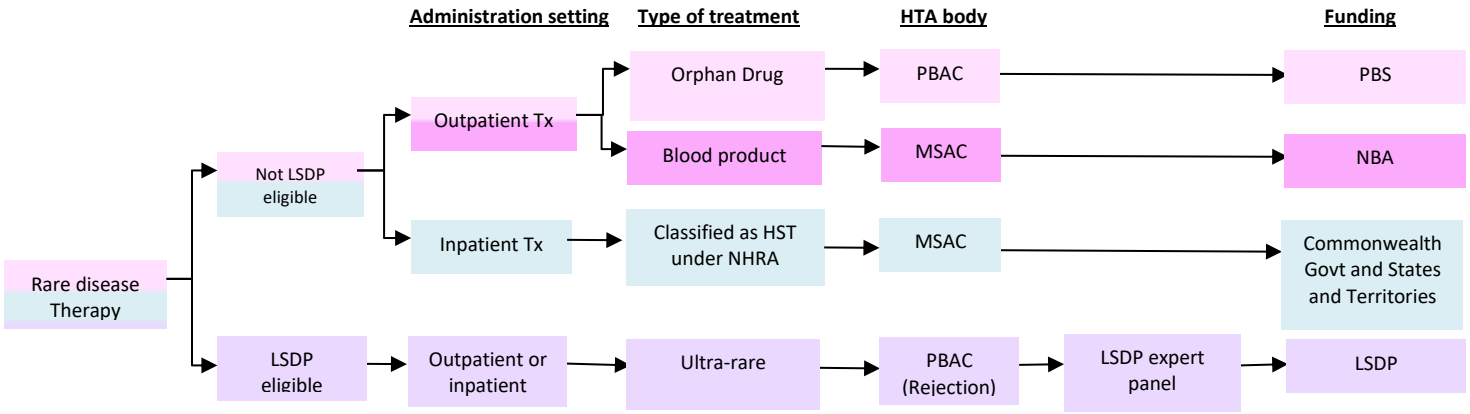
Terms of reference 3: Current or future barriers to equitable access

Increasing access to treatments for rare diseases through streamlined pathways

Access to rare disease treatments for Australian patients is considerably slower than in comparable countries. This is driven by uncertain and ambiguous HTA pathways, an HTA evaluation system that does not make a distinction between treatments for rare and more common conditions, misunderstanding of the rare disease and lack of patient and clinician involvement in evaluation and decision making.

Like cell and gene therapies, rare disease treatments have several HTA and funding pathways:

- Rare disease treatments administered to outpatients are reviewed by the PBAC and funded on the PBS except for blood products which are reviewed by MSAC and funded by the NBA
- Rare disease treatments which are classified as highly specialised therapy (HST) under the National Health Reform Agreement (NHRA) and administered as inpatients are reviewed by MSAC and funded by Commonwealth Government and States and Territories (50:50)
- Ultra-rare treatments for serious conditions that increase life expectancy and where there are no alternative treatments for the condition are rejected by the PBAC, considered by the LSDP expert panel, and funded by the LSDP.



Govt., Government; HST, Highly Specialised Therapy; LSDP, Life-Saving Drugs Program; MSAC, Medical Services Advisory Committee; NBA, National Blood Authority; NHRA, National Health Reform Agreement; PBAC, Pharmaceutical Benefits Advisory Committee; PBS, Pharmaceutical Benefits Scheme; Tx, treatment

The multiple HTA and funding pathways create additional burden, complexity, and cost. These, together with the risk of cost-shifting between payers can result in inequitable access and delays for patients.

Non-traditional evidence

The hierarchy of evidence gives more weighting to the most scientifically rigorous information which can be challenging for rare disease treatments. Rare disease treatments are often associated with other sources of evidence.

When rare diseases are slowly progressive, it is difficult to demonstrate long-term outcomes such as survival in a randomised trial as it is not possible to recruit the patient numbers to deliver results in time. Additionally, heterogeneity in the disease characteristics in addition to disease history (duration, prior treatments) make measuring health outcomes across small patient subgroups problematic. Furthermore, given the size of the patient population, it is challenging to randomise an adequate sample size and conduct an international trial. There are also ethical considerations regarding the use of placebo arms and the duration of studies (e.g., early termination after demonstration of significant treatment effect makes it unethical not to offer treatment to all patients).

