Health Technology Assessment Methods and Policy Review

Consultation 1

AbbVie Pty Ltd Response – June 2023

Executive Summary

About AbbVie

AbbVie Pty Ltd (hereafter AbbVie) is a global, research-based biopharmaceutical company committed to discovering, developing, and delivering innovative new medicines with distinct and compelling benefits for people. Our therapeutic focus areas include immunology, oncology, eye care, virology, and neuroscience. Globally, approximately 57 million people are treated with AbbVie products annually across 60+ conditions and live in more than 175 countries.

In Australia, more than 90,000 Australians currently benefit from our medicines. In the 2020-21 financial year there were over 350,000 PBS prescriptions written for AbbVie products. In 2022, 3000+ Australians received compassionate access to our medicines. AbbVie is also a member of the industry representative body, Medicines Australia.

AbbVie's response to the HTA Review Consultation

AbbVie welcomes the opportunity for consultation on the objectives of the Health Technology Assessment (HTA) Review, one of the key commitments in the Strategic Agreement between the Commonwealth and Medicines Australia[1]. Since the inception of mandatory cost-effectiveness reviews in 1993, the Australian HTA system has facilitated the funding of effective, safe, cost-effective medicines on the PBS for millions of Australians.

Over the last 30 years, significant initiatives have been implemented to improve the performance of Australia's HTA system and the policy settings that support it.[2] Examples include, but not limited to, the introduction of F1/F2 Formularies, TGA-PBAC parallel processing, multiple revisions to technical aspects of the PBAC Guidelines, Stage 1 and Stage 2 PBS Process Improvements, and a revised National Medicines Policy. [3]

While important advances have been made, further progress is required. A recent analysis showed that only 34% of globally approved medicines were PBS listed in Australia from 2012-2021, and only 12% of new medicines were PBS listed in Australia within one year of global first launch.[4] Patients wait 466 days on average for PBS access to a new medicine following ARTG registration.[5] As demonstrated by the evolution of Australia's HTA system to date, the PBAC and Australian Government are well placed to design and implement the ongoing reform that is required to improve on these metrics. This requires stronger investment in innovative medicines on the PBS and a shared commitment to ensuring faster access for Australian patients. COVID-19 has demonstrated what is possible in speeding up access to new treatments when innovation is valued and when health is a collective priority.

[1] Strategic Agreement https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2021/09/Medicines-Australia-Strategic-Agreement-2022-2027.pdf
[2] GSK https://au.gsk.com/media/6259/gsk-viiv-the-pbs-in-australia-feb-2018.pdf
[3] DoHAC https://www.health.gov.au/resources/publications/national-medicines-policy?language=en
[4] PhRMA https://phrma.org/en/resource-center/Topics/Access-to-Medicines/Global-Access-to-New-Medicines-Report
[5] Medicines Australia https://www.medicinesaustralia.com.au/publications/medicines-matter/

Summary of Key Recommendations

The Government must acknowledge it is not acceptable for patients to wait 466 days on average for subsidised access to a new medicine and **set a target of less than 100 days from ARTG listing to PBS access**.

AbbVie makes the following recommendations to achieve this ambitious and achievable target:

1. **Alignment on HTA parameters prior to PBAC submission lodgment, to help reduce the number of resubmissions, and to resolve funding pathways and implementation plans for complex technologies and areas of high unmet need as early as possible.** This could be achieved by replacing the current optional pre-submission meeting process led by the Department of Health and Aged Care (DoHAC) which has limitations around stakeholder attendance, restricted time for consultation and is not a formal part of the HTA process. Instead, a more comprehensive optional pre-submission protocol ratification process could be implemented for complex technologies or areas of high unmet need led by a subset of Committee members, for example the relevant Discussant, PBAC Chair and ESC. It could include elements such as PICO, financial and economic model parameters as well as the opportunity for patient, carer, and clinician input.

2. **Real-time exchange of information between Sponsor and Evaluator during submission evaluations, so that the most comprehensive assessment is provided for PBAC consideration.** Building on the existing plans for an information exchange pilot, this could be achieved by allowing Evaluators to request further information and clarification from Sponsors in real-time via the Health Products Portal (HPP). There should be provisions for Sponsor hearings at ESC meetings. Requests for specific input during evaluations could also be sought from nominated patients and clinicians to reduce the number of resubmissions and deferrals, particularly for new disease areas or where treatment pathways require clarification.

3. **Recalibrate the milestone requirements for parallel processing, so that PBAC recommendations are not delayed due to misalignment with the TGA Delegate's Overview.** This could be achieved by re-anchoring PBAC consideration to the end of the TGA evaluation phase at Milestone 5 or working with the TGA to bring the timing of the Delegate's Overview forward by several weeks.

4. **Improve the transparency and predictability of PBAC decision making, so that Sponsors can better understand the rationale behind PBAC considerations and incorporate these learnings to improve future submissions.** This could be achieved by allowing Sponsors to participate as an observer during the PBAC meeting when their agenda item is discussed. The deliberation of final PBAC recommendations could remain confidential, as would competitor information. Sponsors should also be provided with a copy of Discussant presentations, as well as any communication between the DoHAC, Committee and Evaluators regarding their submission (that is not competitor in confidence). The agenda of all PBAC Executive meetings should be published.

5. **Improve post-PBAC pricing governance so that PBS listings are not unnecessarily delayed due to inconsistent or unclear pricing methodology or interpretation.** This could be improved by reinstating a pricing methods manual as previously used prior to 2014 to ensure transparency and predictability of negotiated PBS prices. Where there are different interpretations between Sponsors and the DoHAC

around the PBAC's pricing recommendations, there should be a pathway to clarify these matters with PBAC in an expedited manner.

6. **Ensure value assessments are person-centred, based on epidemiology and clinical practice rather than a risk-mitigation approach.** This could be achieved by increasing the willingness to pay to a minimum of GDP per capita and updating technical methods with greater weighting given to patient preferences and equity considerations. The PBAC Guideline definition of main comparator should be incorporated into the National Health Act definition of 'alternative therapies'. Utilisation estimates must align with the expected PBS population and represent a fair and credible forecast.

7. **Facilitate early funded access for high added therapeutic value products while further evidence is collected.** This could be done by reforming the current Managed Access Framework, so it is more feasible for Sponsors and delivers for patients. This could be achieved through a range of changes such as greater acceptance of early phase data, or opportunities for a price increase. The current framework is rarely used. Issues from previous agreements include significant risks to the Sponsor such as price reductions with rebates and interest accrued, and no option for a price increase.[6]

[6] Crizotinib PSD http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/public-summary-documents-by-product#C.

Consultation questions

1 Elements or features that are working effectively

Australia's HTA system, since the inception of cost-effectiveness reviews in 1993, has facilitated the funding of effective, safe, cost-effective medicines for millions of Australians. This has been driven by several features of the system that have been working effectively to date. The following section summarises these features and highlights critical items that must be retained and optimised to improve timely and equitable access as well as appropriate value attribution for medicines in Australia.

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

Expertise

The independent Pharmaceutical Benefits Advisory Committee (PBAC) has significant expertise to provide a robust evaluation of technologies. This includes an industry-experienced representative and two consumer representatives on the committee. The additional parties who support the PBAC also have a strong track record of providing well-informed input. These parties include the economic sub-committee (ESC), the drug-utilisation sub-committee (DUSC), as well as the academic evaluation groups. AbbVie considers that these structures currently enable a reasonable level of HTA rigour in Australia. This has fostered Government trust in the PBAC's recommendations and a strong commitment to listing recommended medicines on the PBS. However, as described in Section 2 and Section 4 of this response, there is an opportunity to improve the way in which the expertise and insights of patients, carers and clinical community are included, as well as greater transparency around PBAC decision making for Sponsors.

