evohealth

March 2026

THE COST OF COMPARISON

When the benchmark becomes the barrier

Evohealth acknowledges that we work on the traditional lands of many Aboriginal clans, tribes, and nations.

We commit to working in collaboration with Aboriginal and Torres Strait Islander communities and peoples to improve health, emotional and social well-being outcomes in the spirit of partnership.

About **Evohealth**

The delivery of healthcare is complex.
Our focus is not.

Better health for all.

THE COST OF COMPARISON

When the benchmark becomes the barrier

CONTENTS.

ABOUT **THIS REPORT**

Background

This report was prepared by Evohealth as an independent analysis. Commissioned by Johnson & Johnson Innovative Medicine (Janssen-Cilag Pty Ltd), the report examines how comparator selection within Australia's Health Technology Assessment (HTA) process influences timely access to innovative medicines.

The research explores the implications when medicines under evaluation are compared to the least expensive alternative, when it is not the therapy most commonly replaced in clinical practice. This is referred to as the lowest cost comparator (LCC). This practice can lead to lower price benchmarks, delayed reimbursement decisions, and reduced availability of new treatments for Australian patients.

To develop this report, Evohealth used a mixed-methods approach, combining both qualitative and quantitative research. Key activities included:

- Survey of market access directors from innovative pharmaceutical companies to quantify how comparator selection affects portfolio and launch decisions in Australia.
- Qualitative interviews with policymakers, industry representatives, and HTA experts to capture policy insights, and real-world examples.
- Roundtables with clinicians, patients, carers, and advocacy organisations to understand the broader health, equity, and psychosocial impacts of delayed or limited access to innovative medicines.
- Desktop research to review Australia's policy settings against global best practice.

The findings provide a comprehensive evidence base alongside the recommendations from the *2024 Health Technology Assessment Policy* and *Methods Review* provided by the Health Technology Assessment Policy and Methods Review Reference Committee.

Evohealth acknowledges and thanks the many participants and organisations who contributed their time, experience, and perspectives to this project. Their insights were critical to understanding how comparator-related decisions shape access to innovation in Australia. We also acknowledge Johnson & Johnson Innovative Medicine Australia for funding this research and supporting an evidence-based discussion on policy reform.

ACKNOWLEDGEMENTS

Patient roundtable participants

MEREDITH CUMMINS
Chief Executive Officer
NeuroEndocrine Cancer Australia

CHRISTINE COCKBURN
Chief Executive Officer
Rare Cancers Australia

ELENA SUTCLIFFE
Consumer Engagement Coordinator
Dementia Australia

MONIKA BOOGS
Chief Executive Officer
Painaustralia

MICHELE ROBBINS
Chair
Patients Australia

LOUISE HEALY
Education and Advocacy Manager
Rare Voices Australia

WAYNE MASSUGER
Head - Quality, Research and Support Programs
Crohn's and Colitis Australia

DR **AARON SCHOKMAN**
Research Fellow
University of Sydney

PAIGE PRESTON
General Manager – Policy, Advocacy and Prevention
Lung Foundation Australia

PAM HUBNER
Committee Member
Brain Tumour Alliance Australia

MONICA FERRIE
Chief Executive Officer
Genetic Support Network Victoria

GERRY TYE
Sydney Support Group Lead
Brain Tumour Alliance Australia

MARGARET MACDONALD
Dementia Advocate
Dementia Australia

One participating organisation has requested to remain anonymous.

Clinician roundtable participants

PROFESSOR **JON IREDELL**
Professor Medicine and Microbiology (conj.) Senior Staff Specialist
University of Sydney, Westmead Hospital

PROFESSOR **CHRISTOPHER WARD**
Clinical Haematologist
Royal North Shore Hospital

PROFESSOR **MICHAEL WOODWARD**
Director, Dementia Research and Senior Clinician, Memory Clinic
Austin Health

PROFESSOR **CHRISTINE JENKINS AM**
Head of Respiratory Group
The George Institute for Global Health, UNSW Sydney

PROFESSOR **ADAM JAFFÉ**
Professor of Paediatrics Head, Discipline of Paediatrics and Child Health, School of Clinical Medicine Consultant in Respiratory Medicine
UNSW Sydney, Sydney Children's Hospital

EXECUTIVE **SUMMARY**

Ensuring timely, equitable, affordable access to clinically effective therapies remains a central objective of Australia's health system. The National Medicines Policy (NMP) [1] enshrines this commitment, a priority recently reinforced by the Minister for Health:

> *I want to see those medicines that are coming onto the market... extraordinary medicines that, frankly, we wouldn't have imagined 10 or 20 years ago... I want to see them under the PBS as quickly as possible, so you don't have to pay [that sort] of money.*
>
> **- Mark Butler MP, Minister for Health, Ageing and Disability, Press conference, Friday 21 March 2025** [2]

Despite this ambition, Australia currently faces significantly longer reimbursement timelines than comparable Organisation for Economic Co-operation and Development (OECD) countries. The average time from Therapeutic Goods Administration (TGA) approval to Pharmaceutical Benefits Scheme[1] (PBS) listing is widely reported at around 400 days, more than twice as long as in the United Kingdom, and close to four times longer than in Japan. [4] More recent analysis indicates Australia's delay now exceeds 700 days. [5] This access lag provides important context for understanding the consequences of comparator selection, a critical component of Australia's Health Technology Assessment (HTA) system.

HTA involves evaluation of the quality, safety, clinical effectiveness and cost effectiveness of new therapies. [6] This framework requires economic assessments to compare the costs and health outcomes of an innovative medicine, relative to the therapy or therapies most likely to be replaced in clinical practice. [7, 8] According to the Professional Society for Health Economics and Outcomes Research (ISPOR) Good Practice Task Force, comparator selection should reflect real-world use, including similarities in intended use, place in therapy, method of administration and expected clinical outcomes. [9]

Comparator selection should reflect real-world use, including similarities in intended use, place in therapy, method of administration and expected clinical outcomes. [9]

The choice of comparator shapes every part of HTA evaluation, influencing clinical and economic comparisons, the valuation of incremental benefit and the commercial viability of a PBS listing. Although comparator selection represents only one component of a broader and complex assessment process, its impact is disproportionately large.

[1] The Pharmaceutical Benefits Scheme (PBS) is an Australian Government program that subsidises the cost of medicines across a range of medical conditions. After undergoing HTA, medicines approved for PBS subsidy are listed on the PBS Schedule and can be provided at subsidised prices to patients in community and hospital settings. [3]

The Pharmaceutical Benefits Advisory Committee[2] (PBAC) Guidelines reflect this intent:

> *Where there is more than one comparator, the main comparator should be the therapy that prescribers would most replace with the proposed medicine.*
>
> **- PBAC Guidelines v5.0 (2016), p.13** [8]

Despite this clear directive, comparator selection, in Australia, has diverged from this principle, with implications for the wider equilibrium of the health system. Comparator selection is no longer consistently functioning as intended, instead driving price outcomes, access delays and broader market behaviour. These pressures are most visible in how comparators are defined and applied during assessment, particularly the substitution of clinically appropriate comparators with lowest cost alternatives, a practice that has increased over the past decade.

For the first time, this report captures evidence that examines the true impact of what is commonly referred to as the lowest cost comparator (LCC). The findings are informed by data from an industry-wide survey of innovative medicine companies, interviews with government, industry and independent stakeholders, as well as roundtables held separately with clinicians and patient advocates. These data reveal that the rigid application of LCC is breaking the link between price and value and compromising the economic integrity of our HTA system. This is also actively discouraging global investment, further weakening Australia's position in global launch sequences, and delaying patient access.

Comparator substitution is shaping HTA outcomes

Comparator substitution is a growing and systemic feature of PBAC evaluations, with clinically relevant, sponsor-nominated comparators frequently replaced with the LCC during PBAC assessment. This pattern is observed across different therapeutic areas and types of submissions, indicating a broad shift rather than isolated cases. [11]

Four in five sponsors reported comparator substitution had occurred on submissions in the past five years. Of the substitutions made,

- **100 per cent** were for the lowest cost alternative,
- **95 per cent** affected new medicines seeking first time listing on the PBS. [11]

Because LCCs are typically legacy therapies subject to significant historical price erosion, their application reduces the assessed incremental value of new medicines. This can shift submissions into commercially non-viable territory. [9] Several sponsors reported that, where PBS listing becomes commercially unfeasible, they are increasingly turning to private-only market launches.

[2] The Pharmaceutical Benefits Advisory Committee (PBAC) is an independent, statutory committee responsible for assessing new medicines to determine whether they qualify for the PBS. [3] The Committee are also responsible for assessing vaccines to determine whether they are eligible for subsidised access through the National Immunisation Program. [10]

This shift accelerates reliance on unsubsidised access routes and creates significant risks for equitable patient access, a pillar of Australia's health system.

With use of the LCC becoming routine, it now exerts a much stronger influence on PBS price discussions and listing decisions than in the past.

> *A submission requested that a new strength be [compared] against the currently reimbursed strength, of the same molecule, with identical clinical outcomes. Instead, [the Committee] insisted on the LCC, another medicine and rarely used lower cost product.*
>
> **- Survey respondent** [11]

LCC pricing is constraining access and commercial viability

The shift toward LCC is directly shaping price negotiations and PBS listing outcomes. Sponsors describe circumstances where, even after a positive PBAC recommendation, LCC-anchored price expectations made it commercially non-viable to proceed to listing. Almost all survey respondents also agree that the LCC approach undervalues clinical innovation, with 90 per cent reporting that it discourages investment in Australian HTA submissions. [11]

100 per cent of respondents who did not proceed to price negotiations after positive PBAC recommendation stated LCC-related pricing was a significant factor. [11]

reported it to be the **sole reason** they did not proceed. [11]

reported it to be a **major factor** in their decision not to proceed. [11]

The dynamics of LCC interact with international pricing frameworks. The emergence of the United States' Most Favoured Nation (MFN) policy increases the risk that Australian reimbursed prices could influence willingness-to-pay thresholds of government bodies in other countries, making the case for pursuing Australian listings affected by LCC difficult to justify.

> *The world is small and other countries are looking. Where we have been able to agree to lower prices in the past in Australia, in a MFN world, that will no longer happen.*
>
> **- Director of Market Access**

Comparator selection is reshaping global launch behaviour

The cumulative effect of lowest price comparator substitution is altering both local and global launch strategies. Companies report there is a growing impact on Australia's position in global sequencing.

These decisions are affecting early access, patient outcomes and Australia's attractiveness as a destination for research, clinical trials and investment. Importantly, they are now being felt directly by patients and clinicians.

Comparator selection has a **moderate to extreme impact on:**

AUSTRALIA

73% Local affiliate decisions to **launch new medicines** in Australia. [11]

77% Local affiliate decisions to **launch new indications** in Australia. [11]

GLOBAL

73% Global or head office decisions to **launch new medicines** in Australia. [11]

73% Global or head office decisions to **launch new indications** in Australia. [11]

> *If LCC impacts the lead indication for a new molecule, we may not launch this product in Australia.*
>
> **- Survey respondent** [11]

Patients and clinicians are experiencing widening inequities

Delays to access and decisions to not submit or proceed to listing on the PBS contribute to increasing reliance on older therapies or private market options, that many patients cannot afford. Patient groups and clinicians highlight significant personal and financial strain arising from these access barriers. Advocates described several extreme cases to illustrate the severity of impact.

> *People chose to end their lives rather than go back to the darkness of uncontrolled migraines.*
>
> **- Patient advocate**

Participants in our patient roundtable emphasised the scale of this concern:

Nine in ten patient advocates agree that people they represent do not have access to innovative medicines to meet their clinical needs equivalent to what is available in other countries. [11]

Clinicians also report that they are increasingly unable to offer best practice therapies and are seeing growing misalignment between PBS funded treatments and international standards.

> *We would like to be able to practise in the same way as doctors in the United Kingdom and most European countries, but we're now at risk of being five years plus behind with drug access.*
>
> **- Professor Christopher Ward, Clinical Haematologist**

They also reported broader implications for clinical decision making, system efficiency, and patient experience.

> *Some [patients] can afford $60,000 [out-of-pocket costs each year], but it is beyond reach for the majority. It affects our prescribing, how we manage patients, it affects how patients feel themselves and their autonomy. They blame themselves for not sacrificing their own pennies and superannuation. I think it's perverse.*
>
> **- Professor Michael Woodward, Geriatrician**

These challenges extend to access to research and clinical trials, as comparator misalignment can put our standard of care further behind. This will prevent clinical trials from being launched in Australia. Our analysis reveals that this has already begun, with 45 per cent of sponsors reporting a moderate to extreme impact on local and international willingness to invest in Australian clinical trials. [11] Taken together, these pressures are contributing to a broader decline in trust and predictability across the HTA system.

Declining trust and predictability in HTA processes

A recurring theme in our research was reduced confidence in the transparency and consistency of comparator decision making. Stakeholders note a marked shift in comparator practices over the past decade, without corresponding updates to PBAC Guidelines or public explanation.

> *"There has clearly been a step change... [after] 2017, [the system] shifted totally to the LCC, irrespective of where it sits in clinical practice."*
>
> **- Stakeholder interview**

This erosion of trust limits effective planning for both government and industry and undermines the collaborative foundations of the NMP. These conditions reinforce the need for clear, coordinated reform to restore confidence and ensure comparator selection functions as intended.

The road to reform

Our evidence confirms that comparator selection exerts influence far beyond its methodological role, driving price outcomes, launch sequencing, and Australia's global competitiveness. It is not surprising. This issue has been consistently raised over the past five years: first in the 2021 report, *The New Frontier – Delivering better health for all Australians and* its preceding Parliamentary Inquiry, and then subsequently in *Accelerating Access to the Best Medicines for Australians Now and into the Future*, the final report in 2024 from the HTA Policy and Methods Review. [12-14]

The reform journey has been long. Despite the current HTA Review Implementation Advisory Group prioritising some relevant recommendations, clinicians, patient advocates and the innovative medicine sector are weary, and waiting.

While the final report of the HTA Review explicitly identified the need for greater clarity in comparator selection, the path forward remains contested. Of relevance, Recommendation 40 proposed updating the PBAC Guidelines to confirm when multiple alternative therapies exist, and which alternative therapy should be selected as the main comparator. In the report, Elizabeth de Somer of Medicines Australia offered a different approach, legislative amendment to the *National Health Act 1953 (Commonwealth)* (the Act) to require that the PBAC only consider the therapy (or therapies) most likely to be replaced in clinical practice. [14] With two alternatives, the current path forward for this critical issue remains unclear.

Patients, clinicians and the innovative medicine sector need this to be solved. To move the issue of LCC forward, Evohealth has identified a phased roadmap of short, medium, and long-term actions over the next five years. These actions are designed to resolve a longstanding and contentious HTA issue and ensure that Australia's methodologies are economically valid and scientifically robust. This reform is needed as a sign of good faith and to signal to the global life sciences sector that Australia is a viable environment for next generation medical breakthroughs.

Short term: Contemporise HTA practices in the next 12 months

The reviews of the past five years have revealed that our system overwhelmingly struggles to keep pace with evolving medicines and global best practice, often relying on legacy methodologies and evidence rules that undermine the accuracy and credibility of assessments. Amongst this, anchoring a modern therapy to a comparator that it will not replace in clinical practice produces a fundamentally flawed economic conclusion, particularly when the comparator is not standard of care, or is obsolete.

Four key areas are identified for immediate action, with Actions 1 and 2 designed to be implemented together.

ACTION 1

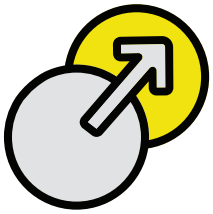
Align the PBAC Guidelines with clinical reality to restore economic validity.

The Guidelines must be urgently amended to reaffirm their original intent, that the default comparator is the therapy most likely to be replaced in clinical practice. This will reinstate alignment with current clinical practice and articulate how the comparator therapy is determined. These changes, along with Action 2, are critical to ensure that the assessment captures the true incremental value of innovation and to restore the validity of Australia's HTA framework.