The best available evidence for rare disease therapies may comprise observational studies (i.e., case-control studies, cohort studies and case series). Single arm studies may also form the sole evidence base for some proposed therapies which raises a further challenge due to the lack of comparative evidence to inform natural history of the disease.

If we are to solve access for Australians living with a rare condition, the HTA system must demonstrate flexibility in the evidence acceptable for decision making. A positive first step would be to place greater weight on clinical opinion which can provide a real-world perspective on the rare disease or proposed therapy. Otherwise, many rare conditions will continue to face an uphill and sometimes futile battle to meet the traditional requirements of the PBAC.

Demonstrating value of the treatment for rare disease

Current HTA methods may not be appropriate for the evaluation of rare disease treatments. A broader consideration of value is important including the magnitude of clinical benefit, unmet need for treatments for the condition, burden of disease, innovation, budget impact, societal benefits, and indirect costs. Australian clinical expert input is important to supplement the evidence included in the HTA submission particularly the importance of the treatment outcomes to the patients. Additionally, patient involvement that gives insight into the lived experience and the day-to-day life impact of a treatment is essential.

Combination pricing of oncology products

Advances in medical science in recent decades are particularly evident in oncology. The more we understand cancer, mechanisms of resistance to treatment and the multiple escape pathways, the potential for the use of combination treatments has become a focus of clinical development programs. Combination therapy is driven by science, with the possibility of additive, enhancing or synergistic effects of combinations of treatments targeting multiple pathways leading to improved health outcomes for cancer patients.

While the reimbursement pathway is not straightforward for any new medicine, there are several additional challenges for innovative medicines used in combination. When combination regimens are comprised of branded constituents sponsored by two or more manufacturers, they may face significant challenges due to strict competition laws that prohibit multi-party discussions. These challenges mean that combination therapies are likely to require more time between regulatory approval and reimbursement than monotherapies, or manufacturers may decide not to seek reimbursement due to the significant complexities and challenges, both of which negatively impact patient access.

Currently, the most significant challenges exist for combinations of treatments with two or more branded (on-patent) components. By improving survival outcomes, both constituents of the combination may be used for a longer duration and where the backbone therapy is a branded (on-patent) therapy, this increases the overall cost of the combination driven by both an increase in the backbone therapy costs, as well as the additional therapy. This leaves very little scope to appropriately value and price the newer add-on therapy.

Critically, at present there is a lack of guidance on methods for the attribution of value between the individual components of a combination regimen in Australia. Arbitrary and/or inequitable attribution of the overall value of the combination between the components could have longer-term access implications. Specifically, if one or more of the components of a combination is either under- or overvalued and this component subsequently forms part of

another combination and/or is a comparator for another innovative (combination) medicine, pricing could become distorted and inconsistent across related medicines.

Overall, these complex challenges for combination therapy pricing are contributing to a growing issue for cancer patients, who may not be receiving optimal standards of care. With increasing numbers of combination therapies in the oncology development pipeline, solutions are urgently required to assure fast, equitable patient access and to ensure that manufacturers continue to invest in the development of future oncology combination therapies.

What is abundantly clear is that there is a need for a formal framework for the assessment, evaluation and valuation of innovative medicines used in combination, including revisions to existing (pricing) policies to ensure future subsidised access to effective and cost-effective combinations. Developing such a framework will require multi-stakeholder engagement and recognition of this as a shared issue.

Terms of reference 4: Elements or features that detract from patient centeredness

The Australian HTA Policy Framework includes a principle to conduct "structured consultation with interested parties, including consumers," implemented by the Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC). The Enhanced Consumer Engagement Process, outlined in the Strategic Agreement between Medicines Australia and the Commonwealth being run concurrently with this review, aims to capture consumer and patient perspectives earlier in HTA to allow enough time for consumer representatives to gather feedback and influence outcomes.