Process

The process for applicant-initiated submissions, aligned with the published PBAC calendar cycle, ensures consistency and visibility of most HTA processes. The timelines for key evaluation milestones are published in advance, leading to visibility and consistency around PBAC deliverables. Applicant-initiated submissions (e.g., sponsors), enables flexibility to propose key submission components based on applicant expertise, commercial considerations, and insights from clinical and patient stakeholders. Opportunities for Sponsor engagement during pre-submission meetings, evaluations, hearings, and post-rejection meetings are welcome, however as outlined in Section 2 of this response, there remains opportunity for improvement. Post-PBAC meeting consideration, Public Summary Documents (PSDs) provide important insights for the public and for current or future applicants. The option to maintain commercially, clinically, and academically sensitive information as confidential supports global pharmaceutical companies such as AbbVie to bring technologies to Australia without introducing significant commercial risk such as international referencing of net prices.

The current process includes an opportunity for consumers to comment on submissions, as well as the recent establishment of the Consumer Evidence and Engagement Unit and recent pilot programs to enhance engagement with patient advocacy groups. This is a welcome approach and there is a need to

further progress a person-centred approach, as outlined in Section 4 of this response. It is essential that these changes are fully supported and continually improved.

The option for PBAC evaluation to occur in parallel with regulatory assessment through the Therapeutic Goods Administration (TGA) should continue to be available. However additional improvements could be made to better align the concurrent evaluations, as outlined in Section 2 of the submission.

The DoHAC and Medicines Australia have been working together since late 2017 to deliver on commitments to streamline medicine listing processes as initially set out as part of the 2017-2022 Strategic Agreement. The Stage 1 PBS process improvements objective, to reduce the time to listing by an average of 2 months appears to have been met, according to the most recent DoHAC analysis[7]. However, the key objective for Stage 2 process improvements, a reduction in the number of resubmissions by 50%, has not yet been delivered on. Strong collaboration between the DoHAC and Industry must continue to ensure the successful outcomes of PBS process improvement measures, in addition to achieving the shared goals of the HTA Review as set out as part of the 2022-27 Strategic Agreement.

Evaluation methods

There are elements of the PBAC's current approach to HTA evaluations that are working effectively. The PBAC may demonstrate flexibility and pragmatism when considering a submission, and this is an important feature that often leads to optimal access for patients. For example, the PBAC currently has the flexibility to recommend equitable patient access and empower clinicians to make prescribing decisions.

This is also reflected in the PBAC's use of a flexible and implicit willingness-to-pay threshold when considering submissions that present cost-effectiveness analyses. Specifically, the PBAC has often expressed different acceptable ICER ranges depending on the therapeutic area being considered and the unmet clinical needs. For example, an ICER of $55K to <$75K per QALY is often stipulated by PBAC for new oncology treatments, compared to an ICER of $355K to <$455K per QALY recently accepted for paediatric patients with Spinal Muscular Atrophy (SMA)[8]. While AbbVie believes the willingness to pay should be increased generally to a minimum of average GDP per capita (approximately 90K AUD in 2021)[9], the current implicit and flexible approach should be retained as a priority. Ultimately, this flexibility allows for the ICER threshold to be considered in light of contextual issues, equity, and person-centredness. Acceptance of a higher ICER for a medicine by PBAC may also reflects a greater acceptance of risk and uncertainty. However, it should not be used as an artificial price and budget impact capping mechanism.

Another element of PBAC evaluations which AbbVie believes should be retained is the current approach and requirements for submissions presenting cost-minimisation analyses. These submissions are often for medicines that are not first-in-class or first-in-indication, yet do expand the treatment options for clinicians and patients. For example, cost-minimisation submissions can include products with new mechanisms of action, improved efficacy (e.g., higher or longer-lasting effects), alternate modes of administration or improvements in ease and convenience for patients. While the incremental improvements offered by

[7] DoHAC https://www.pbs.gov.au/general/process-improvements/Stage-1-and-2-PBS-Process-Improvements-metrics-report-2021-22.pdf
[8] Nusinersen PSD Mar 2022 https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2022-03/files/nusinersen-psd-march-2022.pdf
[9] World Bank https://datacatalog.worldbank.org/search/dataset/0037712

these technologies may not justify a full cost-effectiveness analysis, current HTA policy and methods apply a pragmatic approach to facilitate patient access to these options. Specifically, the economic and budget-impact modelling requirements are reduced, and each new treatment option is able to list on the PBS at price parity to an already-funded treatment. Generally, these treatments achieve first-time PBAC recommendations and timely access for patients. While AbbVie believes that improvements can be made to the process, this pragmatic approach should continue to support and incentivise a wide range of treatment options being made available for patients within a disease area.

Pricing considerations

Two key and interrelated features of Australia's HTA system that work effectively are the use of value-based pricing and indication-based pricing. Value-based pricing ensures that the prices of most medicines, particularly those submitting on the basis of cost-effectiveness, are based on the inherent clinical and economic value provided by that medicine. Indication-based pricing allows each indication to be priced based on the value offered specifically in treating a given group of patients. These features generally support the appropriate valuing of medicines in Australia at the point of HTA evaluation, and should be retained. Another pricing feature that should continue is the ability for sponsors to request a Special Pricing Arrangement, to enable confidential net pricing. This is critical in allowing many sponsors to launch medicines in Australia, in scenarios where, for commercial reasons, sponsors are unable to list on the PBS with the cost-effective price recommended by the PBAC being visible. In addition, the ability for sponsors to request the redaction of price, and any inputs that could be used to back calculate prices, from PSDs, must also be retained.

Prioritisation of treatment choice for patients

The current framework for Australian HTA allows for a range of treatment options to be available for patients within a therapeutic indication and across lines of therapy, rather than limiting treatment choice to one therapy. Funding a range of treatments with varied mechanisms of action, modes of administration and dosing schedules allows treatment choice to be individualised based on patient preference, treatment response and tolerability. In many cases, such as in the use of biologics in immunology, the current framework allows for prescribers to retain the choice of the appropriate molecule, brand, and sequence of molecules for a given patient. Prioritisation of treatment choice also supports equitable access, for example, with administration and accessibility considerations of a treatment due to geographic location.

Summary

The elements and features described in the sections above are working effectively and should be retained and optimised. Critically, these include:

1. **Expertise, flexibility and pragmatism in PBAC decision-making**, allowing this expert independent committee to exercise judgement on willingness to pay and listing details based on important qualitative, person-centred factors.
2. **Streamlined process, published timelines and applicant-initiated submissions** with some opportunity for dialogue before, during, and after a HTA evaluation and decision.
3. **Indication-based pricing** and allowance for cost-effective prices to remain confidential at the request of sponsors.

4. **Approach to cost-minimisations**, allowing medicines that are clinically similar to existing alternatives to list at price parity to appropriate comparators, and retaining patient and clinician choice across treatment options.

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

As described in Section 1.1, AbbVie considers that improvements to the HTA process that have been implemented as part of the Stage 1 and Stage 2 streamlined pathways initiative have helped to facilitate faster patient access to some medicines. This impact, and the opportunity for further improvements, should continue to be monitored into the future.

One example includes PBAC's consideration of venetoclax in acute myeloid leukaemia (AML). As seen in the venetoclax March 2021 PSD, venetoclax was rejected by PBAC at the March 2021 meeting, however the PBAC proposed that an early re-entry pathway would be acceptable if certain parameters were addressed[10]. This enabled AbbVie to resubmit at the earliest possible opportunity, ultimately receiving a positive PBAC recommendation at the July 2021 meeting and, as seen on the Medicine Status Website, a PBS listing in December 2021 which is 4 months earlier compared to a standard resubmission pathway[11].

[10] Venetoclax PSD, March 2021. Available at: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-03/files/venetoclax-psd-mar-2021.pdf

[11] Venetoclax AML Medicine Status Website Entry. Available at: https://www.pbs.gov.au/medicinestatus/document/536.html

2 Current or future barriers to earliest possible access

2.1 What are the elements and features of HTA policy and methods that are acting as a current barrier to earliest possible access?