ACTION 2

Amend the *National Health Act 1953 (Commonwealth)* to reference the PBAC Guidelines.

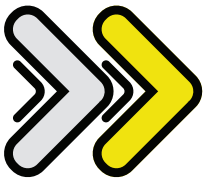
Strengthening the governance of the PBS listing process and PBAC assessment requires a clear legislative link between the Act and the Guidelines amended in Action 1. Formally referencing the Guidelines within the Act, regulations or other related legislative instruments will ensure that decision-making is legally bound to a transparent and economically valid framework. This protects the integrity of the public process by preventing administrative discretion from drifting away from established and agreed best practice now and for any future guideline amendments.



ACTION 3

Transition to a PICO (Population, Intervention, Comparator, Outcome) model where the comparator is agreed with the PBAC during the early stages of the submission pathway.

A partial solution for LCC has been proposed in Recommendation 32 of the *HTA Policy and Methods Review*. Formalising the PICO framework process will ensure that the agreed comparator accurately reflects contemporary practice, and economic evaluations are grounded in real-world treatment pathways. Up front and early agreement with the PBAC on the PICO, as well as clinician input, will be critical to validate the accuracy of the selected comparator. This, alongside strengthened reporting and appeal mechanisms, will support process transparency.



ACTION 4

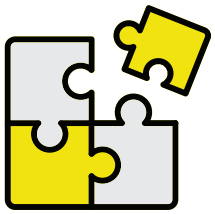
Fast-track implementation of other relevant HTA Review recommendations.

The final report of the HTA Review includes other suggested amendments to HTA methodology to strengthen equitable access to medicines and the alignment of decision-making with global best-practice health economic methodologies. This includes recommendations that improve processes for cost-minimisation submissions, which sponsors identified as most affected by comparator selection issues. [11] This includes: [14]

- **Recommendation 7:** Develop a streamlined pathway for submissions using cost-minimisation analysis.
- **Recommendation 32:** As per Action 3, strengthen PICO development to consider criteria important to patients and clinicians.
- **Recommendation 41:** Investigate mechanisms to differentiate cost-minimisation submissions based on the proportionate benefit and relative cost.
- **Recommendation 42:** Clarify when higher prices for health technologies may be reasonable to accept.

Medium term: Invest in Australia's future over the next two years

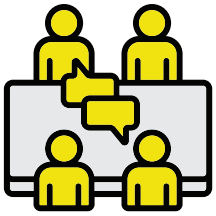
Medicines are the most common health intervention. [1] If we want Australia to be healthier, wealthier and more productive, it follows that PBS investment must increase. However, this will yield limited returns if the underlying value assessment remains distorted by structural barriers, including statutory pricing reductions. Restoring the integrity of the assessment requires decoupling administrative price events from the evaluation of clinical benefit. To repair this value proposition, we propose three structural adjustments.



ACTION 5

Embed flexible approaches for medicines responding to high patient needs, particularly where comparator prices have been eroded from ongoing pricing policies.

The HTA Review recognised a need to improve the pathways and processes for listing therapies with high added therapeutic value on the PBS. This should enable the use of shadow pricing, where a notional and clinically appropriate comparator price is applied to the listed price in circumstances where it no longer reflects real-world value. Additional support measures for these submissions could include fee waivers or adjusted evidentiary requirements to ensure that economic evaluations are not anchored to artificially low comparator prices.



ACTION 6

Initiate structured Government-industry dialogue on the interplay between Statutory Price Reductions (SPRs) and innovation.

In a value-based assessment system, there is a complex interplay between the principles of HTA and systemic and ongoing price reduction policies. Understanding how these two approaches to price setting interplay in the Australian medicine sector is imperative. This should commence with data collection to understand the impact of price cuts and any unintended consequences for launching medicines in Australia.

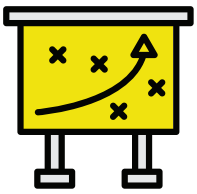
ACTION 7

Increase investment in medicines by aligning PBS funding with the growth in health needs.

As the most accessed health intervention, medicines and vaccines play a central role in our health system. Yet, in recent years, PBS net spending has remained flat, with updated analysis showing a contraction in the last 12 months. [15] Additional investment and indexation is needed to ensure the PBS remains fit for purpose and can sustain access into the future.

Long term: Elevate Australia's global position in the next five years

Remediating comparator selection practices is an essential starting point, but it must be embedded within a broader agenda beyond HTA. To elevate Australia to a priority destination for global investment, we need a unified vision that signals our willingness to value and invest in innovation. Ultimately, a thriving life sciences sector is an effective pathway to secure the health of our nation and guarantee patient access to the next generation of care. To secure sustainable access to innovation, we must shift our focus to building a globally competitive life sciences sector. One key action can ensure we work towards this goal.



ACTION 8

Co-design a national life sciences sector strategy.

This roadmap will ensure our ecosystem is not only scientifically rigorous but economically attractive to the global market. Reform of HTA methodologies is a tactical approach within a broader life sciences sector strategy. Bringing together Government, the innovative medicines and medical technology sectors, and research partners to build this bold, end-to-end plan for Australia's life sciences ecosystem is crucial. Otherwise, we risk continuing to fix the symptom and not the cause.

Implementing this phased roadmap will restore the economic integrity of Australia's HTA system. In ensuring funding decisions are based on accurate clinical and economic signals, we will rebuild trust, improve predictability for investment, and strengthen Australia's life sciences sector. Closer partnership between Government, industry, clinicians and patients is essential to protect the PBS and deliver timely, equitable access to effective therapies. Australia must act now to keep pace with global innovation and secure long-term benefits for patients and the health system.

OVERVIEW OF EVOHEALTH SURVEY DATA

40 innovative pharmaceutical companies were **invited to participate** in the sponsor survey: **25 responded**

TRANSPARENCY AND PREDICTABILITY CONCERNS

70% **agree comparator selection often lacked transparency.** [11]

THE SCALE OF COMPARATOR SUBSTITUTION

80% **experienced comparator substitution** in the past five years. [11] Of substitutions made:

100% **were for the lowest cost alternative.** [11]

95% **affected medicines seeking first time listing on the PBS.** [11]

100% who did not proceed to price negotiations after positive PBAC recommendation **stated the LCC-related price was a significant factor.** [11]

29% **LCC was the sole reason they did not proceed.** [11]

+

71% **LCC was a major factor in their decision not to proceed.** [11]

16% **have intentionally selected the LCC** in their submissions in the last five years. [11]

IMPACTS ON LAUNCH, INVESTMENT AND INNOVATION

95% **agree that the LCC approach undervalues clinical innovation.** [11]

90% **report that LCC practices discourage investment in Australian HTA submissions.** [11]

Nine in ten agree comparator selection affects the **timing of launch or indication** sequencing in Australia. [11]

Four in five identified comparator selection has **moderate to severe impacts** on **Australia's position in sequencing** compared to other markets. [11]

45% report comparator selection bears a **moderate to extreme impact** on local and international **willingness to invest** in Australian clinical trials. [11]

100% **agree major reform** to comparator selection is required. [11]

An economic evaluation in HTA is only valid if it measures the new medicine against what it displaces.

MESSAGES TO THE **MINISTER**

> *We have a responsibility as a well-heeled country to have a leadership position in medicine and science. We should be showing the way, rather than being so reactive. This type of work needs to be much more proactive and much less reactive. It takes a lot of political courage.*
>
> **- Professor Jon Iredell, Infectious Diseases Physician and Clinical Microbiologist**

> *Australia could be healthier, wealthier and wiser if we took the opportunities in front of us right now. This is a good opportunity to bed down your legacy.*
>
> **- Christine Cockburn, CEO, Rare Cancers Australia**

> *Look at the speed of the system. Our patients are falling so far behind their peers elsewhere. We understand the need to run a cost-efficient effective system, but it's not fit-for-purpose when it comes to many of the cancer drugs.*
>
> **- Professor Christopher Ward, Clinical Haematologist**

> *Our communities want change. They want something different to improve their outcomes and quality of life. From a productivity perspective, it makes sense.*
>
> **- Paige Preston, General Manager Policy, Advocacy and Prevention, Lung Foundation Australia**

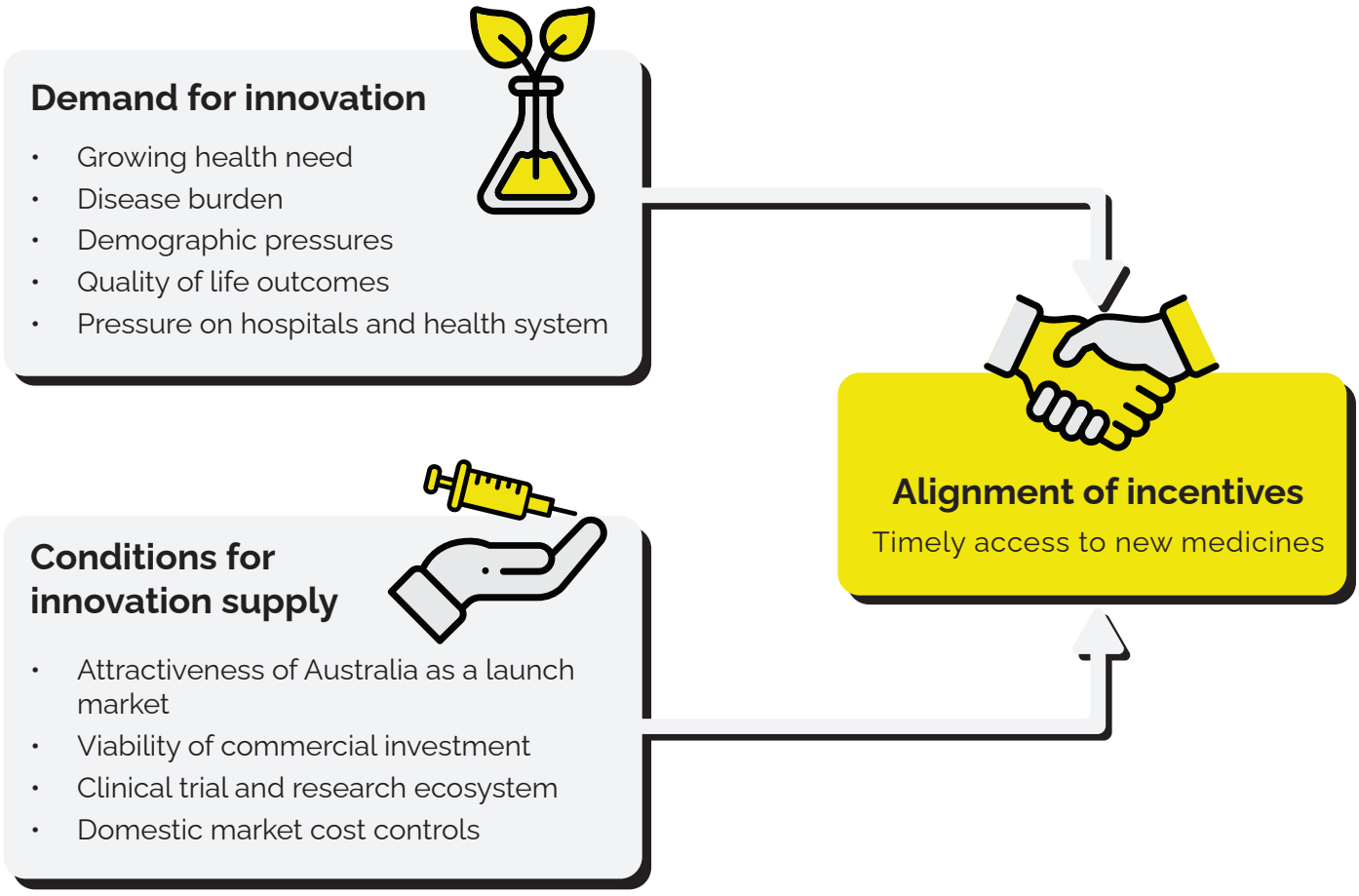
> *We're talking about lives here – all Australians. If we're going to have equitable access for all Australians, we need change.*
>
> **- Meredith Cummins, CEO, Neuroendocrine Cancers Australia**

> *It doesn't have to be better health or economic outcomes. We can be smart about both. We can be economically responsible and improve patient outcomes. Getting this right helps our proactive and preventative health strategy. That is the future path Australian health needs.*
>
> **- Monica Ferrie, CEO, Genetic Support Network Victoria**

AUSTRALIA'S **MEDICINES ENVIRONMENT**

Australia's ability to ensure timely access to effective medicines is shaped by the interaction between the health system's demand for innovation and the factors that enable industry to deliver it for patients. On the demand side, medicines play a central role in preventing disease, improving outcomes and reducing pressure on hospitals, while demographic change and rising chronic disease continues to increase the need for new interventions. On the supply side, Australia's reliance on global research pipelines and the structural features of the domestic market influence how and when companies develop, launch and price new therapies. Figure 1 summarises why aligning these clinical and commercial factors is essential, as timely access depends not only on the health system's need for innovation but also on creating a viable environment for research, development and reimbursement. [16]

Figure 1: How demand and supply interact to shape access to new medicines



Source: Evohealth analysis, adapted from [16]

The role of innovation

Innovative medicines represent advances in the prevention, diagnosis and treatment of disease that improve patient outcomes or transform standards of care. [17] These can include first-in-class therapies introducing new mechanisms of action, or next-generation medicines that improve safety, tolerability or convenience. [18] Beyond their clinical benefit, innovation in medicines delivers broader social and economic value by reducing hospitalisations, improving quality of life (QoL) and supporting greater workforce participation, as shown in Figure 2. [19]

Figure 2: How innovative medicines generate value

Innovative medicines deliver system-wide value

Improved survival

Introduction of new medicines to the PBS between 1996 and 2013 was associated with over **359,000 fewer years of life lost before age 85.**

Reduced hospital care

In 2019 alone, **new medicines** available between 1994 and 2011 was associated with **2.48M fewer bed days**, yielding **savings of $5.97B.**

Improved quality of life

Introduction of new medicines was associated with a **20 per cent reduction of fatal disease** burden between 2003-2015 and enabled patient-reported quality of life gains.

Higher workforce participation

Improved health from better prevention, treatment and diagnosis enables **170,000 more Australians to participate in the workforce.**

Social + economic gains

COVID-19 vaccines are estimated to have yielded **$181B in positive economic benefit for Australia** through preserving education ($26B), tourism ($28B), and employment (~142,000 jobs), equating to $259B in Government savings.

Source: Evohealth analysis, adapted from [17, 19-22]

In recent decades, the treatment landscape has become more complex. Biomedical innovation has delivered major breakthroughs in conditions once considered untreatable, such as targeted cancer therapies, biologics for autoimmune diseases and gene therapies for rare and inherited disorders. [23] These advances have reshaped the expectations of patients, clinicians, and health systems, establishing a new baseline for survival, functioning, and QoL. [24] However, these gains are only sustained when reimbursement systems evolve and recognise the true value of innovation. When this does not occur, investment can stall and treatments for a condition or therapeutic areas can lag patient or population need. This is illustrated in the antimicrobial pipeline example on the following page.