This is an important opportunity for increased transparency, to consider the patient voice and for patients to gain a better understanding of how medicines are valued and considered for reimbursement. Patients have experience-based knowledge gained from living with a health condition and using innovative medical technologies but currently they have little opportunity for feedback. Furthermore, there is little published on how patient input is considered and included in HTA decision making.

Patient participation is provided late in the HTA cycle and participation rates remain low, likely due to the complexity of the process and/or a lack of understanding of how to provide input. Rather than assisting in shaping the HTA approach and decision-making factors, patients are looking through a 'keyhole', trying to piece together information about new medicines, the way reimbursement decisions will be made and unsure how their lived experience influences those decisions.

There is also an opportunity to provide additional resources to support patient engagement in HTA. These resources should help to break down the barriers to participation and explain in plain language the role of each committee and their processes, give clear guidelines on patient involvement opportunities, and provide comprehensive links to tools and advocacy groups.

Pfizer believes more should be done to reinforce and quantify the impact of patient involvement in HTA decision making. If appropriate methodologies are in place, HTA can help physicians understand how novel treatments might best be applied at the population level.

Clearer guidance must be developed for patient reported outcomes and patient values, to influence more relevant data collection, including in clinical trials and for more explicit use of these data in HTA decision making.

Recent initiatives such as the Consumer Evidence and Engagement Unit within the Department of Health and related pilot programs focus on supporting broader consumer participation strategies and better transparency and understanding of HTA decision making processes. While this is promising, further efforts are required. The Enhanced Consumer Engagement Process must be delivered using true co-design and associated principles with clear definitions, roles and responsibilities.

Terms of reference 5: Perverse incentives

Perverse incentives - where an element or feature of HTA policy and methods may be creating an unintended incentive that results in negative consequences – can apply to all stakeholders, not just manufacturers. Pfizer has referenced several perverse incentives earlier in this submission. The following further examples should be addressed as a priority.

Multiple potential approval pathways for gene therapies and cost shifting present unnecessary delays

As referenced in response to TOR 3, the Committee of Chairs i.e., Chair of PBAC, Chair of MSAC and representative of the State Governments decide on the HTA pathway for gene therapies. In the case of outpatient administration, the treatment is assessed by the PBAC and funded by the PBS. Inpatient treatments classified as HST under the NHRA are funded by the Commonwealth and states and territories on a 50:50 basis. Cost-shifting might occur if a product which could appropriately be administered as an inpatient treatment is classified as more appropriately an outpatient treatment, with the result being that funding sits with the PBS. Alternatively, a treatment that could reasonably be administered on an outpatient basis, being determined as an inpatient treatment would result in 50% of the funding sitting with the states.

Of the two gene therapies currently recommended for reimbursement in Australia (Zolgensma and Luxturna), one followed the MSAC pathway with joint Commonwealth-state funding under the NHRA, while the other was the remit of PBAC, having been determined as appropriate for PBS funding There was confusion in the advice from the Department over the choice of evaluation committee for one of these therapies. For industry this approval pathway appears somewhat discretionary and does not provide certainty for planning purposes which is also an important element in ensuring Australia is among first wave launches for these important new treatments.

Furthermore, the ‘yo-yoing’ between state and Federal responsibilities can add unnecessary delays and inequitable access which in some cases can be critical for patients with a narrow treatment window for highly specialised therapies. A clear and consistent approval pathway for gene therapies would remove the potential for funding streams to influence the approval pathway and provide more certainty for industry and other stakeholders. Most importantly, a clear and consistent approach would prevent potential delays to equitable access for Australian patients regardless of their state or postcode.

Use of Lowest Cost Comparators undervalues innovation and may lead companies to avoid or delay listing in Australia

In our response to TOR 2, we outlined challenges to earliest possible access raised by the increasing use of the lowest cost comparator (LCC) rather than the most prescribed therapy. The selection of a LCC does not appropriately value innovation in the context of current Australian therapeutic practice. In addition to potentially limiting early access, this practice can lead to unintended negative consequences:

- The PBS list price of the new medicine may be relatively low on PBS-listing and not reflect appropriate valuation of an innovative medicine.
- There can be flow-on price reductions to other on-patent medicines in F1 which were listed based on cost -minimisation to a medicine(s) within the same reference pricing group.