Multiple PBAC submissions are often required to achieve a positive recommendation

In theory, PBS access in Australia can be achieved within approximately 60 days of ARTG registration if the Sponsor submits at the earliest opportunity under parallel processing, followed by a first time PBAC recommendation, and no delays to post-PBAC negotiations. In practice however, there are very few cases where this is achieved. A recent analysis demonstrates that only 3% of medicines are PBS listed within 0-3 months of ARTG registration, and only 14% of medicines are PBS listed within 3-6 months of ARTG registration.[12] The time between ARTG registration and PBS listing is referred to as the patient access gap.

An analysis of PBS listings between March 2021 and March 2022 indicated that 'ever' cost-effective submissions (where cost-effectiveness was utilised in at least one of the submissions leading to the PBS listing) had a mean patient access gap of approximately 600 days[13]. Updating this analysis to include listings until March 2023 results in a marginally shorter time of 566 days. For listings based on cost-minimisation (typically implying no incremental cost to Government) the mean patient access gap was 360 days.[14] Given that cost-effectiveness is used where the product is considered to offer superior health outcomes over current care, it is a concern that the therapies that are likely to address an unmet need are those that take the longest to be funded. Incremental reforms over time have helped to reduce the patient access gap such as the introduction of parallel TGA/PBAC processing in 2011, and early re-entry pathways in 2021. However, the analyses for both cost-effectiveness and cost-minimisation submissions highlight a substantial delay for Australian patients, compared with the 60 days that is technically possible within the current process.

Resubmissions remain the greatest driver of delayed access. While the Stage 2 PBS Process Improvements aim to reduce the number of resubmissions, the latest DoHAC analysis shows that only 56% of initial submissions were recommended first time. Between 1 July 2021 to 30 June 2022, only 11% of submissions seeking a higher price over the existing alternative(s) were recommended first time (4 out of 37).[15] Approximately 60% of the re-submissions during this time passed via the standard resubmission pathway, which incurs a delay to access for patients of at least 8 months. It is also a very resource intensive exercise for the Sponsor, Evaluators, Committees, and the DoHAC.

Gaining as much alignment as possible on the decision problem and analytical approach at an early stage of the HTA process is expected to be considerably more efficient than addressing these issues via full resubmissions and on average reduce the patient access gap. AbbVie acknowledges that the current process allows for optional pre-submission meetings led by the DoHAC, however there is significant room for improvement.

Limitations of the existing Pre-Submission meetings include:

[12] Medicines Australia https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/04/Medicines-Matter-2022-FINAL.pdf
[13] Millar, D, Commercial Eyes Analysis – Presented by Douglas Millar at ARCS 2022 Conference, ARCS, Australia, 2022
[14] PBS listing data, analyses on file with Medicines Australia
[15] https://www.pbs.gov.au/general/process-improvements/Stage-1-and-2-PBS-Process-Improvements-metrics-report-2021-22.pdf

- Stakeholder attendance: Sponsor and HTA Department representatives only, lacking input from consumers, technical experts and decision makers.
- The meetings are relatively short (1hr maximum) leaving little time for in-depth discussion on any particular topic given there are typically a range of complex considerations to cover.
- Not a formal part of the HTA process.

The increasing complexity of innovative pipeline medical technologies further complicates the issue, for example, in determining the appropriate funding pathways and clinical positioning for disruptive treatments or treatments that cross multiple funding decision bodies and pathways.

Limited opportunity for dialogue with Evaluators, Sub-committees, and patients during the evaluation

The process of commentary responses allows for a very limited opportunity for Sponsors to address questions and points of clarification with Evaluators, ESC and DUSC. This means that often there are issues that remain unaddressed or uncertainty concerns that have not been clarified by the time the submission is considered by PBAC. Insight from patients, carers and clinicians is also limited to consumer comments or a PBAC hearing, where the information provided is often general rather than addressing specific queries or concerns that the Evaluators and Sub-committees may have. This is important to help reduce the number of resubmissions and deferrals, particularly for new disease areas, where treatment pathways and clinical considerations may not be well understood.

Suboptimal alignment with TGA milestones for parallel processing

A significant proportion of Category 1 and Category 2 PBAC submissions are assessed under the parallel processing pathway. Due to the requirement to provide a TGA Delegate's Overview at least one week prior to the PBAC meeting, Sponsors may be required to delay lodging their PBAC submission by a 4-month cycle when a Delegate's Overview may be received shortly after a PBAC meeting, where the TGA Evaluation phase (Milestone 5) may already be complete.

Limited transparency and predictability of PBAC decision making & pricing methods

While Sponsors have some insight into PBAC's considerations through the PBAC minutes and PSDs, it may be unclear how PBAC arrived at a particular recommendation, what prioritisation was applied and shared by the Discussant, if there were any areas of misunderstanding requiring clarification and what additional insights were provided by other parties such as the DoHAC and whether an explicit discussion of risk tolerance was had. There may also be inconsistency of decision making across similar products. It is extremely valuable to have the opportunity for a post-rejection meeting with the PBAC Chair per the current process, however a more complete picture is required to provide the greatest opportunity for a future positive PBAC recommendation.

There is also limited post-PBAC pricing governance leading to inconsistency around pricing finalisation with the DoHAC. Unpredictable or unclear pricing methodology or different interpretations of a PBAC recommendation between Sponsor and DoHAC can delay a Sponsor's ability to lodge a pricing package or accept the price required. This is particularly difficult when Sponsors are required to follow strict internal pricing approvals processes. There is no publicly available pricing methods manual for Sponsors to reference and no clear process to seek clarification from PBAC in an expedited manner where pricing interpretation varies.

Limited functionality of the current Independent Review process

The Independent Review process has only been actioned three times since it was first made available in 2005, under the Australia-US Free Trade Agreement.

Consideration could be given to reviewing the barriers to use of the independent review mechanism, so that it can serve as a proper measure of accountability. However, it is acknowledged that under the current requirements of the National Health Act, the Independent Review process cannot be used to direct PBAC to make a different recommendation. PBAC outcomes are also excluded from administrative appeal.

Given Australia's HTA process is a single-payer system with limited review rights, true transparency for Sponsors around PBAC decision making and deliberations is essential to ensure accountability.

Value assessments that manage uncertainty by preferencing highly conservative scenarios and estimates

A conservative approach to value assessment is observed across many elements of HTA in Australia, and this impacts the willingness of Sponsor companies to prioritise reimbursement in Australia. For example, a recent analysis showed that only a third (34%) of globally approved medicines were PBS listed in Australia from 2012-2021, and only 12% of new medicines are PBS listed in Australia within one year of global first launch.[16] The PBAC often require a price decrement as a proxy for the value of uncertainty with conservative assumptions adopted in base case economic evaluations, and high bars set for establishing clinical superiority or a clinically meaningful difference.

When the PBAC considers economic parameters, it must often rely on modelling to predict cost-effectiveness. Evaluations and considerations are often inconsistent with the PBAC guidelines or with accepted academic best practice. For example, the use of truncated 5-year time horizons, artificial waning of treatment effect, and forced convergence of modelled outcomes are frequently used to manage clinical and economic uncertainty. When combined, the result is an unsupported and clinically implausible value which significantly undervalues the additional benefit therapies offer (i.e., incremental QALY gain) and further reduces the price of medicines. Two analyses of PBAC deliberations have shown that the benefit of some medicines could be undervalued, delaying the ability for patients to access these medicines on the PBS.[17][18] The analyses compared similar HTA processes in the UK, France, Canada and Australia. Australia applied the most conservative approach to analysing new medicines and was the slowest to provide reimbursed access. The methodology applied by the PBAC in the analyses underestimated longer-term trial data on patient outcomes.