A cautionary example of market failure

The antimicrobial pipeline demonstrates the dire consequences of market failure. Despite an alarming increase in antimicrobial resistance, global investment in developing and commercialising new antimicrobials has stalled. This is, in large part, because reimbursement mechanisms do not reward their true societal value. [25] Fifteen of the 18 major innovative medicine companies have exited the field, and some smaller companies have collapsed entirely. [26] Governments worldwide are now scrambling to rebuild incentives. [27, 28] Evohealth's report, *Fighting superbugs: The Path Forward*, highlighted that this market failure has resulted in fewer novel agents, increasing reliance on ageing therapies and ultimately worsened public health risk. It serves as a cautionary example, illustrating why aligning reimbursement with value is critical for sustaining innovation. [26]

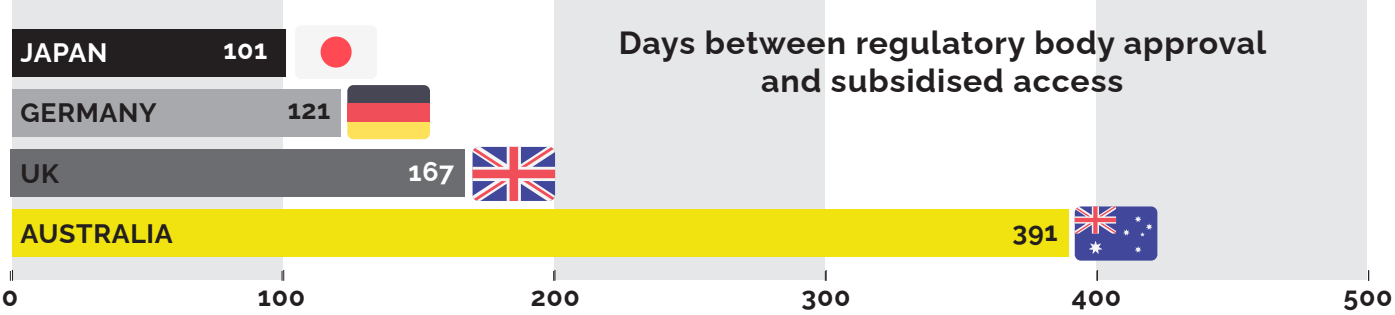
Medicines are both essential healthcare interventions and commercial products that require a viable market to support discovery, development and launch. Bringing such medicines to patients depends on timely and sustainable reimbursement pathways that appropriately recognise value. [29] When reimbursement systems undervalue innovation, patient access is restricted, and countries become less attractive for clinical trials, research partnerships, and future launches. [30] For Australia, this challenge is amplified by its position in the global pharmaceutical market, where structural features of a small, regulated system heavily influence launch timing and investment decisions.

Australia within the global pharmaceutical market

To understand the significance of comparator selection, it is essential to first understand Australia's position globally. Australia accounts for around one per cent of global medicine sales. [31] Although small in size, the strict cost controls, and subsequent listing price is important to global companies. This price can resonate around the world and impact larger markets, ultimately shaping how medicines are launched. Despite being ranked 13th in the world for per-capita spending on healthcare, Australia's combination of a relatively small population, successive reductive pricing policies and complex reimbursement processes means that global companies often launch medicines in Australia later than in larger markets like the United States (US). [32, 33]

The average time from Therapeutic Goods Administration (TGA) approval to Pharmaceutical Benefits Scheme (PBS) listing is approximately 391 days, compared to only 101 days in Japan, 121 days in Germany, and 167 days in the United Kingdom (UK). [4, 34] More recent analysis, however, indicates Australia's delay now exceeds 700 days. [5] Between 2016 and 2021, Australia ranked 16th among Organisation for Economic Co-operation and Development (OECD) nations for the number of reimbursed new molecular entities (NMEs). During this period, Australia reimbursed 27.2 per cent fewer NMEs than the OECD average of 101.5, and 80.5 per cent fewer than leading nations, such as Germany, the UK and Japan. [35] This ongoing lag in access to medicines for Australian patients is highlighted in Figure 3.

Figure 3: International access timelines for new medicines following regulatory approval



Source: Evohealth analysis, adapted from [4]

Australia's 2024 *Health Technology Assessment Policy and Methods Review* confirms this delay, indicating new medicines demonstrating superiority require more than two submissions, with only 50 per cent listed on the PBS within 22 months of TGA approval. [14] These findings highlight ongoing systemic issues, which are occurring, in part, due to structural challenges underpinning Australia's approach to evaluating and reimbursing new therapies. Such challenges include comparator selection, valuation of incremental benefit and price setting mechanisms. [36] These issues sit at the core of Australia's Health Technology Assessment (HTA) framework.

HTA and medicines access

HTA is the process used to evaluate new health interventions such as medicines, devices, and procedures. HTA determines how new medicines are evaluated and funded, and is essential to ensuring that Australians have affordable access to effective treatments while maintaining sustainable public health expenditure. It promotes equity by applying rigorous, consistent, evidence-based criteria to all funding decisions. [37] However, this methodological rigour also contributes to longer assessment timelines in Australia, compared with other systems, challenging timely and equitable patient access. [14]

How Australia evaluates medicines and why comparator choice matters

Before a new medicine can be publicly funded in Australia, its value must be assessed through the HTA process. It considers clinical effectiveness, safety, and cost-effectiveness to determine whether the medicine or vaccine represents value for money (Figure 4). [6] This assessment establishes whether the therapy improves outcomes, compared with existing options, or delivers equivalent health benefit at lower cost. One of two economic evaluation approaches are used in this assessment:

- Cost-effectiveness analysis is used when clinical evaluation determines that a medicine has superior efficacy or safety to its main comparator, and is also more expensive. [7] This analysis determines whether the additional health gain is worth the additional cost. [7] This analysis can also be conducted where the medicine is therapeutically inferior and less expensive than its main comparator. [7]
- Cost-minimisation analysis is used when the medicine provides the same or superior efficacy or safety to its main comparator, and is less expensive. [7] This analysis determines whether equivalent health outcomes can be delivered at the same or lower cost. [7]

In practice, this means the way a new medicine is compared becomes the foundation of its evaluation.

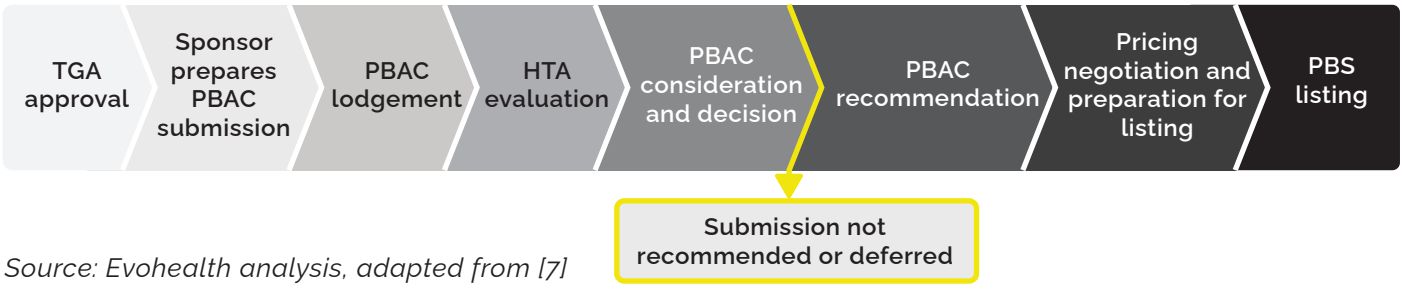
Figure 4: Core components of HTA

Source: Evohealth analysis, adapted from [7]

In Australia, HTA is required to inform decisions for medicines to be listed on the PBS. [10] The Pharmaceutical Benefits Advisory Committee (PBAC) is the independent statutory body responsible for assessing new medicines under section 101 of the *National Health Act 1953 (Cth)* (the Act). [38] According to the Act, the PBAC must be satisfied that the medicine under evaluation provides a clinical advantage or it is no more costly than existing therapies for comparable benefit. [38] The PBAC Guidelines further outline how therapies with non-inferior efficacy and equivalent safety profiles can be considered for cost-minimisation, provided they do not increase costs to the health system. [7] This comparative evaluation underpins PBAC decision making and determines whether a medicine represents value for money for public reimbursement.

Figure 5 summarises the key steps in Australia's HTA and PBS listing pathway.

Figure 5: Overview of the Australian HTA and PBS listing process



Source: Evohealth analysis, adapted from [7]

Comparator determination occurs during PBAC's evaluation and consideration of the submission. While sponsors nominate a comparator in their initial submission, PBAC may question, redefine or replace it. When comparator substitution occurs, it becomes a decisive point in the assessment and a major source of uncertainty. it is important to note that this occurs after the sponsor has completed the clinical and economic modelling, written the submission and paid substantial fees, which can be up to $270,315 for Category One submissions. [39] The consequences of comparator substitution are examined in the next section.

Comparators as the anchor of HTA

Every new medicine must be compared against an existing therapy, or group of therapies, to determine its relative value. [8] The PBAC Guidelines specify that the main comparator should be the therapy most likely to be replaced in clinical practice. [8] This choice anchors both the clinical evidence and the economic modelling, shaping how costs, outcomes, and value for money are interpreted, and the findings of the evaluation. [7]

In practice, industry reports that comparator selection has increasingly shifted towards the use of the lowest cost comparator (LCC), regardless of alignment with real-world clinical practice. [36] The LCC is usually a therapy that has been off patent for many years, may be rarely used in contemporary clinical practice, and/or has experienced significant price erosion from cost-containment policies. [36]

Anchoring an assessment to this low-priced benchmark reduces the estimated incremental benefit relative to current practice, which can lower the assessed value of a new therapy and shape subsequent price expectations. [40] Where outcomes are assumed equivalent, anchoring to a low benchmark leaves little scope to demonstrate a meaningful cost advantage, constraining feasible pricing. Both scenarios can result in commercially nonviable price setting, delaying or preventing PBS listing. [41] In turn, this can lead to delayed patient access, or worse still, withdrawal from PBS listing. Ultimately, treatment choice is reduced, alongside the availability of new therapeutic options in Australia.

Comparator selection in Australia's HTA reform landscape

The calls for examining the impact of LCC are not new, and critical work is currently underway. Key milestones along this journey, including those relating to comparator selection, are summarised in Figure 6. Comparator selection was first raised in the *New Frontier – Delivering better health for all Australians* report, handed down by former Minister of Parliament (MP) Trent Zimmerman, Chair of the Committee, and Deputy Chair of the Committee, Dr Mike Freelander MP. [12] Following this and the *2022-2027 Strategic Agreement* between Medicines Australia and the Government, the HTA Policy and Methods Review (HTA Review) was commissioned to examine whether Australia's HTA system remains fit for purpose. [13, 14]

The HTA Review was initiated in response to long-standing concerns from patients, clinicians, and industry about delays in accessing new therapies, limited transparency in decision-making, challenges in assessing complex technologies and increasing misalignment between HTA processes and contemporary clinical practice. [14] Comparator selection, alongside many other structural features of Australia's HTA system, was recognised as impeding equitable and timely patient access. [14]

Figure 6: Milestones in Australia's HTA reform landscape, 2020 to 2025.

2020

August: Parliamentary Inquiry into approval processes for new drugs and novel medical technology referred to the Standing Committee on Health, Aged Care and Sport.

2021

September: 2022-2027 *Strategic Agreement* is signed between Commonwealth and Medicines Australia.

- Commonwealth agrees to support and resource a HTA policy and methods review.

November: In response to Parliamentary Inquiry, *The New Frontier - Delivering better health for all Australians* report delivered by MPs Trent Zimmerman and Dr Mike Freelander.

- Recommended reform to improve comparator selection flexibility, and to introduce a comprehensive scoping process to inform comparator selection prior to submission.

2022

October: HTA Policy and Methods Review Reference Committee established, HTA Review commences.

2024

September: HTA Policy and Methods Review final report delivered, *Accelerating Access to the Best Medicines for Australians Now and into the Future.*

- Recommendation 40: update PBAC Guidelines to clarify comparator selection.
- Alternative recommendation: update *National Health Act* to require PBAC select the therapy most likely to be replaced in clinical practice.

2025

January: Establishment of the HTA Review Implementation Advisory Group (IAG).

- Includes: government, academia, industry, clinicians and consumer representatives.
- Purpose: prioritise and sequence the 50 recommendations into a roadmap for reform.

August: Comparator selection identified as one of five priority reform areas in IAG's Interim Report 6.

September: Mark Butler MP announces priority review of comparator selection as part of reform activities.

October: Draft HTA Reform Roadmap released for consultation.

Source: Evohealth analysis, adapted from [12, 14, 42-44]

The main priorities of the HTA Review include improving access for underserved populations, reducing delays between TGA approval and PBS listing, strengthening stakeholder engagement and modernising the evaluation of complex technologies. [14] In response to its findings, 50 recommendations proposed to improve transparency, efficiency and equity in the HTA process. [14] This included clarity in comparator selection processes.

Throughout the final report of the Review, comparator selection emerged as a particularly contentious issue. Industry submissions argued that PBAC increasingly selects the LCC even when it is not the therapy most likely to be replaced in clinical practice. The Review acknowledged these concerns but concluded that it did not reflect the PBAC's approach. [14] Recommendation 40 therefore proposed updating the PBAC Guidelines to provide clearer, more consistent direction. However, an alternative recommendation from Elizabeth de Somer of Medicines Australia was also put forward. This called for legislative amendment to the *National Health Act 1953* (Cth) to require PBAC to consider only the therapy (or therapies) most likely to be replaced. [14]

Following the Review, the Commonwealth Government established the HTA Review Implementation Advisory Group (IAG) to oversee the development of a roadmap for reform. The IAG's task is to prioritise and sequence the Review's 50 recommendations, assess feasibility and identify measures of success. Along with the Minister for Health, the IAG have identified review of comparator selection language in the PBAC Guidelines as one of five priority reform areas for action, with outcomes expected in 2026. [44, 45]

This signals clear recognition that improving comparator selection is central to ensuring the HTA system continues to deliver timely, affordable access to effective medicines. The success of this reform is critical. Without it, Australia risks continued delays in access, reduced competitiveness as a launch market and a diminished ability to attract next-generation therapies. [46]

The issue behind the analysis

Although the HTA Review acknowledged concerns raised by industry, clinicians and patient advocates, it concluded that comparator substitution was not occurring to the extent described in stakeholder submissions. [14, 36] This divergence between stakeholder experience and official findings highlights a critical evidence gap. Until now, there has been no comprehensive, independent assessment of how comparator selection is operating in practice, how often lowest-cost comparators are influencing evaluations and what this means for patient access and market functioning. [37, 47]

Addressing this gap matters. Comparator selection determines the benchmark against which new medicines are valued. [40] Yet there is limited transparency about how comparator decisions are made, how closely they align with contemporary clinical practice, and the extent to which they may affect the evaluation of emerging therapies. [48] Without robust evidence, policymakers cannot confidently determine whether current HTA settings are supporting or undermining Australia's access to future medicines. [37] Failing to resolve this uncertainty carries real consequences: patients may miss out on effective and life-extending treatments, and innovation may arrive late to the Australian market, or not at all. [48]

The evidence gathered for this report seeks to clarify the nature and extent of comparator-related challenges by drawing on the perspectives of those directly affected, including industry, clinicians and patient representatives. These insights are essential for informing reforms that protect both the sustainability of the health system and the future availability of innovative therapies for Australian patients.

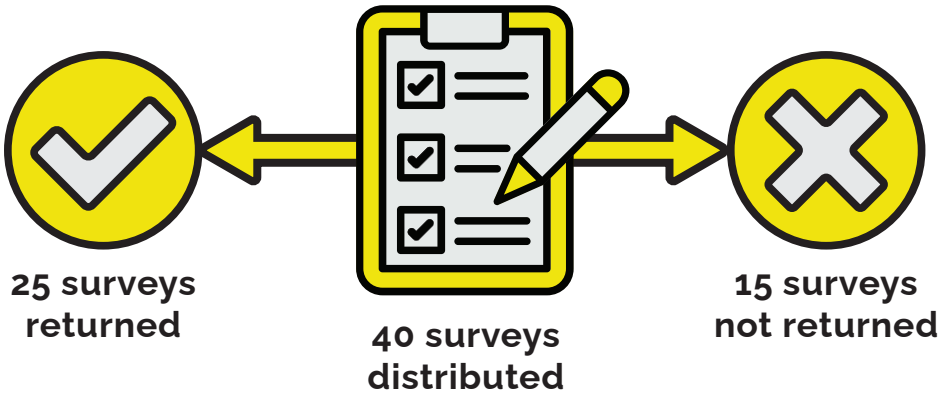
UNDERSTANDING THE TRUE **COST OF COMPARISON**

The aim of this report is to build a clear picture of how comparator selection is working in practice and what it means for patients, clinicians, and Australia's ability to access new therapies. Because no single dataset could show the full picture the analysis combined perspectives from industry, clinicians, patient advocates and experts involved in HTA decision making. Together, these voices helped us understand, not only how comparator decisions are made, but the real-world consequences when they do not reflect clinical practice.