Overall, these price impacts for new innovative health technologies can incentivise companies to avoid, or delay listing in Australia due to the potentially negative international impact. To prevent these unintended consequences, PBAC should make consistent use of the most prescribed comparator for both clinical comparison and pricing purposes to reflect current Australian therapeutic practices and hence provide a more reasonable and acceptable valuation of innovative products.

Interchangeability

Since August 2007, Section 101(3BA) of the *National Health Act 1953* has required that the PBAC include a statement on whether a product should be treated as *"interchangeable on an individual patient basis"* with another product at the time it makes a recommendation to make a product available on the PBS. These determinations are intended to inform the Minister's decision-making as to whether products could potentially be included in a therapeutic group.

Pfizer contends that several of the PBAC's determinations concerning interchangeability in recent years are not justified given the definitions for "interchangeable on an individual patient basis" that have been provided to Government by the Department of Health and by the PBAC. In addition, several of the many more recent determinations that the PBAC has made in relation to interchangeability on an individual patient basis are inconsistent with its earlier determinations.

Determinations on interchangeability that are not founded in clear scientific evidence or appear arbitrary could result in companies deciding not to bring a product to market because of the real or perceived risk of having the product determined to be interchangeable with another older and/or less effective product.

Interchangeability has also been inconsistently applied as shown in the table below outlining determinations for tofacitinib. In March 2019, tofacitinib was determined to be interchangeable despite being of different therapeutic class and mechanism of action. bDMARDs considered prior to this had been determined not to be interchangeable. In July 2020, Pfizer lodged a minor submission challenging PBAC's determination which was unsuccessful.

Date	Drug	Class	Administration	Economic analysis	Comparator	Interchangeability	Comment
July 2014	Infliximab	TNF- α inhibitor	IV infusion	Cost-effectiveness		N/A	
March 2015	Vedolizumab	α4β7 integrin inhibitor	IV infusion	Cost-minimisation	Infliximab IV	Not interchangeable with infliximab IV	Appropriate – different classes and mechanisms of action
March 2016	Adalimumab	TNF- α inhibitor	SC	Inferior to infliximab – to be reflected in price	Infliximab IV	Not interchangeable with infliximab IV and vedolizumab IV	Appropriate – for drugs to be interchangeable must have same therapeutic outcomes
March 2018	Golimumab	TNF- α inhibitor	SC	Cost-minimisation against least costly bDMARD Less costly than infliximab to account for inferiority in induction therapy	Least costly bDMARD	Not interchangeable with any drug	

Date	Drug	Class	Administration	Economic analysis	Comparator	Interchangeability	Comment
March 2019	Tofacitinib	JAK inhibitor	Oral	Cost-minimisation against least costly bDMARD	Least costly bDMARD	Interchangeable with infliximab, adalimumab, vedolizumab and golimumab	Not appropriate – different therapeutic class and mechanism of action. Other drugs deemed to be not interchangeable
March 2022	Ozanimod	Sphingosine l-phosphate receptor modulators	Oral	Cost-minimisation against least costly bDMARD	Least costly bDMARD	No determination	
July 2022	Ustekinumab	MAB	IV and SC	Cost-minimisation against least costly bDMARD	Least costly bDMARD	No determination	
November 2022	Upadacitinib	JAK inhibitor	Oral	Cost-minimisation against least costly bDMARD	Least costly bDMARD	No determination	In PSCR, sponsor indicated was amenable to accepting listing of upadacitinib on cost minimisation basis with infliximab, tofacitinib or vedolizumab, however argued adalimumab and golimumab would be inappropriate comparators due to inferior efficacy, based on PBAC's prior advice that infliximab, tofacitinib and vedolizumab should be treated as interchangeable on individual patient basis, but not adalimumab or golimumab (paragraph 4.17, tofacitinib interchangeability PSD, November 2020)

The broken market dynamic for novel anti-infectives disincentivises research and development in AMR

As discussed earlier, in order to preserve the effectiveness of new antimicrobials for as long as possible and prevent AMR, their use is restricted. While these restrictions reflect best practice for antimicrobial stewardship, they have the significant unintended negative consequence of limiting research and development as companies that invest in this area might see no return as their highly effective drug is held back in case of emergency. [xxvi]

To better incentivise investment in this critical area of drug development, Pfizer endorses the recommendations of AAMRNet that the Australian Government should invest in the rapid establishment of its own fit-for-purpose fund (incorporating learnings from a similar pilot underway in the UK) with payments for antimicrobials based on their value to the health system and wider public health.