AbbVie considers that this approach to uncertainty may not be reflective of more liberal societal risk preferences. It is possible that a conservative approach to modelling and extrapolation creates a bias towards valuing medicines with short term-trial based outcomes. The perceived lower level of risk tolerance may also lead to submission deferrals or rejections for medicines where the outcomes are more difficult to measure quantitatively or require longer term studies to measure outcomes. Between March 2021 and March 2022, the PBAC rejected 62 major (Category 1 and 2) submissions. Uncertainty in the ICER

[16] PhRMA 2023 https://phrma.org/en/resource-center/Topics/Access-to-Medicines/Global-Access-to-New-Medicines-Report
[17] Spiteri C et al: Predicting the unknown – how health technology assessment agencies deal with uncertainty, and the impact this has on patient access for immuno-oncology therapies; ISPOR Asia 2020.
[18] Phan K et al: Comparison of Long-Term Overall Survival With Extrapolated Overall Survival for Pembrolizumab Assessed by Australian Reimbursement Authorities; ISPOR Asia 2020

or magnitude of benefit was mentioned in 37 (60%) of the cases.[19] On average, it takes 2.2 submissions for medicines with superior efficacy claims supported by a cost-effectiveness analysis to receive a positive PBAC recommendation compared with 1.2 submissions for medicines where a cost-minimisation approach is taken.[20]

Willingness to pay, as determined by the cost per QALY, is typically <$75k which is significantly lower than the value placed on a life compared with other Government departments such as Prime Minister & Cabinet who state '*based on international and Australian research a credible estimate of the value of statistical life is $5.3m and the value of statistical life year is $227,000 in 2022 dollars'*[21]. If any areas of uncertainty are identified within a submission, this often translates into further downward pressure on the ICER that the PBAC is willing to accept.

AbbVie considers that the PBAC's current approach to uncertainty and low risk tolerance also impacts budget impact modelling, with the most conservative assumptions for parameters such as patient population and uptake often being adopted in utilisation estimates. In scenarios where a risk sharing arrangement (RSA) is then recommended, these conservative utilisation estimates underpin the yearly subsidisation caps applied. When this is coupled with a high RSA rebates above caps, the benefits that eligible patients are receiving from treatment are ultimately under-valued or, in the case of 100% rebates, valued at less than zero (taking into account fees and mark-ups).

One example which illustrates conservative PBAC behaviour to utilisation estimates is the RSA currently in place for the severe atopic dermatitis (AD) PBS indication, applying to both dupilumab and upadacitinib. When dupilumab was first recommended for use in severe AD, the PBAC recommended that patients with severe AD of the whole body as well as patients with severe AD of the face and/or hands be included in the restriction [22]. However, the PBAC noted it would not be appropriate for the utilisation estimates to include any uplift for these patients, as data in a subgroup that matched the recommended restriction wording was not available. This was despite the PBAC and ESC agreeing that the treatment of these patients was clinically appropriate and that dupilumab appeared to be effective across all anatomical regions, as outlined in the dupilumab March 2020 PSD[13].

<u>Comparator selection</u>

Selection of a comparator is crucial for determining the content and structure of any HTA submission. Once the comparator is identified, the economic analysis, and subsequently the price and budget impact of a new treatment, is anchored to this comparator.

Section 1.1.3 of the current PBAC Guidelines stipulates that the main comparator for any given submission should be "the treatment most likely to be replaced in practice"[23]. This definition is largely consistent with other HTA bodies around the world, including England.

Section 101 (3B) of the National Health Act (1953) states that the PBAC should not recommend a therapy to the Minister that is "substantially more costly" than an "alternative therapy", unless the PBAC is satisfied

[19] Millar, D, Commercial Eyes Analysis – Presented by Douglas Millar at ARCS 2022 Conference, ARCS, Australia, 2022
[20] MAESTrO Database. Analysis of PBAC submissions and their related outcomes & timelines. December 2020
[21] PM&C 2023 https://oia.pmc.gov.au/sites/default/files/2023-05/value-of-statistical-life.pdf
[22] Dupilumab https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2022-07/files/dupilumab-psd-july-2022.pdf
[23] PBAC Guidelines, v 5.0. https://pbac.pbs.gov.au/content/information/files/pbac-guidelines-version-5.pdf

that ”the therapy, for some patients, provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy”[24]. These terms are not explicitly defined in the Act and they do not differentiate between cost-effectiveness or cost-minimisation submissions.

The PBAC’s broad interpretation of alternative therapy leads to recommending new medicines relative to the price of the lowest cost comparator (LCC). This approach is enforced even if the LCC identified would not satisfy the PBAC Guidelines definition of a comparator and/or is a real alternative therapy in clinical practice. For example, the LCC can be a product that is seldom used in practice or has different features to the new medicine, such as mode of administration.

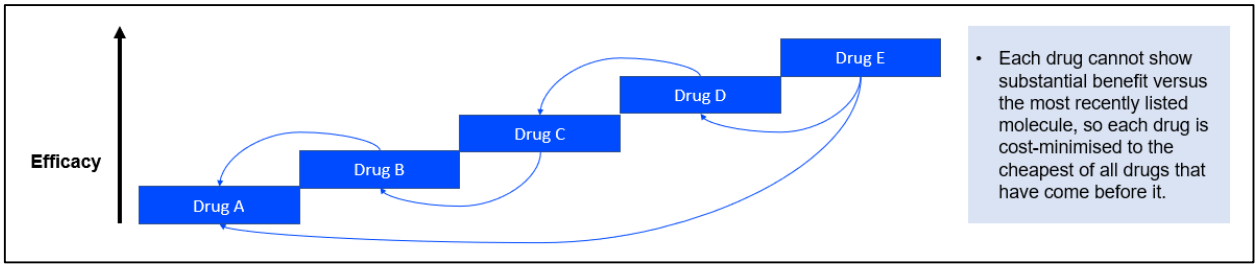
The consequence of this approach is that many new medicines are inappropriately undervalued. This is particularly true when the LCC price used is based on a molecule that is in F2 or has otherwise received multiple statutory price reductions following listing on the PBS. Through the application of LCC, new innovative medicines may be required to list at parity to LCC. This also includes new presentations of existing PBS medicines that benefit patients , that are then required to list at an LCC price rather than the relevant price of an existing presentation. Ultimately, the prices resulting from LCC for new medicines or new presentations of existing medicines can be prohibitively low, preventing access for Australian patients to new therapies.

AbbVie considers that the issue of comparator selection and LCC is amplified by the PBAC’s level of evidence requirements to support a claim of substantial improvement over alternative therapies. In many cases, indirect treatment comparisons are not accepted as a basis for demonstrating clinical superiority over alternative medicines. However, even with a head-to-head, blinded, randomised controlled trial demonstrating superiority of a new medicine to an alternative therapy, the PBAC may still recommend the new medicine on a cost-minimisation basis to the LCC. A relevant example for this can be found within the July 2019 PSD for risankizumab for the treatment of chronic plaque psoriasis (CPP). The PSD states: ‘The PBAC considered the claim that risankizumab is superior to ustekinumab in terms of effectiveness and non-inferior in terms of safety to be supported by the direct evidence presented’[25]. However, the PBAC go on to state there is unlikely to be any clinically significant difference between any biologics listed for CPP and that risankizumab should be listed on a cost-minimisation basis to the least costly alternative of all CPP biologics[16].

Ultimately, the application of LCC currently leads to “daisy chains” of products being linked together for pricing purposes, with new innovative medicines being priced the same as older, cheaper, and less effective medicines due to each incrementally better treatment being cost-minimised to the LCC. Over time, the newer medicines are significantly undervalued when compared to the original listings and often, the LCC. This is visually depicted in **Figure 1** below.

[24] National Health Act (1953), Section 101. http://classic.austlii.edu.au/au/legis/cth/consol_act/nha1953147/s101.html
[25] Risankizumab PSD July 2019. https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2019-07/files/risankizumab-psd-july-2019.pdf

Figure 1 The "daisy chain" effect of requiring each new medicine to cost-minimise to the LCC



Managed access

As per existing legislation, the PBAC is an advisory committee by nature and is not able to make conditional recommendations that are binding on the Minister of Health. However, as described in the 2015 Overview of the Managed Access Program (MAP) for PBS listings, the PBAC is able to propose the use of a MAP when considering a treatment in an area with high unmet need but uncertainty surrounding the evidence available at the time[26]. This mechanism was originally introduced as the Managed Entry Scheme (MES) framework in 2011 and has the intention of enabling earliest possible funded access to treatments for patients, while further evidence is collected to support PBAC decision-making.