Sponsor survey

Market access and policy leads from innovative pharmaceutical companies were invited to complete a short survey. The survey was distributed via direct email to 40 companies and included a combination of multiple choice and open text questions about their experiences with comparator selection over the past five years.

Figure 7: Survey participation overview



Source: Evohealth [11]

Figure 7 shows that, of the 40 surveys distributed, 25 companies responded, representing a response rate of 62.5 per cent. A small number of companies did not participate due to having no recent submissions or internal governance constraints. All responses were anonymised before analysis. Quantitative responses were summarised descriptively, and open text comments were grouped into common themes to capture shared experiences and recurring concerns.

Stakeholder interviews

Stakeholders across the HTA system were also consulted to understand how comparator decisions play out in practice. In total, 25 stakeholders took part in interviews, including policymakers, Department of Health, Disability and Ageing representatives, former PBAC committee members, HTA specialists and industry experts.

25 stakeholder interiews

Interviews explored how comparators are chosen, how guidelines are interpreted and the practical factors that shape decisions during an evaluation. These conversations highlighted the day-to-day realities that are not always visible in the Public Summary Documents (PSDs) of PBAC deliberations.

Clinician and patient advocate roundtables

To understand how comparator decisions affect people beyond the formal HTA process, a series of focused discussions were held with patient advocates and clinicians. Two roundtables created space for participants to share real-world experiences that are often not captured in submissions or economic evaluations.

Held in October 2025, the sessions brought together five clinicians across oncology, microbiology, neurology, respiratory medicine and rare disease, and separately 14 representatives from patient advocacy groups. Conversations explored what happens when the comparator chosen for a PBAC assessment does not reflect contemporary practice and the practical consequences that this has for patient outcomes, care pathways and equity.

For those unable to attend in person, follow up virtual interviews ensured their perspectives were included. The insights gathered through these discussions helped ground the analysis in lived experience and provided important context for the broader findings.

Case study development

Case studies were also identified. Each case was analysed to understand the comparator nominated by the sponsor, the comparator applied by the PBAC, and whether this aligned with clinical practice. These exemplars were assessed for how comparator decisions influenced economic analysis, listing outcomes, launch timing and investment feasibility, illustrating systemic patterns manifested in individual submissions.

Together, these insights point to a system in which comparator decisions are increasingly inconsistent, frequently misaligned with clinical practice, and often influential in delaying or limiting access to new therapies. The following section sets out the major themes that emerged, highlighting the implications for patients and clinicians, and the risks this poses to Australia's future access to innovative medicines.

THE IMPACT OF **COMPARATOR SELECTION IN PRACTICE**

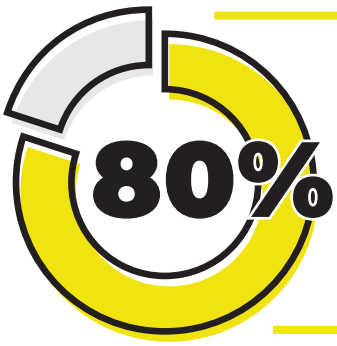
Comparator selection is intended, under the PBAC Guidelines, to anchor HTA decisions to real clinical practice. The Guidelines specify that *"where there is more than one comparator, the main comparator should be the therapy that prescribers would most replace with the proposed medicine"*. [8] Our findings demonstrate that current practice does not align with this principle, nor is it applied consistently. Patterns in recent evaluations reveal shifts in how comparators are selected, how those choices are interpreted within assessments, and the influence they exert on decision-making. The following sections outline how these dynamics affect Australia's medicines market and what they mean for patient access, clinical practice and equity.

What stakeholders told us

Stakeholders across industry, clinical practice and patient advocacy consistently report that a significant change to comparator decisions by the PBAC occurred around 10 years ago. The subsequent experiences of the last decade reveal patterns of comparator substitution, shifts in sponsor behaviour and declining confidence in the transparency and predictability of the HTA process.

Comparator substitution is increasing

Four in five surveyed sponsors report that the PBAC had requested a change in comparator over the past five years (survey question period). In every instance the substitution was to the lowest cost alternative, and was most likely (95 per cent) to affect new medicines applying for initial listing on the PBS. [11] This recurring pattern indicates a departure from the requirement of the Guidlines that the comparator reflects the therapy (or therapies) most likely to be replaced in practice.



Four in five sponsors report comparator substitution had occurred on their submissions in the past five years. Of the substitutions made,

- **100 per cent** were for the lowest cost alternative,
- **95 per cent** affected new medicines seeking first time listing on the PBS. [11]

This departure is most likely to affect submissions anticipated to result in equivalent or lower costs to the health system, also known as cost-minimisation submissions. The majority of sponsors (76 per cent) identify LCC as a major issue for cost-minimisation submissions, compared with only 32 per cent for cost-effectiveness submissions. [11] Where a lower cost alternative is substituted on a cost-minimisation submission, it creates a lower benchmark against which the submitted medicine is assessed. This can artificially lower the price of the new medicine, indication, or presentation, and distort the outcomes of the economic evaluation.

In practice, stakeholders described examples where these benchmarks to lower cost alternatives have been set against medicines rarely prescribed, deemed clinically inappropriate or not registered for the relevant indication. This included cases where different medicines were nominated, despite the submission being for a change in device with no change to the active ingredient. [11] This is explored in Case Study 1, where a new device presentation of an existing respiratory medicine triggered LCC-derived price cuts.

Case Study 1: New device triggered LCC-derived price cuts

The case of Breztri® Aerosphere DFP-EvoCap (budesonide / glycopyrronium / formoterol triple-therapy inhaler) for chronic obstructive pulmonary disease (COPD) illustrates how the comparator selection guides decision-making, even in device changeovers with identical active ingredients.

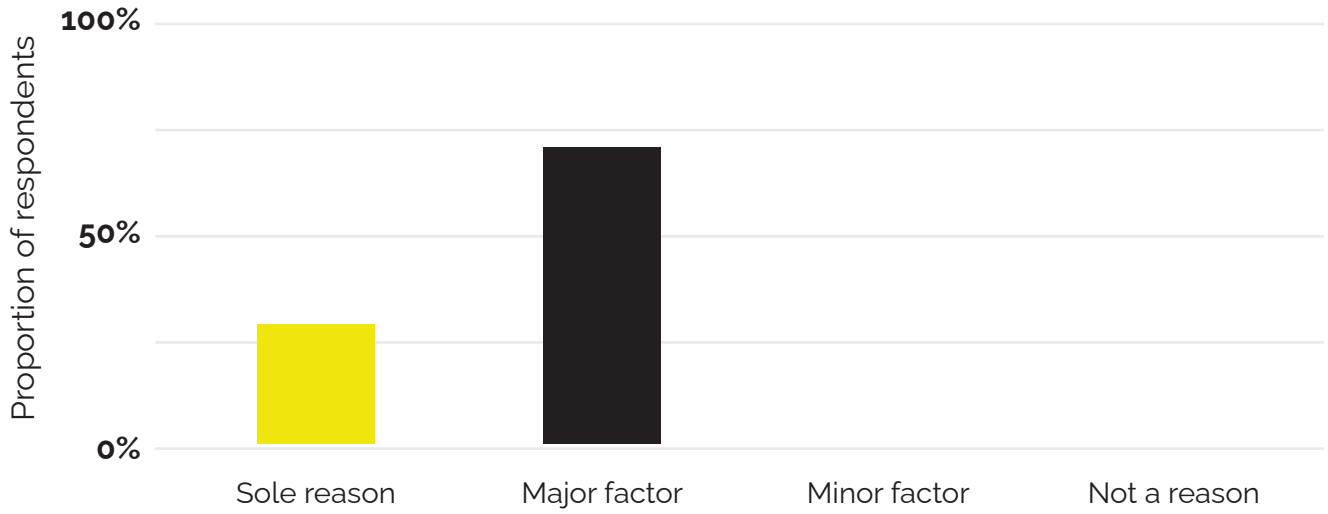
- **November 2022:** Submission sought to replace the existing version of Breztri® with a new DFP-EvoCap device designed to address issues with clogging, unintentional firing and dosing confusion. The active ingredients remained identical, with the new inhaler defined as bioequivalent, and intended to replace the previous device before it was completely phased out. [49] In its November 2022 decision, "The PBAC considered that the DFP-EvoCap should be cost-minimised to the lowest cost alternative agent, including any combination of long-acting muscarinic antagonist (LAMA), long-acting beta-antagonist (LABA) and corticosteroid used for the treatment of COPD, whether in fixed dose combinations or open combination (i.e. individual products)." This required comparison to the individual component inhalers, rather than to the original Breztri® device, despite the submission relating solely to a delivery-device upgrade. [49]
- **June 2023:** Resubmission requested reconsideration of this advice, and PBAC subsequently clarified that no change to the listing or price was required. The sponsor also sought prompt listing to avoid supply disruption during the phase-out of the original device, which the PBAC supported, provided the price remained unchanged. [49]
- **August 2023:** Breztri® with a new DFP-EvoCap device was listed on the PBS.

Summary: This case demonstrates how LCC-driven assessments can influence device transitions. Anchoring the evaluation to the lowest cost alternative, rather than to the predecessor device it is intended to replace, can affect price expectations, market strategy and the continuity of patient access, even when the therapeutic ingredients are identical and only the delivery mechanism has changed.

Comparator substitution is affecting sponsor behaviour

As a result of this practice, sponsor companies of PBS submissions are making difficult choices. This has resulted in negative impacts for subsidised access. Following a PBAC recommendation, all respondents report LCC-related pricing to have a significant influence on decisions not to proceed to PBS price negotiation and listing. Visualised in Figure 8, this was reported to be sole decision for 29 per cent of respondents, and a major factor for the remaining 71 per cent.

Figure 8: Extent to which LCC influenced the decision not to proceed to listing post PBAC recommendation



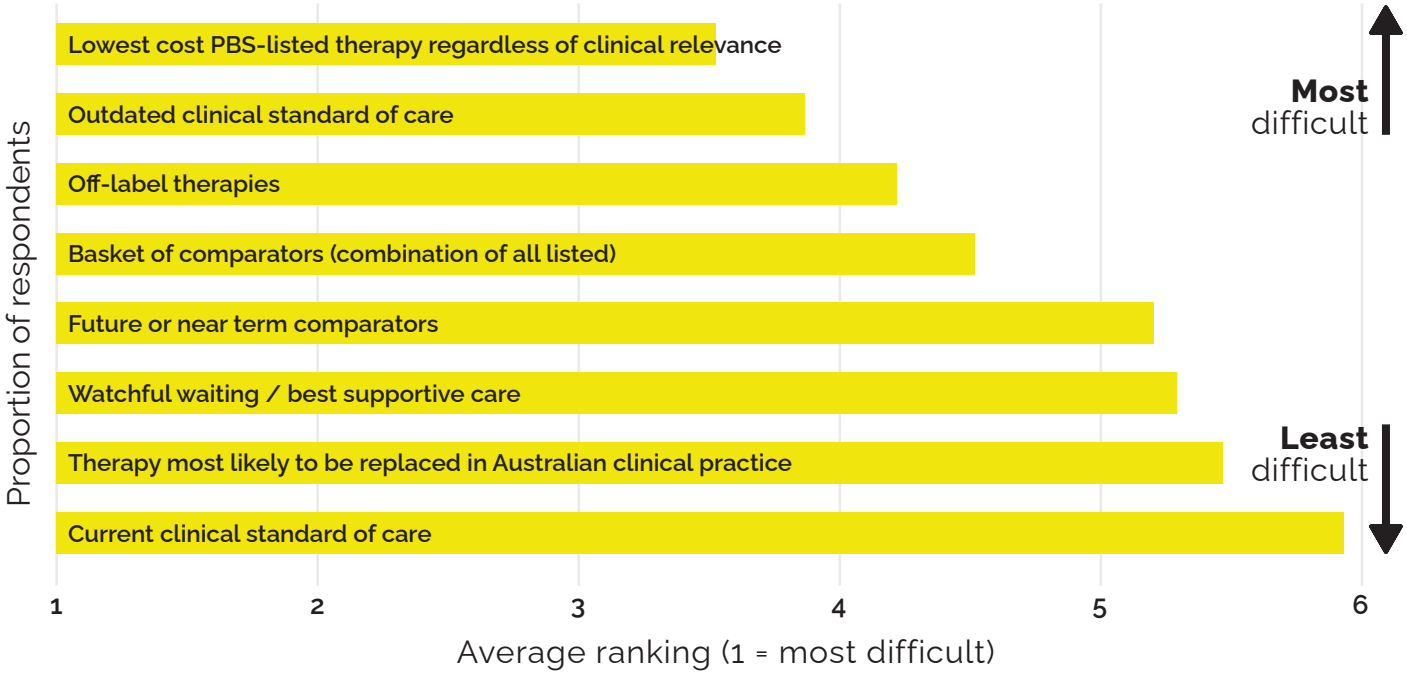
Source: Evohealth [11]

This behaviour change is also occurring further upstream, with companies adjusting their strategies to minimise risk of comparator substitution in a less predictable environment. Sixteen per cent of sponsors report having intentionally nominated the LCC in the last five years, even when it is not the therapy most likely to be replaced in clinical practice.

16 per cent of sponsors intentionally selected the LCC in their submissions over the past five years, even when it was not the therapy most likely to be replaced. [11]

Survey findings in Figure 9 highlight the practical consequences of this shift, with sponsors identifying the LCC as the most difficult comparator for achieving a positive recommendation and progressing to PBS listing. Beyond difficulties in achieving PBS listing, companies intentionally nominating the LCC risks anchoring new products to prices that do not reflect their clinical value or their place in therapy. If this practice continues, it may compound price erosion, distort incremental value assessment and influence whether new therapies are brought to the Australian market at all.

Figure 9: Difficulty of comparator types throughout PBS listing and patient access, ranked by sponsors



Source: Evohealth [11]

Continued application of lowest cost alternatives has also increased the risk of companies choosing to not pursue PBS listing altogether. Sponsors may choose to forgo PBAC submission if they anticipate comparator substitution will result in a commercially nonviable price. An example of this is seen in Case Study 2, where perceived risk of LCC application for a human immunodeficiency virus (HIV) medicine led to MSD Australia not submitting for PBS listing.

Case study 2: Decision not to seek reimbursement due to anticipated LCC practices

In February 2019, the TGA registered doravirine (Pifeltro®) for the treatment of HIV-1 infections in adults. Doravirine is a once-daily medicine indicated in combination with other antiretroviral therapies (ART). It offers an alternate treatment option for those experiencing adverse effects or at risk of drug-drug interactions from other therapies. [50]

MSD elected not to seek PBS reimbursement because the anticipated PBS price was commercially nonviable. While clinical evidence indicated doravirine would replace higher cost therapies, justifying a weighted price of $11.36 per day, PBAC precedents suggested nevirapine would be the comparator. Nevirapine as a lower cost alternative would have resulted in a price benchmark of $3.41 per day, a price that was commercially nonviable for MSD to pursue listing. Consequently, MSD did not proceed with the application, leaving Australian patients without subsidised access.

Together, submissions being abandoned, deliberately tailored to anticipate PBAC behaviour, or not made in the first instance signals declining confidence in HTA processes. This reflects a system with growing uncertainty about how comparator decisions are reached.

A process that feels increasingly opaque

Across interviews and survey responses, stakeholders describe difficulty in understanding why the PBAC substituted comparators, and why the selected comparators frequently conflicted with clinical practice. Seventy per cent of surveyed sponsors agree that comparator decisions often lack transparency. [11]

These experiences contribute to a perception that the PBAC's rationale is unclear and that decisions are increasingly detached from both the Guidelines and clinical reality.