PBS eligible populations are often narrower than TGA approved indications which limits access for patients who could benefit from new treatments

Restrictions on eligibility for subsidised treatment form part of the recommendation by the PBAC when providing advice to the Minister about which medicines or vaccines should be subsidised, which is based on consideration of medical and cost-effectiveness. It is common for new medicines and vaccines in Australia to be provided for subsidised treatment on the PBS or NIP, respectively, in a restricted group of patients compared to the population included in TGA approved indication.

PhRMA's Global Access to New Medicines Report indicates more than a third (37%) of new medicines launched globally from 2015-2020 and reimbursed by the PBS are not reimbursed for all indications and lines of therapy; half of new medicines with limited PBS reimbursement are cancer therapies.[xxvii]

While recommendations for restricted eligibility for subsidised medicines and vaccines are intended to ensure cost-effective use of healthcare funding, this practice has a number of unintended negative consequences. Most importantly, these restrictions deny access to treatment for groups of patients who could benefit within the TGA approved indication. Similarly, these restrictions limit the discretion of clinicians to make individualised treatment choices for patients who could benefit from treatments which are registered but not subsidised.

Fundamental to these restricted recommendations for subsidy, are the range of HTA policy and methods issues raised in our submission which do not recognise the full value of these technologies. As discussed in our responses to survey questions 2 and 3, these issues include limited inclusion of elements of value in decision making, the need for greater inclusion of the patient's voice in decision making, comparator price erosion, increasing utilisation of lowest cost comparators rather than accepted clinical comparators, high discount rates applied in cost-effectiveness base case evaluations, underutilisation of RWE to support understanding of efficacy and/or safety (pre- and post-product launch), and unclear assignment of value for combination oncology products. As a result of one or more of these challenges, sponsors of new medicines and vaccines may seek PBS reimbursement for less than the full TGA eligible population. The result can be patients missing out on advances in treatment, particularly in comparison to the accessibility of new medicines in other countries with comparable health systems and standards of care.

Throughout this submission Pfizer has provided more detailed and specific recommendations to address each issue which leads to undervaluing of innovative medicines and vaccines. When these are addressed, we will be closer to the shared goals of providing access as early as possible for Australian patients and to maintaining the attractiveness of Australia as a first-launch country for new medicines and vaccines.

International HTA comparisons

Throughout our response to this consultation, where appropriate, Pfizer has indicated how comparable HTA markets have approached specific challenges. In approaching HTA reform, Australia can sample significantly from other countries, their interventions and experience in tackling access issues.

While each HTA system should fit within the health care context of the country or region, all should meet a minimum standard of rigor and employ a comprehensive and transparent assessment process that permits deliberation, flexibility, and pragmatism, given the wide range of therapeutic areas and needs. Much policy debate on HTA has focused on the use of quality-adjusted life years (QALYs) as a metric to indicate the clinical benefits of a new medicine - as used in Australia and other HTA agencies such as NICE in England and the Dental and Pharmaceutical Benefits Agency (TLV) in Sweden.

QALYs are not the only way to measure the value of new health technologies, and many health care systems have taken different approaches. France, Germany, and Denmark have created systems where the relative clinical benefit of a new medicine is ranked on a five- or seven -point scale, and reimbursement and pricing are negotiated through a separate process with payers/insurers.

Generally, there has been little consensus on these different approaches and the choice of either should be based on the local, social, and economic contexts and available resources.[xxviii] No country has a "perfect" HTA system. Where it is already part of the health care system, Pfizer supports efforts to enhance HTA policies and methods to ensure individual patient needs are taken into consideration, and new clinical data and real-world evidence is incorporated and assessed.