However, to date, there has been low uptake of MAPs. The few programs that have been initiated have demonstrated the complexity of participation for sponsors including the resource-intensity of collecting further evidence, the potential for near-term competition and subsequent change in relevant treatment landscape during the MAP timeframe, and pricing risks with no price increases realised even in the presence of favourable mature data. Furthermore, fewer than a third (8) of the 29 non-COVID medicines that have been Provisionally Approved by the TGA have resulted in a PBS listing from the inception of Provisional Approvals (2018) to May 2023, with only half ever submitting to the PBAC. These insights highlight the need for a more effective reimbursement framework that allows earliest possible patient access to treatments that are plausibly cost-effective in high unmet need areas while further evidence is developed.

The 2022-2027 Strategic Agreement (Clause 6.4) states that the Government and the industry both acknowledge this need to consider a reimbursement pathway that complements the TGA's Provisional Approval Pathway. The Clause notes that these parties will work together to identify possible options that:

(a) Use the current MAP arrangements, and
(b) Establish transparent and robust criteria for reviewing funding and managed exit.

AbbVie is aligned to the goal of pursuing earliest possible access for patients to treatments in high unmet need areas where evidence is still under development. As above, one feasible option for the achieving this goal is to improve the existing Managed Access Program framework in a way that better considers the needs of industry, the Government, patients, and clinicians. This will be described in more detail in **Table 1**, Section 2.3.

[26] Overview of Managed Access Program, 2015. Available at: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-outcomes/2015-03/Overview-of-managed-access-program.pdf

2.2 What are the elements and features of HTA policy and methods that may act as a future barrier to earliest possible access?

If the considerations described above are not addressed, there will continue to be significant barriers to earliest possible access for Australian patients. In particular, the continued application of LCC will disincentivise future innovative medicines from launching in Australia. This will ultimately impact health outcomes of patients.

In addition, as discussed in Section 2.1, AbbVie considers that the PBAC's current approach to utilisation estimates coupled with high RSA rebates is currently leading to eligible patients being treated, but the cost of treatment borne by the Sponsor and minimal (or no) value attributed by the Government. If this approach continues, it will likely further disincentivise Sponsors from launching future treatments in Australia due to the impacts on commercial viability.

While improved transparency of PBAC decision-making supported in-principle, the ability to keep commercially sensitive information confidential remains paramount. Any initiatives, however well intended, that risk exposing information that is commercial-in-confidence would threaten Australia's position as an early launch country and significantly limit or delay patient access to medicines available elsewhere.

2.3 Would you like to provide feasible options or suggestions you have to improve elements of HTA policy and methods that are acting as a current or future barrier to earliest possible access?

As described in Section 2.1-2.2, there are several elements of HTA policy and methods in Australia which are acting as current or future barriers to earliest possible access for patients. For barriers that AbbVie has a feasible option or suggestion to improve the related element, this has been presented in the below table.

AbbVie also notes that while the National Medicines Policy was updated throughout 2022 to better reflect the challenges and opportunities relevant to today, the Department of Health's policy on Health Technology Assessment and the underlying principles which underpin the evaluation of technologies has not been updated since 2009[27]. Following the outcome of this HTA Review, AbbVie recommends that this policy be revisited and updated in line with the Review recommendations.

Table 1 Feasible options to improve HTA elements identified as current or future barriers to earliest possible access

Relevant barrier	Proposed option or suggestion
Multiple PBAC submissions are often required to achieve a recommendation	• Alignment on HTA parameters prior to lodging, so that resubmissions are minimised, and funding pathways and implementation plans for disruptive or complex technologies can be resolved early. • This could be achieved by replacing the current pre-submission meeting process led by the DoHAC, with an optional pre-submission protocol ratification led by Committee members. It could include elements such as PICO, financial and economic model parameters as well as the opportunity for patient, carer, and clinician input. • Alternatively, there could be a focussed meeting between ESC/DUSC and the Sponsor to agree a base case economic model and utilisation assumptions which represent the most plausible scenario. • There is also an opportunity to leverage the existing PBAC intra-cycle process, by optimising accessibility and transparency for stakeholders. While the increased formalisation of May, September, and December PBAC intra-cycle meetings, including their presence on the PBAC Calendar, represents a positive step forward for predictable timing, there is still an opportunity to improve the intra-cycle meeting process in order to facilitate earliest possible access. Specifically, AbbVie considers that the criteria used to select what submissions are eligible or ineligible for intra-cycle consideration should be more clearly stated and agreed to between the Department and the industry. For example, this could include any medicine that

[27] Health technology assessments – Department of Health and Aged Care: https://www.health.gov.au/topics/health-technologies-and-digital-health/health-technology-assessments

Relevant barrier	Proposed option or suggestion
	has received a prior deferral but new information has become available, or medicines that offer high therapeutic added value. The process and timing behind an intra-cycle consideration should also be made clear. For example, it could be stated that any information provided to the PBAC Secretariat within 2 weeks of the intra-cycle meeting could be expected to be considered at an intra-cycle meeting, if it is relevant to the reason for prior delay. Overall, optimising this process would provide more clarity for Sponsors and other stakeholders on what is required for intra-cycle consideration and how an earliest possible recommendation can be achieved.
Limited dialogue between applicants, evaluators, and other stakeholders during evaluation	• Real-time exchange of information during submission evaluations, so that the most comprehensive assessment is provided for PBAC consideration. • Building on the existing plans for an information exchange pilot, this could be achieved by allowing Evaluators to request further information and clarification from Sponsors in real-time via the Health Products Portal (HPP) and introducing provisions for more dynamic information sharing between PBAC Evaluators/Committee members and TGA Clinical Evaluators. • There should be provisions for Sponsor hearings at ESC meetings. • Requests for specific input during evaluations could also be sought from nominated patients and clinicians. To facilitate improved dialogue throughout evaluation, a DoHAC HTA case-manager could be assigned for each submission.
Suboptimal alignment with TGA milestones for parallel processing	• Recalibrate the milestone requirements for parallel processing, so that PBAC recommendations are not unnecessarily delayed due to misalignment with the TGA Delegate's Overview. • This could be achieved by re-anchoring PBAC consideration to the end of the TGA evaluation phase at Milestone 5 or working with the TGA to bring the timing of the Delegate's Overview forward by several weeks.
Limited transparency and predictability of PBAC decision making & pricing methods	• Improve the transparency and predictability of PBAC decision making, so that Sponsors can better understand the rationale behind PBAC considerations and incorporate these learnings to improve future submissions. At a minimum, this could include a presentation of clear rationale behind the selection of base-case assumptions and how contextual factors, such as unmet need, are taken into account.

Relevant barrier	Proposed option or suggestion
	• This could be achieved by allowing Sponsors to participate as an observer during the PBAC meeting when their agenda item is discussed. • Sponsors should also be provided with a copy of the Discussant presentation, as well as a summary of communication between the DoHAC, Committee and Evaluators regarding their submission. This could be implemented for all submission and recommendation types, and provided to Sponsors at the same time that the PBAC minutes are currently shared (i.e., 3 weeks after PBAC meeting for positive recommendations, and 6 weeks after PBAC meeting for all other recommendations). • The agenda of all PBAC Executive meetings should also be published. • Predictability around pricing methodology post-PBAC recommendation should also be improved by reinstating a pricing methods manual as previously used prior to 2014
Value assessments that manage uncertainty by preferencing highly conservative scenarios and estimates	• Ensure value assessments are person-centred, based on epidemiology and clinical practice rather than a risk-mitigation approach, so that Sponsor companies continue to prioritise early registration and reimbursement in Australia. • This could be achieved by increasing willingness to pay to a minimum of GDP per capita (~90K AUD) • Agree base case economic model and utilisation assumptions upfront, to represent the most plausible scenario and separate the modelling assumptions from the PBAC budget impact and price assessment • Update technical methods with greater weighting given to patient preferences and equity considerations.
Comparator selection that does not reflect the therapy most likely to be replaced in clinical practice	As described in Section 2.1 and Section 2.2, the PBAC's current interpretation of the National Health Act (NHA) 1953 is not aligned to HTA best-practice and is often at odds with the PBAC's own guidelines on comparator selection. Specifically, the PBAC have interpreted the legislation broadly to select the lowest cost alternative therapy as the comparator for pricing purposes. However, HTA best-practice and the PBAC Guidelines define a main comparator as the most likely to be replaced therapy in practice. Consequently, the resulting prices recommended for new medicines to list onto the PBS are undervaluing medicines and can delay patient access. • In order to address this issue, AbbVie believes the most effective and feasible solution would be to align the NHA with the PBAC Guidelines definition of main comparator. Ideally, the legislation should be changed to include a definition for "alternative therapies" which is the medicine/intervention likely to be most replaced in clinical practice.