Examples included substitutions involving:

- **therapies rarely or no longer used,**
- **medicines not registered for the relevant indication,**
- **products that were not therapeutic substitutes, or**
- **cases where a simple device change, such as a vial to a pre-filled syringe, triggered an entirely different medicine as the comparator.**

> *A submission requested that a new strength be referenced against the currently reimbursed strength, of the same molecule, with identical clinical outcomes. Instead, [the Committee] insisted on the LCC comparator, another medicine and rarely used lower cost product.*
>
> **- Survey respondent** [11]

> *We compared to ourselves and the currently listed form, but were cost-minimised to the LCC, which no patient uses.*
>
> **- Survey respondent** [11]

Real-world accounts of these experiences can be clearly seen in Case Study 3, where the PBAC required comparison to an unapproved and clinically inappropriate therapy, significantly increasing evidentiary requirements and delaying access. Case Study 3 also illustrates the longevity of comparator-related issues throughout the Australian HTA process, with impacts on time to market and patient access evident as early as 2013.

Case Study 3: Requests for an unapproved comparator delayed access to ranibizumab

The assessment of ranibizumab for treatment of vision impairment due to macular oedema secondary to retinal vein occlusion (RVO) and due to diabetic macular oedema (DME) provides a clear example of the PBAC requesting a comparator that was neither TGA approved, nor PBS listed for the indication.

- **November 2012:** In the RVO submission, the PBAC agreed the comparators were appropriate, but also stated that bevacizumab was a relevant comparator because it was widely used in practice. [51] This was despite bevacizumab not being TGA approved for RVO, not being formulated for intravitreal use and having no evidence of safety and cost effectiveness for this population. Ultimately, the submission was rejected due to high uncertainty of cost effectiveness. [51]
- **March 2013:** The same issue recurred for the DME indication. [52] The PBAC again acknowledged laser treatment as the appropriate comparator but insisted that bevacizumab was also relevant due to its widespread off-label use. The submission was again rejected, due to uncertainty in the incremental cost effectiveness ratio and unresolved questions about long-term safety and benefit. [52]
- **November 2013:** In resubmissions made for both RVO and DME, the sponsor reiterated that bevacizumab was inappropriate as a comparator because it was unapproved and not intended for intravitreal administration. [53, 54] The PBAC maintained that bevacizumab was still relevant because it was commonly used and requested further departmental investigation into how bevacizumab could be considered as a comparator and how a clinical and economic comparison could be undertaken. Both submissions were deferred. Novartis publicly disagreed that bevacizumab was an appropriate comparator. [53, 54]
- **March 2014:** A minor resubmission again resulted in deferral. [55] The PBAC reiterated that bevacizumab remained a relevant comparator because it was widely used in patients who would be eligible for ranibizumab if listed. The PBAC noted that more robust comparative evidence was required and pointed to ongoing head-to-head trials that may strengthen the evidence base. The PBAC also advised that, if compounded bevacizumab were ever considered for PBS listing, pricing would likely mirror bevacizumab used in oncology and funded under the Efficient Funding of Chemotherapy Program. [55]
- **July 2014:** Ranibizumab for DME and RVO was ultimately recommended after almost two years of repeated submissions, deferrals and requests for comparative evidence against an unapproved therapy. [56, 57]

Summary: This case shows how the PBAC's interpretation of comparator rules can escalate evidentiary requirements. By insisting on evaluation against an unapproved and unevaluated therapy, the PBAC introduced additional layers of clinical and economic comparison that delayed listing and required multiple submissions, even when appropriate, approved comparators were acknowledged.

A shift driven by unseen interpretations

Around 2015, interpretation of section 101(3B) of the *National Health Act 1953* (Cth) appears to have changed, although information around this is limited. [6] Patterns in subsequent PBAC evaluations show a parallel move toward greater use of LCC, materially affecting confidence in the consistency of the HTA process.

> *There has clearly been a step change… up until 2017 there was still willingness, in certain circumstances, to apply some discretion. It has shifted totally to the LCC, irrespective of where it sits in clinical practice*
>
> **- Director of Market Access**

This shift in approach altered how companies interpret PBAC decision-making and how predictable the evaluation pathway feels in practice. As the basis for comparator decisions has become less clear, confidence in the stability of the HTA process has weakened.

Diminishing trust in the HTA process

Several interview and survey responses point to a growing loss of confidence that the PBAC will apply its own Guidelines consistently, particularly to select comparators reflecting the therapy most likely to be replaced in clinical practice. This unpredictability is identified as a key driver of declining trust, with sponsors noting the inconsistent application of the Guidelines leading to uncertainty on when to lodge submissions and how to plan evaluation strategies.

> *There is such a lack of trust – that is our biggest issue across the board, beyond comparators. How do we write that into a strategic agreement? Until you build trust, there is no improvement.*
>
> **- Senior Manager, Access and Funding**

This erosion of confidence was not limited to industry. Clinicians and patient advocates also report reduced trust in the PBAC and the Department, citing examples where comparator decisions did not align with clinical practice and where the rationale for substitution was unclear.

> *Seeing [inappropriate comparator substitution] occurring – it's such an erosion of trust.*
>
> **- Patient advocate**

The cumulative effect of a wider deterioration of trust, across and between all groups, has implications for the collaborative environment required to support timely medicines access. Stakeholders expressed concern that comparator uncertainty is now undermining the cooperative, transparent relationships required by the National Medicines Policy (NMP), [1] where decision-making relies on effective partnerships between government, industry, clinicians and people with lived experience. The result is growing concerns that comparator selection undermines both individual evaluations and the wider HTA ecosystem, shaping how the medicines market operates in practice.

How comparator selection distorts Australia's medicines market

The impacts of comparator substitution are not occurring in isolation. There are clear and consistent links between comparator substitution and broader market dynamics. These interactions with Australia's price and reimbursement settings affect commercial viability, investment decisions, launch timing and Australia's position within global development pipelines.

Cost containment policies amplifying the effect of LCC

Australia's pricing architecture has been shaped over decades by layers of cost containment policies, including statutory price reductions (SPRs), anniversary cuts, first new brand reductions and successive rounds of price disclosures. [58] These mechanisms erode the prices of older medicines and, when new medicines are anchored to these benchmarks through substitution, the combined effect reduces PBS prices to levels that no longer reflect the clinical value.

There are multiple examples where comparators aligned with clinical practice at the time of submission, then diverged when a separate product in the same therapeutic class later took a raft of price reductions. Despite representing a small share of the market, the cheaper product was then substituted as the LCC and was then used as the benchmark for evaluation.

> *We have examples where the comparator nominated was a therapeutic analogue which was the most likely to be replaced in therapy. During the evaluation, another treatment took a price disclosure-related reduction, and although this treatment accounted for a disproportionately minuscule share of the market, it was deemed to be the appropriate comparator [by PBAC]. This resulted in a commercial decision not to launch this product in Australia.*
>
> **- Survey respondent** [11]

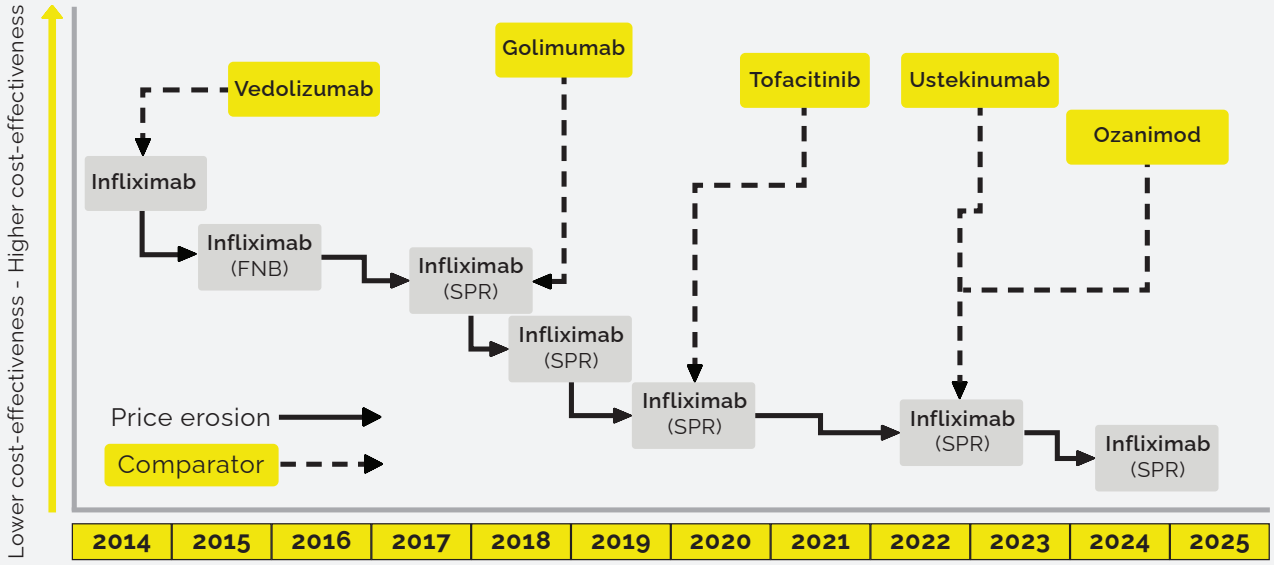
This dynamic is exemplified in Case Study 4, which shows how successive SPR and price-disclosure reductions on infliximab created a long-term, structurally-depressed benchmark that shaped the PBAC evaluation of ozanimod, irrespective of its clinical positioning.

These experiences reveal how LCC substitution compounds the effect of SPRs, driving price expectations to levels described by sponsors as commercially nonviable, particularly in a small, regulated market.

Case Study 4: LCC pricing history shaped the assessment of ozanimod for ulcerative colitis

The assessment of ozanimod for moderate to severe ulcerative colitis (UC) highlights how long-standing LCC practices can predetermine price expectations for new therapies. Figure 10 shows that, over more than a decade, PBAC decisions have repeatedly benchmarked UC medicines to infliximab, creating a durable price floor that shaped ozanimod's evaluation.

Figure 10 Infliximab-anchored price has defined the ulcerative colitis cost floor for more than a decade



Source: Constructed by Evohealth using PBAC Price Disclosure Reduction announcements [59-63] and PSDs (2014–2023) for infliximab, [64] vedolizumab, [65] golimumab, [66] tofacitinib, [67] ozanimod, [68] and ustekinumab. [69] Comparator selection, clinical positioning and price dynamics were validated against PSDs, including instances where PBAC substituted to infliximab (LCC).

Note: FNB = First New Brand statutory price reduction and SPR = statutory price reductions applied at legislated anniversaries of PBS listing.

2014—2021: Across multiple UC treatments, the PBAC consistently applied cost-minimisation to infliximab, embedding a price anchor for the entire therapeutic area. As shown in Figure 10, this history created a very low comparator price that all subsequent therapies were expected to match.

November 2022: When considered by the PBAC, ozanimod was deemed cost effective only if priced at parity with the LCC, again infliximab. [68] Although the PBAC recognised the value of an oral option, these benefits did not support pricing above the established LCC anchor. The PBAC also acknowledged evidence that ozanimod is superior to adalimumab and may provide, for some patients, a significant improvement in efficacy or reduction in toxicity. [68] However, these comparative advantages were not sufficient to justify pricing above the established LCC benchmark, given the PBAC's view that ozanimod could substitute for all listed biological disease-modifying anti-rheumatic drugs (bDMARDs) and targeted-synthetic disease-modifying anti-rheumatic drugs (tsDMARDs).

2023: Ozanimod was ultimately recommended for listing, and was made available on the PBS in March 2023, but only within the constraints of the long-standing infliximab-based LCC benchmark. [70] The economic outcome reflected historical comparator practice rather than ozanimod's distinct mechanism of action, oral administration or patient-experience advantages.

Summary: The case illustrates how entrenched LCC pricing in UC continues to shape HTA outcomes. For ozanimod, the predominant influence on pricing was not comparative effectiveness but the expectation that all UC therapies align with an infliximab-defined price floor.

Distortions from unintended reference price linkage

Industry stakeholders also report scenarios where LCC substitution results in unintended linkages between products that should not be reference priced against each other. Under the PBS, reference price is intended to apply only to:

- Formulary 1 (F1) medicines,
- Combination products on the Combination Drug List, and
- Medicines within established Therapeutic Groups. [71]

However, some sponsors report that once an F1 medicine was cost minimised to a Formulary 2 (F2) comparator through LCC substitution, reference price arrangements then flowed this benchmark into the broader therapeutic area.

The key issue is not the reference price itself, but where comparator substitution enables cross-formulary linkages never intended in regulation. Together with other cost-containment mechanisms, this creates downward price pressures that extend well beyond Australia's borders, setting the stage for the additional risks introduced by contemporary pricing policy issues, such as Most Favoured Nation (MFN).

> *We have experience of a new therapy being listed on a cost-minimisation basis to the LCC, and then reference pricing being used to flow this lower price to all treatments cost-minimised to each other within this [therapeutic area]. This practice is very challenging commercially… it can result in unanticipated and accelerated price erosion for products still on patent, [or] decisions not to launch in Australia due to accelerated erosion of prices.*
>
> **- Survey respondent** [11]

MFN policies intensifying global consequences for Australia

The challenges associated with LCC substitution are being magnified by the emergence of the MFN policy environment in the United States (US). Sponsors report that PBS prices are now scrutinised more heavily by global headquarters because price reductions in Australia may trigger unwanted flow-on effects in MFN-linked markets.

Following LCC substitution and recommendation by the PBAC, survey respondents noted three factors most influential in whether companies proceed to price negotiation:

1. Directives from global and internal teams to not list
2. Commercially nonviable prices for medicines
3. Potential to impact on price and reimbursement in other markets. [11]

Stakeholders report the interaction between comparator selection policies and MFN has moved Australia from a market automatically included for rollout of a new medicine, to one requiring justification for access, and increasingly seen as "high-risk, low-value."

This reduces flexibility allowed during price negotiations and, where the required price cannot be reached, increases the probability of a new medicine not being PBS listed. This dynamic is illustrated in Case Study 5, where extended global price negotiations for ustekinumab demonstrate how LCC-driven assessments can delay access even for established therapies.

These perspectives constrain investment and launch planning for Australia, with downstream consequences for equitable patient access to innovative medicines.

> *Demonstrating [cost-effectiveness] is extremely difficult in Australia. LCC made it worse, and our global colleagues were absolutely unwilling to compromise given the price reference was such an old medicine that was far from clinically relevant anymore.*
>
> **- Survey respondent** [11]

Case Study 5: Global price constraints delayed access to ustekinumab for ulcerative colitis

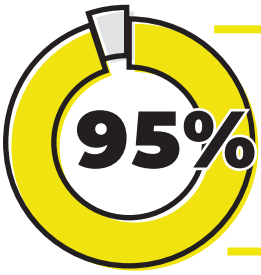
The experience of ustekinumab (Stelara®) for ulcerative colitis (UC) illustrates how LCC price requirements delay access even when clinical evidence is well established. Though clinicians and patients supported the therapy's value, Johnson & Johnson Innovative Medicine Australia could not progress to a PBAC submission for several years due to inappropriate price anchoring to the LCC.

- **2019—2021:** J&J Australia intended to pursue PBS listing for ustekinumab in UC at the earliest opportunity but was not able to submit to the PBAC, given the low price expected from an LCC recommendation not representing the value of the medicine.
- **March 2022:** J&J Australia were able to submit to the PBAC. The submission challenged the LCC through real-world evidence, advocacy and strengthened arguments around comparative effectiveness. The submission occurred more than two years after the initially planned submission, and was much closer to anticipated ustekinumab biosimilar entry. [72]
- **July 2022:** The PBAC recommended ustekinumab be listed on the PBS, on the basis it was cost-minimised to the LCC. [72]
- **February 2023:** After the PBAC recommendation, ustekinumab was progressed through the post-PBAC PBS listing process, including negotiation on listing arrangements. Ustekinumab was finally listed on the PBS on 1 May 2023, almost three years after being TGA registered on 19 May 2020, and closer to the anticipated ustekinumab biosimilar entry. [72, 73]

Summary: This case shows how comparator-driven price expectations can result in multi-year delays in patient access.