HTA Review

In the absence of a clear willingness to invest in new technologies, HTA can become a cost-containment tool, which regardless of process or methodology, may be harmful to the interests and health outcomes of patients. Pfizer understands the fiscal and budgetary pressures that many health systems are facing, however using HTA to deny or undervalue the benefit of new medicines in order to limit spending discourages the development of future treatments and cures and inappropriately creates barriers to patients accessing medicines they need.

As part of the HTA review consultation process Pfizer welcomes the work of the independent HTA experts in identifying what can be learned from appropriate comparable jurisdictions. We would be concerned if, for example, New Zealand is proposed as a comparable jurisdiction to Australia. Pfizer is proud to have operations in New Zealand and to have partnered with the New Zealand Government to respond to the threat of the COVID pandemic but as the recent Medicines New Zealand 'Medicines Landscape' report outlines, New Zealand ranks last in the OECD for access to publicly funded modern medicines. Between 2011 and 2021, just 7% of the medicines launched in the OECD were publicly funded in NZ. The OECD average was 29%. As Medicines NZ outlines, the NZ approach to medicines access is underpinned by procurement and tendering due to capacity and capability constraints. The current funding model prioritises upfront savings on the cost of medicines rather than downstream impacts on, and cost to patients, whānau, the wider health system and the economy.[xxix] The selection of comparable jurisdictions must be based on a clear and transparent set of criteria that can be agreed among all stakeholders.

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[ii] The New Frontier - Delivering better health for all Australians – Parliament of Australia (aph.gov.au)

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[xiii] Health Technology Assessment of Gene Therapies: Are Our Methods Fit for Purpose? - OHE

[xiv] Commonwealth of Australia and Medicines Australia 2022-27 Strategic Agreement in relation to reimbursement, health technology assessment and other matters

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[xviii] International | Therapeutic Goods Administration (TGA)

[xix] Commonwealth of Australia and Medicines Australia 2022-27 Strategic Agreement in relation to reimbursement, health technology assessment and other matters

[xx] Pharmaceutical Benefits Scheme (PBS) | Review of discount rate in the PBAC guidelines

[xxi] Real world evidence (RWE) – a disruptive innovation or the quiet evolution of medical evidence generation? - PMC (nih.gov)

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Appendix 1: Glossary of acronyms

AAMRNet – Australian Antimicrobial Resistance Network
AMR - Antimicrobial resistance
ANDAR – Applicant Developed Assessment Approach
ALK - anaplastic lymphoma kinase
ATAGI - Australian Technical Advisory Group on Immunisation
bDMARDs - biological disease-modifying antirheumatic drugs
CADTH – Canadian Agency for Drugs and Technology in Health
CHERE - Centre of Health Economics Research and Evaluation
EHRs - electronic health records
EMA – European Medicines Authority
ESMO – European Society for Medical Oncology
FDA - U.S. Food and Drug Administration
FIMEA – Finish Medicines Agency
HST - highly specialised therapy
HTA – Health Technology Assessment
HTAB - Health Technology Assessment Body
KCE – The Belgium Health Care Knowledge Centre
LCC - lowest cost comparator
LSDP - Life Savings Drugs Program
MA - Medicines Australia
MSAC - Medical Service Advisory Committee
NBA - National Blood Authority
NCCN – National Comprehensive Cancer Network
NHRA – National Health Reform Agreement
NICE – National Institute for Health and Care Excellence
NIP - National Immunisation Program
NITAG - National Immunisation Technical Group
NMES - New Molecular Entities
NMP - National Medicines Policy
NSCLC – Non-small cell lung cancer
PASC – PICO Advisory Sub-Committee
PBS - Pharmaceutical Benefits Scheme
PBAC – Pharmaceutical Benefits Advisory Committee
PhRMA - Pharmaceutical Research and Manufacturers of America
QALYs - quality-adjusted life years
RCA - randomised controlled trials
RWE - real world evidence
TGA – Therapeutic Goods Administration
TLV - Dental and Pharmaceutical Benefits Agency in Sweden