Relevant barrier	Proposed option or suggestion
	• Another alternative, albeit more limited, approach could be to allow new presentations for molecules which have been listed for less than 5 years to list at the existing price of that molecule. Given that the most plausible scenario is that a new presentation of a molecule will simply replace an existing presentation, this is still generally aligned with the intention of the NHA in comparing a therapy to it's alternative therapies. • While legislative change is pursued, AbbVie considers that an interim approach could be to allow the use of a weighted economic comparator in the case of cost-minimisation submissions. This would see new medicines list at a price weighted based on real utilisation of each possible alternative therapy, and could feasibly be considered as appropriate under the existing legislation. • In summary, the issues surrounding comparator selection and LCC all arise from a discrepancy between the PBAC Guidelines and the NHA. As such, the most effective solution would be to re-align the two, with the NHA better reflecting the PBAC Guidelines which were developed based on HTA best practices.
Managed Access Framework that does not support early funded access for patients in its current form	AbbVie believes a feasible and effective approach to supporting earlier treatment access for patients in high unmet need areas where further evidence is needed is to improve the existing Managed Access Program (MAP) framework. A renewed framework should be co-designed by the industry and the Government and involve meaningful consultation with patients, clinicians, and other stakeholders. This will ensure that the framework better reflects the needs of all stakeholders involved and ultimately increase incentives for sponsors to pursue earlier reimbursed access in Australia. An overview of elements that should be considered in the design of a renewed MAP framework are outlined below: • **Clearly defined eligibility:** The types of treatments suitable for the framework should be clearly defined. This could be aligned to the Pricing Pathway A definition already in use by the Department of Health: *"the medicine is expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over any alternative therapies; and the medicine addresses a high and urgent unmet clinical need; and it would be in the public interest for the submission to be recommended to follow this pathway".* • **Clearly defined targets with shared commitment:** the framework should clearly outline targets that reflect the shared goals of industry and the Government, including improving time from TGA provisional approval

Relevant barrier	Proposed option or suggestion
	to initial reimbursement. This increases transparency and the incentive for sponsors to apply via the MAP framework rather than progressing through standard PBAC processes. While different for each medicine, the time from initial reimbursement to completed re-assessment should also be clearly defined at the beginning of a MAP. • **Applicant or PBAC proposed:** A MAP should be able to be proposed by either a submission applicant or the PBAC. When proposed by the PBAC, the applicant should not be required to proceed with the approach and should retain the ability to return to a future PBAC meeting and propose an alternative. • **Management of uncertainty:** appropriate recognition of value by the PBAC upfront is paramount. The PBAC should be able to recommend a MAP price based on plausible estimates which will require some increased acceptance of early-phase clinical data. • **Appropriate sharing of risk:** AbbVie does not consider that the current MAP framework represents appropriate sharing of risk in practice. Any renewed framework should include more predictable and manageable risks around future price impacts and not mandate sponsor paybacks if data is ultimately less favourable. This acknowledges risks taken by the Government and sponsors, in pursuit of early access. • **Transparent and consistent approach to competition:** Consistent and transparent mechanisms should be described in order to address the scenario of a product with similar efficacy and safety to a MAP product being introduced during the MAP timeframe, which changes the treatment landscape. Competition can always be expected, yet a consistent and transparent approach to managing the potential pricing impacts of new entries, along with ensuring a timely and efficient MAP process overall, can ensure the MAP framework still provides a meaningful opportunity for sponsors. • **Clearly defined re-assessment:** evidence requirements, approaches to evaluation, and timelines should be clearly defined and agreed to upfront for each MAP. A commitment to price increases, when supported by the evidence, should be made. • **Hierarchy of evidence requirements:** evidence collection should prioritise existing trials and expected data readouts in the first instance. In the absence of expected data readouts that are relevant to the PBAC's identified uncertainties, existing registries and infrastructure should be considered as a second source. If these approaches are insufficient, new data collection sources or studies should then be considered.

Relevant barrier	Proposed option or suggestion
	• **Clearly defined exit from subsidy:** an approach to managed exit should be clearly articulated in the description of a renewed MAP framework. The approach should be risk-sharing and represent a joint commitment to addressing managed exit and impacts to patients who are receiving treatment. For example, this could involve the Department subsidising treatment up to the PBAC's perceived cost-effective price and the remainder of treatment cost being the responsibility of the sponsor. • **Pilot approach:** AbbVie considers that any renewed MAP framework should be implemented through a pilot program, where learnings from initial evaluations can be openly discussed and addressed in a final framework. Ultimately, AbbVie considers that improving the existing MAP framework and addressing current disincentives for sponsors to select this pathway for funding is crucial with the goal of achieving earliest possible access for Australian patients. However, overall, it is worth noting that the balance of incentives across the medicines landscape should always ensure that companies continue to pursue and develop medicines that address all types of health needs for diverse groups of patients.

3 Current or future barriers to equitable access

3.1 What are the elements and features of HTA policy and methods that are acting as a current or future barrier to equitable access?

Equitable access is a key tenant of the National Medicines Policy: 'Irrespective of diversity, background, age, disability, location or personal circumstance, all Australians should have equitable access to safe, effective and high-quality medicines, culturally appropriate medicines-related services and medicines-related information'.

Currently, HTA policies and methods in Australia do little to enable meaningful consideration of how technologies address equity issues. While the guidelines state that equity is part of PBAC decision-making, there is no clarity or further detail on how this occurs and what factors are considered. There are also no accepted methods or guidelines for how applicants should discuss equity in a meaningful way in submissions or present the value of therapies that improve access for the groups identified in HTA Review Terms of Reference:

a) First Nations people
b) people from culturally and linguistically diverse backgrounds
c) children and older people
d) people with disability
e) people living in rural and remote areas
f) people of low socioeconomic status
g) people living with rare and under-recognised diseases
h) people with mental illness
i) lesbian, gay, bisexual, transgender, queer or questioning, intersex and/or other sexuality and gender diverse people (LGBTQI+)
j) other populations in circumstances and at life stages that give rise to vulnerability.

For example, there is currently no basis for the PBAC to recognise the benefits offered by a therapy which is orally administered (rather than injectable) or doesn't have specific cold chain storage requirements. These types of therapies have a positive impact on those living in geographically rural and remote areas, by not requiring any assistance or facility for administration (for example, instead of an infusion treatment administered at a hospital) or by reducing quality use of medicines concerns regarding storage. These benefits are not formally considered when assessing a therapy and therefore the full value of the product may not be recognised.

AbbVie also notes that inequities related to access on a socio-economic or geographic basis are exacerbated when earliest possible access for medicines is not achieved. In a scenario where a PBAC recommendation is delayed or never achieved, patients who can pay privately or those based near a clinical trial location for that medicine may be able to receive treatment. However, patients with lower socioeconomic status or those not geographically located near a clinical trial centre may become further disadvantaged by lack of access to the best possible care and health outcomes. As such, AbbVie considers that addressing barriers to earliest possible access will also support improving equity of access in Australia.

3.2 Are you able to provide any details of feasible options/suggestions to improve elements of HTA policy and methods that are acting as a current or future barrier to equitable access?

As described in Section 3.1, HTA policy and methods in Australia are currently doing little to appropriately consider equity issues when evaluating therapies. In ***Table 2***, feasible options for improving this are proposed.