Reducing Australia's attractiveness for innovation and investment

Australia's attractiveness as a destination for innovation and future investment is at risk due to comparator substitution with lower cost alternatives. Almost all (95 per cent) survey respondents agreed the LCC approach undervalues clinical innovation, with nine in 10 reporting the practice discourages investment in Australian HTA submissions. [11] A clear example of how comparator selection undervalues incremental innovation can be seen in pneumococcal vaccines, described in Case Study 6.



of survey respondents agree the LCC approach **undervalues clinical innovation.** [11]

of survey respondents report that LCC practices **discourage investment in Australian HTA submissions.** [11]

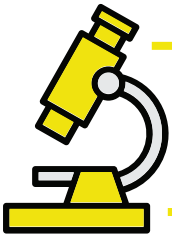
Case Study 6: Comparator selection fails to recognise incremental innovation for pneumococcal vaccines

Australia's assessment of pneumococcal vaccines shows how comparator selection can systematically undervalue incremental innovation. In its 2023 response to the HTA Review, Pfizer highlighted that successive conjugate vaccines were recommended by the PBAC based on cost-minimisation against earlier and lower valent products, even when newer vaccines offered broader serotype coverage and the potential to reduce invasive pneumococcal disease. [74]

The 13 valent and 10 valent vaccines were both recommended by the PBAC for inclusion on the National Immunisation Program (NIP) at the same price as the original seven valent vaccine, despite adding six and three additional serotypes. [74] The 15 valent vaccine was then recommended at price parity with the 13 valent vaccine for adult and paediatric populations, and most recently the 20 valent vaccine received a cost-minimisation recommendation for both groups. [75, 76] As a result, the 20 valent vaccine has been valued at approximately the same price as the seven valent vaccine that was listed on the NIP more than 20 years ago. This approach treats each new vaccine as if it provides no additional value, regardless of epidemiological gains or reductions in severe disease and mortality.

Summary: After being recommended by the PBAC in November 2023, Prevenar 20 replaced Prevenar 13 and Pneumovax 23 on the childhood and adolescent NIP schedule from 1 September 2025. [77] This example illustrates how incremental innovation needs to be supported via our HTA system to improve public health protection, and signal globally that incremental advances will be appropriately valued.

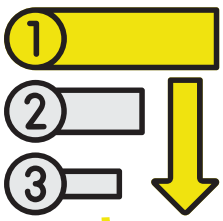
Where sponsors do not perceive the Australian market as worth effort or investment, there is risk that this perception may also affect industry support for research and scientific infrastructure. More than four in 10 sponsors report comparator selection bears a moderate to extreme impact on local willingness to invest in Australian clinical trials, rising to five in 10 for international willingness. [11] These factors risk how global industry views Australia as an attractive destination for innovation and investment, which includes the nation's priority for new medicine launches.



45 per cent of sponsors report comparator selection bears a moderate to extreme impact on local and international willingness to invest in Australian clinical trials. [11]

Australia is moving down the global launch order

Impacts from comparator substitution, combined with cost containment policies, MFN pricing, and declining investment appeal, has moved Australia further down the global sequencing order. Survey findings show that nine in 10 sponsors agreed comparator selection affects the timing of launch or indication sequencing, and four in five reported moderate to severe impacts on Australia's position relative to other markets. [11]



Nine in ten agree comparator selection affects the timing of launch or indication sequencing in Australia. [11]

Four in five identified comparator selection has moderate to severe impacts on Australia's position in launch sequencing compared to other markets. [11]

Evidence suggests that once a product is cost-minimised to a low benchmark, global organisations view Australia as a high-risk, low-return environment. In some cases, LCC-driven price expectations were described as incompatible with global price corridors, leading to delays in lodging submissions or decisions not to proceed after a positive PBAC recommendation.

The issue is reflected in Case Study 7. Sponsors described cases where LCC substitution directly results in decisions not to launch, even when the PBAC had recommended the medicine.

Case Study 7: Inability to launch a new treatment for rheumatoid arthritis in Australia due to application of LCC

November 2018: Sanofi applied for listing of their treatment sarilumab, an interleukin-6 (IL-6) inhibitor used to treat rheumatoid arthritis. This listing was sought on the basis of cost-minimisation to another IL-6 inhibitor (tocilizumab) that was already listed on the PBS for the same indication. [78]

The PBAC recommended sarilumab but on a cost-minimisation basis 'with the least costly bDMARD for severe active rheumatoid arthritis.' [78] This comparator treatment was not considered a pharmacological analogue and used by less than five per cent of patients, thus not the treatment most likely replaced in clinical practice. It was a first-generation treatment for rheumatoid arthritis that had been subject to substantial price erosion due to the length of time it had been listed on the PBS and the application of pricing policies including price disclosure.

Summary: As a result, Sanofi were unable to launch sarilumab in Australia. [79] At the time patients still had access to tocilizumab, however during the global COVID-19 pandemic, demand resulted in shortages of this treatment and necessitated patients to switch to alternate formulations or treatments. This created challenges beyond simple treatment choice; it directly impacted disease management and treatment continuity for patients and clinicians. [80] Furthermore, the administrative burden of managing these shortages required pharmacists and prescribers to divert substantial time and professional resources away from patient care. [81] In this case, the valuation approach resulted in restricted options, creating broader operational and clinical pressures across the healthcare system.

Sequencing decisions determine when, and if, Australia is to receive new medicines or new indications for existing medicines. Sponsors surveyed report a moderate to extreme impact from LCC substitution on local and international decisions to launch new medicines or indications in Australia, as summarised in Figure 11.

The result is that innovative therapies may enter Australia later than comparable markets, or not at all, compounding existing access delays and reducing Australia's attractiveness as a destination for innovation.

Comparator selection has a **moderate to extreme impact on:**

AUSTRALIA

73% Local affiliate decisions to **launch new medicines** in Australia. [11]

77% Local affiliate decisions to **launch new indications** in Australia. [11]

GLOBAL

73% Global or head office decisions to **launch new medicines** in Australia. [11]

73% Global or head office decisions to **launch new indications** in Australia. [11]

What this means for patients, clinicians and equity

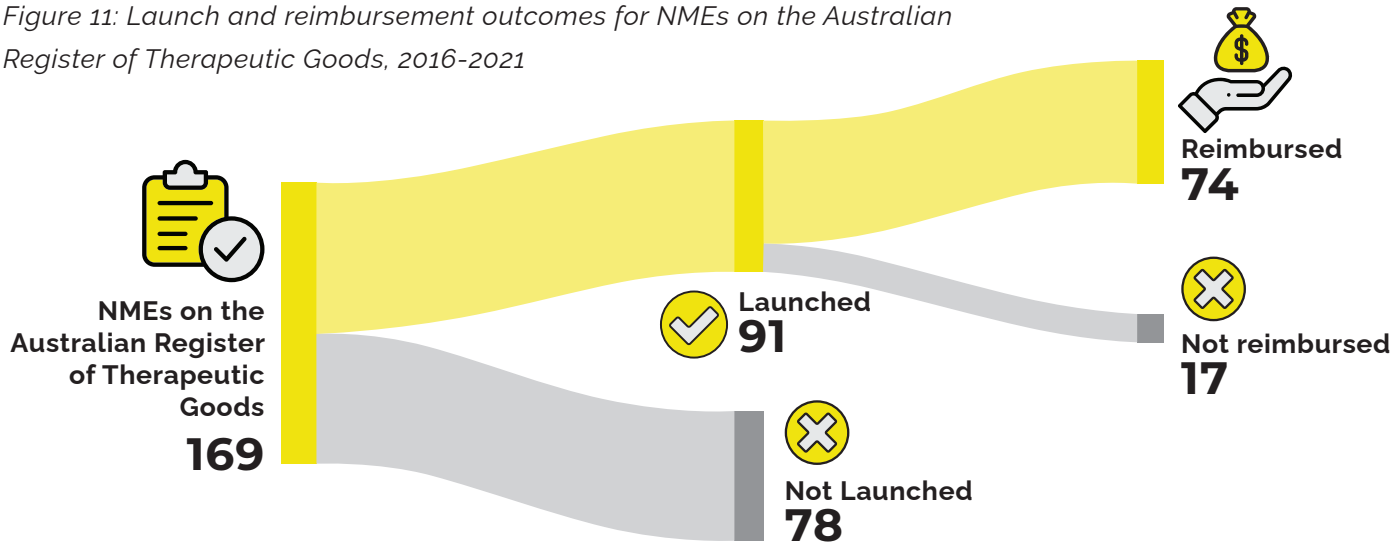
The market effects of comparator selection translate directly into real-world consequences for patients and clinicians. Delayed, uncertain or commercially nonviable PBS pathways influence affordability, treatment choice, clinical practice and participation in research. These pressures shape patient wellbeing, equity of access and Australia's broader healthcare environment.

Australia's growing private market and rising inequity

There is increasing concern of unaffordable and inequitable access, amid a growing private market trend. In response to assessments that undervalue newer therapies, companies are increasingly pursuing or considering exclusively launching medicines via the private market. Some industry stakeholders report that their global office will not launch a new product in Australia if subsidised access appears unachievable, whilst others are preparing to lean into private market activity by increasing resources and infrastructure.

Between 2016 and 2021, there were 10 per cent fewer registrations for NMEs in Australia, compared to other OECD nations. [35] Of the 169 NMEs that were registered, the proportion of those that were reimbursed in Australia was 27.2 per cent lower than the average across other OECD countries, described in Figure 11. [35] Concurrently, private out-of-pocket prescription spending now represents 15 per cent of the total retail market in 2024, up from nine per cent in 2019. [82]

Figure 11: Launch and reimbursement outcomes for NMEs on the Australian Register of Therapeutic Goods, 2016-2021



Source: Evohealth adapted from [35]

Increasing private market spending raises significant concerns for equitable access for patients, as 21 per cent of Australians report delaying or foregoing medicines due to cost in the last three years. [83] Without improvement, this inequity will broaden the existing gaps in these challenges, and further disadvantage communities, including:

- Aboriginal and Torres Strait Islander peoples,
- People living in areas of lower socioeconomic advantage,
- People living in regional, rural and remote areas,
- Culturally and linguistically diverse people, and
- Older Australians.

These gaps occur in direct contrast with our NMP and other public health priorities. Australia's *Ninth National HIV Strategy 2024-2030* prioritises access and equity as a key principle, stating "the health system must ensure care reaches those who need it when they need it". [84] Case Study 8 describes an eight-month access delay that faced Cabenuva®, owing in part to comparator selection. This is despite the role of Cabenuva® in the treatment of HIV. Case Study 8 is described on the following page.

Case Study 8: LCC Application in HIV Treatment

ViiV Healthcare's experience with the long acting injectable, cabotegravir and rilpivirine (Cabenuva®), demonstrates how the LCC approach can influence outcomes even in high priority public health areas such as HIV. In this case, the assessment framework shaped both the timing and complexity of the pathway to listing, despite strong alignment with public health goals and clear potential to improve the treatment experience for people living with HIV.

- **March 2021:** The initial submission was not recommended, with the PBAC considering it was unclear whether the availability of a long-acting injectable alternative to oral ART would provide tangible improvements in patients' QoL. [85] Ultimately, the PBAC also considered that the most appropriate basis for a listing would be if Cabenuva® was cost-minimised to the least costly alternative
- **November 2021:** ViiV Healthcare resubmitted the medicine in November 2021 for the treatment of HIV infection. The PBAC updated its consideration of Cabenuva®, recognising that the availability of a long-acting injectable option for the management of HIV is likely to offer some QoL and adherence benefits for a small number of patients. The PBAC further considered that a price advantage over the least costly alternative would be acceptable. [86]
- **April 2022:** PBS listing commenced in April 2022, more than a year after TGA registration (February 2021). The patient access gap from registration to PBS access was primarily driven by strict LCC based requirements from the initial consideration.

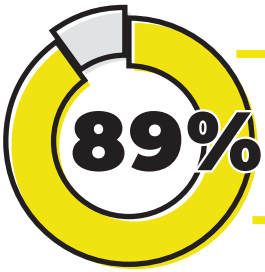
Summary: The experience with Cabenuva® highlights how the LCC mechanism can extend timelines and complicate access pathways for innovative therapies, even where they closely align with public health priorities. In this instance, the requirement to anchor price to the least costly alternative constrained recognition of broader benefits, introduced additional procedural steps and delayed access for a population that could have benefited from earlier availability of a long-acting treatment option.

Without equitable access to innovative medicines that reflects the global standard of care, Australia faces a widening gap in equitable healthcare across population groups.

> *Our healthcare environment is insidiously moving towards a user-pays situation. We need to be more outspoken when we see it is actually moving away from equity-based principles to variable levels of accessibility and affordability - which we as a country should not be wanting to see happen.*
>
> **- Professor Christine Jenkins, Respiratory Physician**

Australians are experiencing physical, psychosocial and financial impacts

Undervaluing of innovative medicines, driven in part by comparator selection practices, is building barriers to subsidised access, with direct impacts on patient outcomes. Advocates and clinicians described predictable, yet avoidable, consequences of delayed access, including higher disease burden, reliance on older therapies and increased financial strain.

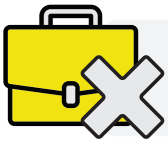


of patient advocates agree that the people they represent **do not have access** to innovative medicines to meet their clinical needs that are equivalent to other countries. [11]

Without access to innovative medicines,

Disease progression is more likely to become irreversible.

Patients remain on older therapies that may provide inferior control or greater toxicity.



The ability to work or participate in daily life declines.

Psychological distress increases due to uncertainty, worsening symptoms, and financial pressure.

> *The other outcomes are that patients get left on profoundly suboptimal therapy, progressively and incrementally. This won't happen overnight, but it will happen progressively.*
>
> **- Professor Christine Jenkins, Respiratory Physician**

Financial strain and unsafe coping behaviours

There is also widespread financial stress among patients who pay privately, when PBS-subsidised access is not available because of LCC-related price. Behaviours described in our research include:

- Withdrawing large sums from superannuation,
- Selling homes or taking on substantial debt,
- Travelling overseas for treatment at significant personal expense, and/or
- Sharing purchased medicines within patient communities, raising additional concerns for safety.

These examples affect patients from a broad range of disease areas and are universally reported to be an overwhelming burden. Advocates describe instances where delays or unaffordable access are associated with avoidable deterioration and mortality. This includes patients who died waiting for access to treatments, or because they could not afford to source them.

> *People chose to end their lives rather than go back to the darkness of uncontrolled migraines.*
>
> **- Patient advocate**

This highlights how comparator selection decisions made upstream have negative consequences for patients' health and financial outcomes. They also shape the clinical environment itself, influencing how clinicians can practice.

> *Some [patients] can afford $60,000 [out-of-pocket costs each year], but it is beyond reach for the majority. It affects our prescribing, how we manage patients, it affects how patients feel themselves and their autonomy. They blame themselves for not sacrificing their own pennies and superannuation. I think it's perverse.*
>
> **- Professor Michael Woodward, Geriatrician**

Clinical practice is being constrained

Comparator selection is influencing the availability of medicines in clinical practice, in turn limiting the ability of clinicians to follow contemporary best practice and forcing reliance on older or less effective therapies. This has direct implications for clinical decision making and system-wide resource use.

Clinical care impact

Therapies used as LCCs that would not be considered standard of care, creating an ethical and clinical misalignment.

Moral injury arises from being unable to offer treatments routinely available in comparable countries.

Increased use of invasive procedures, including surgery, when less invasive options are inaccessible.

Forced reliance on outdated treatments when innovative therapies are not available on the PBS.

Additional strain on general practice, outpatient services, and emergency departments as clinicians manage avoidable disease progression.

As best practice standards drift further from PBS funded options, the effects extend into Australia's research environment, where the standard of care determines which trials can be run.

> *"We would like to be able to practise in the same way as doctors in the United Kingdom and most European countries, but we're now at risk of being five years plus behind with drug access."*
>
> **- Professor Christopher Ward, Clinical Haematologist**

Clinical trial activity at risk

Comparator-driven delays and inaccessibility also pose risks for Australia's clinical trials environment, with implications for research capability and patient opportunities. Patient advocates, clinicians, and industry highlighted three risks:

- Australia's standard of care falls further behind, and becomes a less desirable site for global trial participation,
- Patients lose access to early stage or investigational therapies only available through trials, and
- Reduced trial activity weakens Australia's research workforce and infrastructure.