Table 2 Feasible options to improve HTA elements identified as barriers to equitable access

Relevant barrier	Proposed option or suggestion
No guidelines or clarity on equity informing PBAC decision-making	• AbbVie proposes that the PBAC guidelines be updated to include a section on equity considerations. The guidelines should clearly describe what type of information should be included in submissions to discuss how therapies address access for the groups mentioned above that are relevant to the product and disease. • AbbVie also proposes that Public Summary Documents consistently include a summary of how relevant equity issues were considered during the evaluation of each medicine and how this contributed to a final decision by the PBAC.
Broader recognition of innovation and value	• AbbVie supports a broader recognition of innovation and a medicine's value, where the benefits that a treatment can offer for priority groups, and improving their level of access, are considered when attributing valuing to a medicine. • This could be implemented by allowing these equity considerations to be an acceptable basis to not be considered interchangeable with other medicines. Specifically, if a medicine can demonstrate that an equity issue is addressed by listing onto the PBS, that medicine is not able to be deemed interchangeable on an individual patient basis with other medicines who do not provide the same equity benefits. • In addition, if a medicine offers similar clinical efficacy and safety to other treatments yet can address a specific need or existing inequity experienced by a priority group, the PBAC guidelines should stipulate that the medicine is not mandated to cost-minimise to the least costly comparator and is not linked to other therapies for reference pricing purposes. This approach has been observed in a limited number of prior PBAC evaluations and could be stipulated in the PBAC guidelines. For example, when the PBAC considered a long-acting cabotegravir presentation in November 2021, benefits provided to the Aboriginal community in regard to adherence to treatment and improved quality of life, were considered an appropriate basis to grant a price premium compared to alternative therapies[28].

[28] Cabotegravir/Cabotegravir and rilpivirine PSD November 2021. https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-11/files/cabotegravir-rilpivirine-psd-nov-2021.pdf

4 Elements and features that detract from person-centredness

4.1 Are you able to provide details of any elements and features of HTA policy and methods that may be detracting from person-centredness?

Limited resources to support consumer engagement in HTA

Documents such as Public Summary Documents are highly technical and do not contain a plain language summary which limits the accessibility for consumers. There are limited tools and resources that clearly explain how the HTA process in Australia works.

Limited opportunity for consumer engagement

Recent initiatives such as the Consumer Evidence and Engagement Unit within the DoHAC 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.

There is no consumer engagement and consultation early in the HTA process to determine true lived experience and unmet need of patients. Consumer participation is provided late in the decision process and participation rate remains low. This limits the ability for PBAC to make fully informed, person-centred decisions about the impact of a certain disease state and the potential impact of the medicine, including considerations for implementation. Many patients may not even be aware that a submission for a medicine that treats their condition is being considered and miss the opportunity for input.

The approach to consumer engagement is one-way with no formal feedback loop. Consumers have little insight or understanding as to how their input has been considered during an evaluation, the value of their participation and how it could be improved.

In terms of consumer hearings, consumers have the opportunity for direct communication with the PBAC regarding medicines that seek PBS listing. However, participation in a consumer hearing is by invitation only, and mainly between patient groups and PBAC representatives and take place only when deemed necessary by PBAC. Decisions to include a consumer hearing are usually ad-hoc and with very short notice. Attendees therefore have limited time or guidance to adequately prepare.

In terms of stakeholder meetings, these are only convened where a submission for a medicine that treats a serious, disabling or life-threatening condition has not been recommended. Patient group representatives and PBAC consumer representatives are invited to provide input only at the request of PBAC.

Current HTA methodology does not adequately capture broader patient benefits and preferences

Value in healthcare can come in many forms. Non-economic value as well as indirect benefits should play a more substantial role in healthcare funding decisions. For example, patient preferences are not regularly addressed or recognised in current HTA methods. A new medicine may provide significant value delivered through innovation in formulation, mode of administration, acuity of care setting required, patient satisfaction etc, none of which significantly change the final clinical outcome, yet nevertheless have attributes that are important to the patient and deliver value through innovation.

4.2 Are you able to provide details of feasible options/suggestions to improve elements of HTA policy and methods that are detracting from person-centredness?

As described in Section 4.1, HTA policy and methods in Australia have several areas for improvement to ensure that a more person-centred approach is adopted. when evaluating therapies. In **Table *3*** feasible options for improving this are proposed. Many of these align with a report prepared by Bristol Myers Squibb, '*Broadening the Evidence'*[29].

Table 3 Feasible options to improve HTA elements that may detract from person-centredness

Relevant barrier	Proposed option or suggestion
Limited resources to support consumer engagement in HTA	• Provide additional resources to support consumer engagement in HTA. These should explain in plain language the role of each committee and their processes, give clear guidelines on consumer involvement opportunities, and provide comprehensive links to tools and advocacy groups. • Development of plain language summaries of Public Summary Documents • The use of electronic alerts to advise interested stakeholders of a product entering the PBAC process, and prompts for submission deadlines
Limited opportunity for consumer engagement	• Formulate a robust and formal framework for consumer engagement in HTA for input from consumers before, during and after the HTA process. • Feedback on consumer comments to provide greater clarity on how the input helped to inform the PBAC decision, demonstrate the value of input, increase understanding, and improve participation. • Inclusion of advocates in a technical consultation prior to the PBAC meeting, for example through the proposed early engagement step
Current HTA methodology does not adequately capture broader patient benefits and preferences	• More meaningful incorporation of patient preferences is critical to understand what matters most to Australian patients. Inclusion of a broader set of health indicators could be done through robust methodology such as discrete choice modelling, patient and consumer value mapping or social return on investment analyses. • In the MSAC Guidelines, there is now provision for a clinical claim based on the 'value of knowing' as alternative evidence to clinical utility. The value of knowing 'encompasses any consequence for the wellbeing of a patient beyond the changes in the health outcomes attributed to changes in the health care provided'. A similar approach could be taken to capture the value of patient preference or patient benefit.

[29] BMS https://www.bms.com/assets/bms/australia/documents/Broadening-the-evidence.pdf

	• Recent international guidance has been published on the topic of patient preferences: '*A Roadmap for Increasing the Usefulness and Impact of Patient-Preference Studies in Decision Making in Health: A Good Practices Report of an ISPOR Task Force'*. This could be used as a framework to align on agreed metrics or indicators for inclusion in the Statement to ensure a more comprehensive picture of health is captured and valued.

5 Perverse incentives

5.1 Are you able to provide details of elements or features of HTA policy and methods that are causing or could cause unintended consequence or perverse incentives?

As outlined in the HTA Review consultation questions, a perverse incentive is where an element or feature of HTA policy and methods may be creating an unintended incentive that results in negative consequences. There are several perverse incentives that exist in the current HTA system.

Firstly, the application of lowest-cost comparator when recommending any new medicine based on cost-minimisation to multiple other therapies is resulting in very low benchmark prices. This can deter the PBS listing of new therapies, as well as new presentations, which can offer patient benefit yet are priced lower than the original presentation due to the application of LCC.

For example, two new 150 mg presentations of risankizumab in the treatment of chronic plaque psoriasis (CPP) were considered by the PBAC in November 2021. The presentations included a sub-cutaneous syringe and pen containing 150 mg risankizumab in each unit. These were proposed to replace the existing 2 x 75 mg syringe presentation of risankizumab, halving the number of injections required each time a patient is treated. For CPP patients living with a lifelong condition, this benefit is significant from a convenience, pain, and quality use of medicines perspective. However, the PBAC recommended this presentation at the lowest cost comparator of 8 other molecules; 'the PBAC advised that risankizumab PFP and PFS should be cost-minimised to the lowest cost biological agent available for severe CPP'[30]. The other severe CPP agents have been listed onto the PBS over the span of two decades and have experienced significant price erosion due to statutory price reductions and reference pricing. The PBAC's recommendation of listing at the LCC contrasted with AbbVie's position proposed in the submission; 'the submission considered that the 150 mg PFP and 150 mg PFS should be cost-minimised to the existing PBS-listed risankizumab 75 mg PFS rather than the lowest cost comparator'[21]. As per the Medicine Status Website entry for the new presentation of risankizumab, AbbVie has not progressed to PBS listing following the November 2021 consideration[31].

Currently, perceived uncertainty in clinical data and economic assumptions is often managed by the PBAC by adopting the most conservative assumptions rather than the most plausible. This ultimately impacts the base-case assumption and ICER estimates, leading to significant price decrements being applied to support a positive recommendation. While AbbVie acknowledges that some uncertainty will always exist in HTA and that this must be addressed, the current approach favours treatments that provide short-term and more 'certain' benefits where no/less extrapolation is required. This may introduce systematic bias in the valuation between treatments with short terms versus longer-term benefits.

The PBAC's current approach to assessing budget-impact and utilisation estimates also reflects cost-containment behaviour, leading to restrictive risk sharing arrangements being recommended with low subsidisation caps and high rebates. Ultimately, the benefits that eligible patients are receiving from treatment end up being undervalued, which is not aligned with the intention of RSAs.

[30] Risankizumab November 2021 PSD. https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-11/files/risankizumab-psd-nov-2021.pdf
[31] Risankizumab 150 mg Medicine Status Website entry: https://www.pbs.gov.au/medicinestatus/document/660.html

5.2 Are you able to provide details of feasible options/suggestions to improve elements of HTA policy and methods that are creating unintended outcomes or perverse incentives either current or in the future?

Approaches to improve the PBAC's current approach to comparator selection (LCC), their approach to risk and uncertainty in assumptions, and other barriers to timely access have been described in **Table 1**.

6 Areas for further investigation or analysis

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

No country has a perfect HTA system. AbbVie notes that adoption of international models or elements into Australia must be made in consultation with stakeholders and with a thorough consideration of our local context including economic health, patient perspectives and preferences, the design of the broader health system, the political landscape including national and state priorities, policy settings and societal values including risk tolerance and willingness to pay for health. In fact, AbbVie considers that any elements considered under this section of the consultation will ultimately require localisation in order to make them effective in achieving the intended goal in Australia.

With this in mind, the following international elements have been identified by AbbVie as those which may contribute towards achieving earliest possible and equitable access to medicines for Australians. Notably, many of these elements are from the United Kingdom's HTA system, where HTA is undertaken by the National Institute of Health and Care Excellence (NICE). The UK's overall health system and the position of HTA within it is similar in nature to Australia. In addition, the UK is within the top 5 OECD nations for timely access to medicines with the gap between registration and reimbursement at 156 days or less than 6 months[2]. As such, the examples provided below are considered relevant and may plausibly contribute to improved access in Australia.

<u>Alignment on HTA parameters prior to submission lodging:</u>

As discussed earlier in this response, AbbVie notes that many reimbursement submissions in Australia are rejected or delayed for reasons that could be resolved through pre-submission alignment on HTA parameters.

This could be achieved by replacing the current optional pre-submission meeting process led by the Department of Health and Aged Care (DoHAC) which is often uninformative, with an optional pre-submission protocol ratification process for complex technologies or areas of high unmet need led by a subset of Committee members, for example the Discussant, PBAC Chair and ESC.

Elements discussed could include the PICO, financial and economic model parameters, and even allow for an early consideration of patient, carer, and clinician perspectives. A relevant analogue of where this early alignment occurs is with NICE in the **United Kingdom**. Specifically, the scoping process performed by NICE

before a reimbursement submission is made covers the elements mentioned here[32]. The outputs of the scoping processes are made public on the NICE website, and while they are not strictly binding, they produce an informative guide and base for applicants and evaluators to progress from, while also identifying areas of potential uncertainty early in the process. This enables applicants to make more informative submissions from the outset and even begin to address areas of uncertainty without delay.

Meaningful engagement with patients and patient advocacy groups:

Currently, Australia's engagement with patients and patient advocacy groups is very limited. Meetings between the PBAC and these stakeholders are only available at the request of the PBAC. There is also only one opportunity for consumer input which is considered late in the evaluation process. There is also limited transparency on how the input collected through the Consumer Comments process ultimately informs decisions, with no guidance or feedback available to patients to consider how input may be improved.

AbbVie believes that elements of the HTA systems in the **United Kingdom** and **Scotland** could be adopted to improve engagement and input from patients into the HTA process.

Specifically, NICE in the UK proactively ensures that a patient representative with experience relevant to the disease area under consideration is present when a treatment is considered[33]. This, combined with NICE meetings being open to the public and recorded extensively, increases NICE's accountability to consider the patient voice and patient input in a meaningful way.

The Scottish Medicines Consortium (SMC) which undertakes HTA in Scotland has a particularly robust approach to incorporating the patient voice which is generally well regarded by industry and patients. There are three main components to their approach which could be considered for adoption in Australia. Firstly, the SMC has established a Patient Group Partner System, where patient groups are able to register with the SMC in order to contribute to future treatment reviews. The groups then gather contributions from their members including patients and caregivers[34]. Detailed guidelines for making a contribution are available for these individuals on the SMC website. Secondly, the SMC also has a Public Involvement Network (PIN). This group consists of patients, carers, SMC team members, and other stakeholder groups and act to ensure that patient and carers perspectives are involved in SMC processes. The group engages on topics such as how to strengthen public involvement, incorporating patient and carer views in decision-making, and maintaining awareness of patient and public engagement activities[35]. Thirdly, the SMC also runs a Patient and Clinician Engagement (PACE) meeting for medicines for end of life and rare conditions. This meeting aims to allow better description of the benefits of a medicine, from both patient and clinician perspectives, outside of conventional clinical and economic assessment. For example, this includes issues related to convenience, independence, dignity, or impact on patient and carer ability to work[36].

[32] NICE technology appraisal guide: The scope. *https://www.nice.org.uk/process/pmg36/chapter/the-scope*.
[33] NICE involvement and participation https://www.nice.org.uk/process/pmg36/chapter/involvement-and-participation#clinical-experts-and-patient-experts
[34] SMC: Patient Group Partners. https://www.scottishmedicines.org.uk/about-us/public-involvement/patient-group-partners/
[35] SMC: Public Involvement Network: https://www.scottishmedicines.org.uk/about-us/public-involvement/public-involvement-network-advisory-group/
[36] SMC: Patient and Clinician Engagement: https://www.scottishmedicines.org.uk/how-we-decide/pace/

AbbVie notes that in parallel to this HTA Review, there is work underway to consider how consumers can have a more meaningful role in HTA. Specifically, Clause 6.3 of the Strategic Agreement commits to co-designing an Enhanced Consumer Engagement Process. AbbVie believes that the elements outlined above from the United Kingdom and Scotland should be considered for adoption/adaptation in Australia as part of this Review and ongoing work outside of the review.

7 Other details of importance

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

Subsiding new life saving and life improving therapies should be viewed as the investment that it is, reaping broad societal benefits. This was demonstrated in the 2019 research paper: Measuring the Impact of Pharmaceutical Innovation in Australia 1998–2018, authored by economist, Professor Frank Lichtenberg[37]. The paper showed that PBS-listed pharmaceutical innovation improves patient outcomes, reduces hospital demand, and is cost-effective. The paper was focused on cancer medicines, yet the findings and concepts are transferrable to any new treatment that generates improvements in health outcomes.

The overall impact of Government investment in innovative medicines on the PBS is not routinely assessed in terms of health benefits delivered. For example, comparing total costs with national health targets. Government scrutiny is focussed on growth in the costs of the PBS rather than the efficiency and value delivered through Australia's rigorous HTA system. It is counter-productive to view increased PBS expenditure as a trigger to introduce additional reforms to limit that spending. Allocation of funds and investment in the PBS should be in concordance with health outcomes it delivers.

An increase in PBS investment would allow for an appropriate increase to the risk appetite within Australia's HTA system and would ultimately allow many of the barriers described in this response to be addressed and help achieve the ambitious but achievable target of **PBS access within 100 days of ARTG registration.**

[37] Measuring the Impact of Pharmaceutical Innovation in Australia1998–2018: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2020/11/Med-Aus-Lichtenberg-Report-12pg-Booklet.pdf