Conducting trials can become ethically challenging when there is no realistic pathway to patient access after the trial concludes.

The consequences for Australian clinical trials are at odds with efforts to strengthen the environment by Australian policymakers. This includes through the Inter-Government Policy Reform Group's efforts to encourage more translation of research into healthcare, and $13.6 million recently announced "to make Australia a leading destination for more clinical trials". [88, 89] Efforts seeking to "drive a consistent national approach so that more Australians get early access to emerging treatments" risk being undermined well before they can take effect. [88]

Improving comparator selection is necessary to ensure Australian HTA processes remain aligned with best-practice economic methodology. Current approaches have affected the way incremental value is assessed, contributed to delays or uncertainty in progressing PBS listings, and influenced the availability of new therapies in the Australian market. These effects flow through patient access, clinical practice, and research activity. Timely and coordinated reform is required to support consistent, methodologically sound decision making and to maintain Australia's ability to provide equitable access to innovative therapies.

CHARTING THE **PATH FORWARD**

Successive reviews have highlighted that Australia's HTA framework is no longer functioning as intended. The evidence presented in this report reveals current comparator selection practice is contributing to delayed or foregone access, distorted price expectations, weakened investment signals and declining trust across the HTA ecosystem. Stakeholders across industry, clinical practice and patient advocacy are united in calling for reform. The question is not whether change is required, but how quickly it can be delivered.

of survey respondents agree **major reform** to comparator selection is required. [11]

The 2024 *HTA Policy and Methods Review* acknowledges gaps in comparator selection, yet the solutions diverge. Recommendation 40 of the Review proposes updates to the PBAC Guidelines, effectively treating the issue as one of guideline interpretation. [14] In contrast, the alternate recommendation put forward by Elizabeth de Somer of Medicines Australia calls for legislative reform, framing the issue as a failure of Guideline governance. [14]

The reality is that both are required.

- **Interpretation:** The PBAC Guidelines must be updated to clearly articulate that the "main comparator" is the therapy that prescribers would actually replace in clinical practice. This technical clarity is essential to maintain the value and intent of economic evaluation.
- **Governance:** Guidelines alone are insufficient if they are not consistently applied. The call for legislative change highlights a need to strengthen the governance of the process. Without a stronger mechanism to tether decision-making to these Guidelines, administrative discretion risks undermining the economic validity of the assessment.

Therefore, the path forward is not binary. It requires a dual approach: technical refinement of the Guidelines to restore economic validity, reinforced by statutory improvements to protect the integrity of the process. What is clear across all evidence sources is that the call is not for minor technical adjustments but for meaningful, system-level change to ensure comparator selection supports timely, equitable and sustainable access to innovative medicines. This sentiment is echoed in the direct messages to the Minister for Health provided during this project, included on page 19.

WORKING TOWARDS REFORM

Work is already underway to reform comparator selection, driven by the IAG within the broader context of the HTA Review. The actions identified in this report are intended to inform and support these critical processes.

To guide these efforts, Evohealth has developed a phased roadmap with short, medium and long-term actions. These recommendations are designed to ensure Australia's HTA methodologies remain economically valid and clinically robust. Crucially, they also serve to strengthen Australia's position as a viable destination for innovation and investment.

Short term: Contemporise HTA practices in the next 12 months

Immediate action is needed to restore the integrity of economic modelling in Australia's HTA process. To ensure Australia's system keeps pace with global best practice in HTA and valuing of innovative medicines, we must act with urgency to eliminate the distortions that may arise from using outdated therapies as baselines. The integrity of an assessment relies on the accuracy of its inputs. Where use of lower cost alternatives has anchored a modern therapy to an obsolete standard of care, a fundamentally flawed economic conclusion is produced. Correcting this requires structural clarity, process transparency and decision-making agility.

Recent progress has seen Recommendation 40 of the HTA Policy and Methods Review proposing updates to the PBAC Guidelines to improve clarity in comparator selection. [14] This creates an immediate opportunity to clarify the intent of our HTA framework. This report proposes an alternate to how we can restore economic validity to the Australian evaluation process. Both Actions 1 and 2 must be implemented together to ensure both the interpretation and application of comparator selection are protected by standard legislative safeguards.

Implementing these changes must be an urgent priority to set the tone for genuine partnership between Government and industry. Progress will demonstrate a clear commitment to resolving comparator-related barriers, and affirm the mutual value placed on innovation.

ACTION 1

Align the PBAC Guidelines with clinical reality to restore economic validity.

The PBAC Guidelines must be urgently updated to reaffirm their original intent, that the default comparator is the therapy likely to be replaced in clinical practice. Over time, the language in the Guidelines has been diluted, creating ambiguity that enables selection of theoretical or legacy comparators disconnected from contemporary practice.

The updated Guidelines must reinstate and embed the core principles of earlier versions - clinical alignment for the relevant population, and transparent reasoning. This should adapt language from the alternate recommendation submitted to the HTA Review by Medicines Australia to state 'the Committee must consider the alternative therapy or therapies for the relevant patient population and any sub-populations to be the therapy or therapies most likely to be replaced in clinical practice for the largest number of patients.' Justification for any deviation to the comparator throughout the evaluation process will need to be provided to the sponsor company by the PBAC.

Additionally, the Guidelines need to clearly articulate how the comparator is determined, including the role of alternative mechanisms of action or delivery. This simple but critical clarification ensures the assessment captures the true incremental value of the innovation, rather than an artificial price difference against a legacy drug. This technical clarity is essential to maintain the validity, value and intent of economic evaluation.

These changes are necessary as an economic evaluation is only valid if it measures the new medicine against what it displaces. When assessments are anchored to theoretical comparators that are no longer standard of care, the entire basis of the value calculation is compromised. Establishing technical clarity on this point is essential to prevent the selection of irrelevant medicines that distort the economic profile of new innovations.

ACTION 2

Amend the *National Health Act 1953 (Commonwealth)* to reference the PBAC Guidelines.

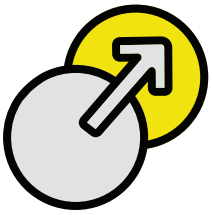
While Action 1 would restore economic validity to the Australian evaluation process, it is not a standalone solution. Action 2 must be implemented concurrently to ensure both the interpretation and application of comparator selection are protected by standard legislative safeguards. This action calls for an urgent amendment to the *National Health Act 1953 (Cth)* or subordinate legislation to explicitly reference the PBAC Guidelines. Currently, the Act does not strictly bind the PBAC or sponsor companies to compliance with these Guidelines. This creates a governance gap, with Guidlines not legally tethered to the legislative authority of the listing process.

Strengthening the governance of the PBS listing process requires a clear legislative link between the Act, regulations and the Guidelines. Formally referencing the Guidelines within the Act or related legislative instruments will ensure that decision-making is legally bound to a transparent and economically valid framework. This protects the integrity of the public process by preventing administrative discretion from drifting away from established scientific and health economic best practice. Without this statutory link, the improvements made in Action 1 remain vulnerable to inconsistent application.

This model offers a distinct strategic advantage over prescriptive and isolated legislative reform. By ensuring that the requirement to follow Guidelines is enshrined in legislation rather than encoding the methodology itself, the system retains the flexibility to adapt to future challenges without requiring ongoing legislative amendments. This approach addresses the core intent of Medicines Australia's call for greater accountability and governance, specifically, Elizabeth de Somer's alternate Recommendation 40 which sought to include a clause in the Act stating that the 'Committee must consider the therapy or therapies most likely to be replaced in clinical practice.' [14] While aligned in principle, our proposed model achieves this standard without creating a rigid system that cannot evolve. It ensures that enforceable requirements balance the need for certainty with the necessity of administrative agility.

To implement this, the Government should expedite exploration of appropriate legislative mechanisms to formalise the legal status of the PBAC Guidelines. This may involve identifying the most effective statutory instrument to create a binding requirement for the PBAC to comply with the Guidelines when formulating their advice.

Ultimately, this reform will help to rebuild trust between Government and industry by providing the assurance of statutory governance without constraining the discretionary levers needed for priority populations or future system reforms.



ACTION 3

Transition to a PICO (Population, Intervention, Comparator, Outcome) model where the comparator is agreed with PBAC during the early stages of the submission pathway.

Several changes are needed to support better HTA methodologies, and the bigger picture of HTA more broadly. This includes a more formal process for the formulation and testing of the comparator to be evaluated.

This would involve a formalised pre-submission milestone where the PICO criteria, including the comparator, are agreed upon between the sponsor and the PBAC and publicly documented prior to submission. This follows the precedent set by the Medical Services Advisory Committee (MSAC), where the PICO is developed in consultation with an independent HTA group and sponsor input before it is confirmed by the PICO Advisory Subcommittee. [90] This model allows sponsors to provide input and even attend subcommittee meetings before the full assessment commences to ensure alignment on the clinical baseline. [90]

Our research reveals that predictability of comparator agreement with the PBAC has diminished. This forces sponsors to increasingly prepare submissions around anticipated PBAC behaviour rather than clinical reality. When a submission is anchored to a comparator that clinicians no longer use, we argue that the resulting economic evaluation is flawed. Confirming the comparator upfront is essential to stop inappropriate LCC substitution, remove avoidable uncertainty, and ensure evaluations reflect contemporary best practice. Without this early agreement, the system generates significant churn and wastes resources on submissions with economic models destined to be rejected.

To operationalise this transition, Recommendation 32 of the HTA Policy and Methods Review should be implemented in the short term. This recommendation represents a step forward by proposing a framework that governs when and how the PICO should be developed. [14] This should involve establishing a formal confirmation step within the PBAC pathway that mirrors the MSAC process and allows for sponsor engagement and PICO agreement with the PBAC prior to submission. Furthermore, it is critical to mandate the inclusion of clinician input during this phase to validate that the selected comparator accurately reflects that most likely to be replaced in practice, cognisant of contemporary clinical approaches and real-world treatment pathways.

This process should mirror transparency principles exhibited in MSAC's processes, including the public release of the ratified PICO and summarised consultation input. It could also be strengthened by providing justification of why the outcome is in the interest of consumers and clinicians. Furthermore, the improved process must include a formal appeal mechanism for sponsors. This is critical for instances where a positive PBAC recommendation varies from the previously agreed PICO.

ACTION 4

Fast-track implementation of other relevant HTA Review recommendations.

Modernising Australia's HTA framework requires the fast-tracked implementation of relevant technical recommendations from the HTA Review. Specifically, the Government must prioritise Recommendations 7, 32 (see action 3), 41, and 42 which directly address HTA methodology. These reforms are critical to ensure the HTA framework can accurately assess and value the complex profile of innovative medicines. This includes strengthening processes for cost-minimisation submissions, which, according to sponsors, are the submission type most affected by comparator selection issues. [11] By focusing on these areas, the system can support equitable access and future-proof the alignment of decision-making with best-practice health economic methodologies worldwide.

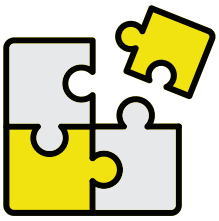
Many of the pressures undermining Australia's HTA system are already noted in the HTA Review, but are yet to be implemented. Specifically, recommendations that should be progressed include:

- **Recommendation 7** – *Streamlined pathway for submissions applying for PBS listing using cost-minimisation analysis*. Submissions using cost-minimisation analysis are most commonly affected by issues in comparator selection. [11] Where substitution with LCC occurs, this can result in multiple submissions being made, which use significant time and resources. System improvements are needed to prevent these submissions, which is "reduced to a cost comparison" from being delayed by avoidable methodological debates. [7] Additionally, improving transparency of the effective comparator price would help to address the information asymmetry that contributes to submissions being resubmitted or delayed. This is currently scheduled for action over Year 1 and Year 2 by the IAG. [14, 44]
- **Recommendation 32** - *Creating a framework for PICO development to support HTA submissions*. As per Action 3, earlier agreement on PICOs that reflect real-world clinical practice is essential to preventing inappropriate comparators from being utilised. Fast-tracking this ensures evaluations begin with clinically relevant anchors and strengthens economic analysis for decision-making. This is currently slated for action in Year 1 by the IAG. [14, 44]
- **Recommendation 41** - *Cost-minimisation submissions.* In alignment with Recommendation 7, process improvement is needed to streamline cost-minimisation submissions. Compared to the therapy most likely to be replaced in practice, these submissions are made for medicines with equivalent or greater clinical and safety benefits, at the same or lower cost. [7] To ensure these submissions do not unnecessarily complicate evaluations, the methods and level of appraisal required for cost-minimisation analysis should be commensurate to their risk and benefit. This is currently scheduled for action over Year 1 and Year 2 by the IAG. [14, 44]
- **Recommendation 42** – *Value and pricing*. This includes clarifying when higher prices for health technologies may be reasonable to accept. Accelerating this work is critical where current LCC practices often undervalue innovation, create rigid price anchors that are increasingly misaligned with global norms, and contribute to delayed or foregone launches in Australia. Establishing when higher prices may be reasonable is therefore essential to prevent LCC from continuing to act as a structural barrier to timely access. Research on higher pricing usage is mapped for action in Year 1 by the IAG. [14, 44]

The IAG roadmap has identified these areas for action in the first three years. However, in a global market increasingly constrained by MFN considerations, Australia cannot afford to wait. The urgency of the current environment demands these reforms be actioned more quickly. Accelerating these reforms will strengthen and modernise evaluative methods. This ensures Australia recognises the full value of innovation over a medicine's lifecycle, improves transparency in comparator selection, and reduces disincentives for sponsors to bring new treatments to market.

Medium term: Invest in Australia's future over the next two years

Medicines are the most common health intervention. [1] If we want Australia to be healthier, wealthier and more productive, it follows that the level of PBS investment must increase. Increasing investment in the PBS yields limited returns if the underlying value assessment remains distorted by structural barriers. Currently, statutory price reductions function as administrative mechanisms rather than market signals. Consequently, they artificially depress the economic baseline for new innovations and sever the link between price and value. Restoring the integrity of the assessment requires decoupling these administrative price events from the evaluation of clinical benefit. To repair this value proposition, we propose three structural adjustments.



ACTION 5

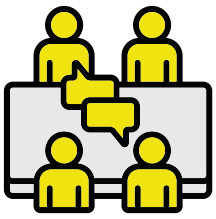
Embed flexible approaches for medicines responding to high patient needs, particularly where ongoing pricing policies have eroded comparator prices.

The HTA Review recognised a need to improve the pathways and processes for listing therapies with high added therapeutic value on the PBS.

This is necessary because current pricing policies effectively punish innovation by anchoring new therapies to the price of old medicines that have undergone years of statutory price reductions. When a comparator's price is driven down by these administrative mechanisms, it no longer reflects its real-world health value. This creates a distortion where a new and patent-protected medicine is deemed "not cost-effective" simply because the baseline has been artificially lowered. Consequently, valid clinical advancements are blocked from the PBS because they cannot mathematically compete with an administratively depreciated comparator.

To correct this, the Government must implement flexible approaches that decouple the economic evaluation from these artificial price floors for therapies that respond to high or unmet patient needs. This approach to HTA must allow the use of shadow pricing. This is where a notional and clinically appropriate comparator price is applied to the listed price in circumstances where it no longer reflects real-world value. To accurately measure value where multiple pricing policies apply, shadow prices should reflect the medicine's initial cost-effective price, prior to any erosion.

Additional measures could include fee waivers or adjusted evidentiary requirements to ensure that economic evaluations are not anchored to artificially low comparator prices.



ACTION 6

Initiate structured Government-industry dialogue on the interplay between Statutory Price Reductions (SPRs) and innovation.

In a value-based assessment system, there is a complex interplay between the principles of HTA and of systemic and ongoing price reduction policies. Understanding how these two approaches to price setting interplay in the Australian medicine sector is critical.

Alongside use of LCCs, application of five- and 10-year anniversary price cuts disincentivise innovation, whilst triggering two sets of price cuts. These overlapping pricing levers compound uncertainty in launch planning, narrow commercial viability and have already contributed to submissions being delayed, abandoned or not made. There is a need to rebalance how these are applied in the broader landscape of pricing policies and innovation needs.

Open and constructive dialogue between Government and industry is needed to rectify this issue. This should commence with data collection to understand the impact of price cuts on innovative medicines access, including submissions abandoned due to price cuts levied on comparators, and any unintended consequences for launching medicines in Australia.

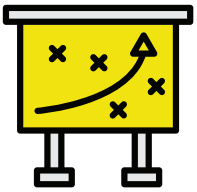
ACTION 7

Increase investment in medicines by aligning PBS funding with the growth in health needs.

Medicines and vaccines play a central role in Australia's health system, yet net PBS spending has remained relatively flat in recent years, with more recent analysis showing a contraction in the last 12 months. Between 2016-17 to 2023-24, net PBS expenditure increased only modestly from $8.5 billion to $12.4 billion, before contracting to $12.3 billion in 2024-25. [15] Declines in PBS expenditure risk Australia falling further behind in growth of disease burden, reinforcing the need for funding indexation to maintain equitable and timely access. Strengthening PBS funding growth is essential to ensure the system can sustainably accommodate the cost of innovation, rather than relying on eroded comparator prices that perpetuate LCC-driven access challenges.

Long term: Elevate Australia's global position in the next five years

Beyond remediating the effects of comparator selection, a broader agenda is needed to elevate Australia to a priority destination for global investment. In the age of MFN and increasing global competition, Australia needs a unified vision that signals a national willingness to value and invest in innovation. This is necessary to create a more connected and thriving life sciences sector which can secure the health of our nation and guarantee patient access to innovative medicines. To ensure continuing access to the next generation of care, our focus must shift from short-term fiscal perspectives to building a globally competitive life sciences sector. One key action can ensure we are all working towards this goal.



ACTION 8

Co-design a national life sciences sector strategy.

This action calls for the development of a unified national life sciences strategy, co-designed by Government, industry, research, patient and clinical partners. Currently, Australia's policy landscape is fragmented, creating uncertainty that dampens global investment. A bold, end-to-end plan is required to align these disparate elements into a cohesive ecosystem. This strategy offers a practical way to position Australia for long-term success by integrating the pharmaceutical, medical technology, and research sectors under a shared national vision.

To counter growing concern about Australia's attractiveness for innovation, this strategy must strengthen support for the entire product lifecycle. This involves coordinating priorities across clinical trials, regulatory pathways, and reimbursement settings. By aligning these pillars, the strategy can support sustainable innovation and improve equitable access to advanced therapies. This approach is critical to prevent the fragmentation of care and reduce the leakage of patients into the private sector due to gaps in public access.

Australia has a clear opportunity to follow the blueprint set by the UK's Life Sciences Sector Plan. [91] Published in 2025, the UK's strategy successfully focuses on strengthening research and development, growing local companies, attracting global capital, and delivering better patient outcomes. Adopting a similar framework would strengthen the connections between industry, Government, clinicians, researchers and patient advocates, ultimately securing Australia's place in the competitive global innovation landscape.

By acting on this phased roadmap, Australia can restore the economic integrity of its HTA process; ensuring that how medicines are assessed, priced and valued reflects true clinical reality. This restoration of rigorous, valid methodology is the foundation for rebuilding trust. Alongside this, stronger collaboration between Government, industry, clinicians, and patient groups will provide the predictability needed for companies to invest, innovate, and bring new therapies to market. These steps are needed to ensure Australians have timely, safe and affordable access to the medicines they need.

The actions outlined in this report lay the groundwork for a viable and sustainable life sciences sector, a PBS that delivers equitable access to clinically and cost-effective medicines for all, and a system that uses resources judiciously. Together, they strengthen the foundations of the NMP and ensure Australians are not left behind as global innovation accelerates. Now is the moment for Government and industry to commit to these changes and secure Australia's future as a leader in life-changing medical innovation.

ABBREVIATIONS

Abbreviation	Description
ART	Antiretroviral therapy
AMR	Antimicrobial Resistance
bDMARD	Biological disease modifying anti-rheumatic drug
CEO	Chief Executive Officer
Cth	Commonwealth
COPD	Chronic obstructive pulmonary disease
DFP	Dry powder formulation
DME	Diabetic macular oedema
F1	Formulary 1
F2	Formulary 2
FNB	First new brand
HIV	Human immunodeficiency virus
HTA	Health Technology Assessment
IAG	Implementation Advisory Group
IL-6	Interleukin-6
ISPOR	Professional Society for Health Economics and Outcomes Research
LABA	Long-acting beta-agonist
LAMA	Long-acting muscarinic antagonist
LCC	Lowest cost comparator
MA	Medicines Australia

Abbreviation	Description
MP	Member of Parliament
MFN	Most Favoured Nation
MSAC	Medical Services Advisory Committee
NIP	National Immunisation Program
NME	New molecular entity
NMP	National Medicines Policy
OECD	Organisation for Economic Co-operation and Development
PBS	Pharmaceutical Benefits Scheme
PBAC	Pharmaceutical Benefits Advisory Committee
PSD	Public Summary Document
PICO	Population, Intervention, Comparator, Outcome
QoL	Quality of life
RVO	Retinal vein occlusion
SPR	Statutory Price Reduction
TGA	Therapeutic Goods Administration
tsDMARD	Targeted synthetic disease-modifying anti-rheumatic drugs
UC	Ulcerative colitis
UK	United Kingdom
US	United States
WHO	World Health Organization

REFERENCES

1. Department of Health and Aged Care. *National Medicines Policy 2022*. 2022; Available from: https://www.health.gov.au/sites/default/files/2022-12/national-medicines-policy.pdf.
2. Mark Butler MP. *Press Conference Adelaide Friday, 21 March 2025*. 2025; Available from: https://www.markbutler.net.au/news/transcripts/press-conference-adelaide-friday-21nbspmarch-2025.
3. Pharmaceutical Benefits Scheme. *About the PBS*. 2025; Available from: https://www.pbs.gov.au/info/about-the-pbs.
4. Medicines Australia. *The patient access gap: Speed up access to new medicines and medical technologies to reduce the Australian patient access gap*. 2022; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2022/11/HTA-DP-Patient-Access-Gap.pdf.
5. Amgen Australia. *Australian Patient Access Gap Tracker Edition 8 - January 2021 to Dec 2025*. 2025; Available from: https://www.amgen.com.au/responsibility/-/media/Themes/CorporateAffairs/Redesign/Amgen-com-au/Amgen-com-au/Documents/Amgen-Patient-Access-Gap-Tracker-and-Infographic-July-2025-APPROVED.pdf.
6. Department of Health Disability and Ageing. *Health technology assessments*. 2025; Available from: https://www.health.gov.au/topics/health-technologies-and-digital-health/health-technology-assessments.
7. Pharmaceutical Benefits Advisory Committee. *Section 3 Economic Evaluation: Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (PBAC)*. 2016; Available from: https://pbac.pbs.gov.au/section-3-economic-evaluation.html.
8. Pharmaceutical Benefits Advisory Committee. *1.1 Clinical issue addressed by the submission: Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (PBAC)*. 2016; Available from: https://pbac.pbs.gov.au/section-1/1-1-clinical-issue-addressed_by-the-submission.html.
9. Kristensen, F.B., et al., *Identifying the Need for Good Practices in Health Technology Assessment: Summary of the ISPOR HTA Council Working Group Report on Good Practices in HTA.* Value Health, 2019. **22**(1): p. 13-20.
10. Department of Health Disability and Ageing. *HTA for Australian Government subsidy*. 2025; Available from: https://www.health.gov.au/topics/health-technologies-and-digital-health/health-technology-assessments/for-subsidy?language=en.
11. Evohealth, *Survey of innovative pharmaceutical companies: Exploring how comparator choice is shaping access to innovative medicines in Australia*. 2025.
12. House of Representatives Standing Committee on Health, A.C.a.S. *The New Frontier - Delivering better health for all Australians*. 2021; Available from: https://parlinfo.aph.gov.au/parlInfo/download/committees/reportrep/024755/toc_pdf/TheNewFrontier-DeliveringbetterhealthforallAustralians.pdf;fileType=application%2Fpdf.
13. Pharmaceutical Benefits Scheme. *Strategic Agreements with the Medicines Industry*. 2021; Available from: https://www.pbs.gov.au/info/general/medicines-industry-strategic-agreement.
14. Review Reference Committee. *Health Technology Assessment Policy and Methods Review - Final Report*. 2024; Available from: https://www.health.gov.au/sites/default/files/2024-09/health-technology-assessment-policy-and-methods-review-final-report_0.pdf.
15. Department of Health Disability and Ageing. *Annual reports*. 2025; Available from: https://www.health.gov.au/topics/about-the-department/corporate-reporting/annual-reports?language=en.
16. Organisation for Economic Co-operation and Development (OECD). *New Health Technologies: Managing Access, Value and Sustainability*. 2017; Available from: https://www.oecd.org/content/dam/oecd/en/publications/reports/2017/01/new-health-technologies_g1g72f2b/9789264266438-en.pdf.
17. Medicines Australia. *Funding Innovative Medicines*. 2023; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/06/Funding-Innovative-Medicines-1.pdf.
18. The Pharmaceutical Benefits Scheme. *4.1 Types of submissions*. 2025; Available from: https://www.pbs.gov.au/info/industry/listing/procedure-guidance/4-presubmission-requirements/4-1-types-of-submissions.
19. Medicines Australia. *04. The Value of Medicines & Australia's Medicines Industry*. 2020; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2020/11/4.-The-value-of-medicines-and-Australias-medicines-industry.pdf.
20. Lichtenberg, F.R., *Number of drugs provided by the Pharmaceutical Benefits Scheme and mortality and hospital utilization in Australia, 2002–2019.* SSM - Population Health, 2023. **24**: p. 101514.
21. Research Australia. *Creating a dynamic and resilient economy: Interim Report Submission*. 2025; Available from: https://researchaustralia.org/wp-content/uploads/2025/09/Response-to-the-Productivity-Commissions-Five-Pillars-of-Productivity-Inquiries-Research-Australia-Submission.pdf.

22. Fox, N., et al., *The Value of Vaccines: A Tale of Two Parts.* Vaccines, 2022. **10**(12): p. 2057.
23. Mahara, G., et al., *Revolutionising health care: Exploring the latest advances in medical sciences.* Journal of Global Health, 2023. **13**(03042).
24. Moses, H., III, et al., *The Anatomy of Medical Research: US and International Comparisons.* JAMA, 2015. **313**(2): p. 174-189.
25. O'Neill, J. *Tackling drug-resistant infections globally: final report and recommendations*. 2016; Available from: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf.
26. Evohealth. *Fighting superbugs: The Path Forward*. 2025; Available from: https://www.evohealth.com.au/work/fighting-superbugs-the-path-forward/.
27. Theuretzbacher, U., et al., *The global preclinical antibacterial pipeline.* Nat Rev Microbiol, 2020. **18**(5): p. 275-285.
28. Outterson, K., et al., *Repairing the broken market for antibiotic innovation.* Health Aff (Millwood), 2015. **34**(2): p. 277-85.
29. World Health Organization. *Medicines reimbursement policies in Europe*. 2018; Available from: https://www.who.int/europe/publications/i/item/9789289053365.
30. Lee Mendoza, R., *Incentives and disincentives to drug innovation: evidence from recent literature.* Journal of Medical Economics, 2019. **22**(8): p. 713-721.
31. Medicines Australia. *Facts Book 2021: Fifth Edition*. 2021; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2021/06/Medicines-Australia-Facts-Book-2021.pdf.
32. Mulcahy, A.W., *Comparing New Prescription Drug Availability and Launch Timing in the United States and Other OECD Countries.* Rand Health Q, 2024. **11**(3): p. 4.
33. Australian Institute of Health and Welfare. *Health Expenditure*. 2025; Available from: https://www.aihw.gov.au/reports/health-welfare-expenditure/health-expenditure.
34. Medicines Australia. *Stronger PBS*. 2025; Available from: https://www.strongerpbs.com.au/.
35. Medicines Australia. *Medicines Matter 2022: Australia's Access to Medicines 2016-2021*. 2022; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/04/Medicines-Matter-2022-FINAL.pdf.
36. Medicines Australia. *HTA comparators: Evaluations of innovative medical technologies should compare their benefits and costs against standard clinical practice in Australia*. 2022; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2022/11/HTA-DP-Comparators.pdf.
37. Department of Health Disability and Ageing. *About the HTA Review*. 2024; Available from: https://www.health.gov.au/our-work/hta-review/about.
38. Commonwealth Government, *National Health Act 1953 (Cth) s 101(3B)*. Australasian Legal Information Institute.
39. Pharmaceutical Benefits Scheme. *Cost Recovery Fees and Charges*. 2025; Available from: https://www.pbs.gov.au/info/industry/listing/elements/fees-and-charges.
40. Medicines Australia. *Fact Sheet: Comparator Selection*. 2024; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2024/10/Fact-sheet-Comparator-selection.pdf.
41. Medicines Australia. *Re: ANAO audit of PBS Administration 2023-24 - Medicines Australia submission 2*. 2024; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2024/11/20240405_ANAO_PBS_MedicinesAustralia_Submission2_FINAL.pdf.
42. Parliament of Australia. *Inquiry into approval processes for new drugs and novel medical technologies in Australia*. 2021; Available from: https://www.health.gov.au/sites/default/files/2023-11/inquiry-into-approval-processes-for-new-drugs-and-novel-medical-technologies-in-australia.pdf.
43. Department of Health. *Strategic Agreement in relation to reimbrusement, health technology assessment and other matters*. 2022; Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/10/ma-strategic-agreement-22-27.pdf.
44. Health Technology Assessment Review Implementation Advisory Group. *Draft Roadmap Consultation*. 2025; Available from: https://www.health.gov.au/sites/default/files/2025-10/hta-review-implementation-advisory-group-october-webinar-slides_0.pdf.
45. The Hon Mark Butler MP. *Speech from Minister Butler, Australian Parliament House – 3 September 2025*. 2025; Available from: https://www.health.gov.au/ministers/the-hon-mark-butler-mp/media/speech-from-minister-butler-australian-parliament-house-3-september-2025.
46. Health Technology Assessment Review Implementation Advisory Group. *Interim Report - 6 August 2025*. 2025; Available from: https://www.health.gov.au/sites/default/files/2025-09/hta-review-implementation-advisory-group-interim-report.pdf.
47. Novartis. *HTA Policy and Methods Review: Response to Consultation 2*. 2024; Available from: https://ohta-consultations.health.gov.au/ohta/hta-review-consultation-2/results/novartis_c2response_publishattributed_redacted.pdf.
48. Medicines Australia. *Access*. 2022; Available from: https://www.medicinesaustralia.com.au/publications/issues-briefs/access/.

49. Pharmaceutical Benefits Advisory Committee. *Breztri Aerosphere® DFP-EvoCap - Public Summary Document - November 2022 PBAC Meeting with June 2023 OOS Addendum* 2023; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2022-11/files/budesonide-with-glycopyrronium-and-formoterol-psd-11-2022-oos-06-2023.pdf.

50. Therapeutic Goods Administration. *PIFELTRO doravirine 100 mg film-coated tablet bottle (297701)*. 2019; Available from: https://www.tga.gov.au/resources/artg/297701.

51. Pharmaceutical Benefits Advisory Committee. *Lucentis® - Public Summary Document - November 2012 PBAC Meeting* 2012; Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2012-11/ranibizumab-lucentis.

52. Pharmaceutical Benefits Advisory Committee. *Lucentis®- Public Summary Document - March 2013 PBAC Meeting* 2013; Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2013-03/ranibizumab.

53. Pharmaceutical Benefits Advisory Committee. *Lucentis® (DME) - Public Summary Document - November 2013 PBAC Meeting* 2013; Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2013-11/ranibizumab-dme.

54. Pharmaceutical Benefits Advisory Committee. *Lucentis® (RVO) - Public Summary Document - November 2013 PBAC Meeting* 2013; Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2013-11/ranibizumab-rvo.

55. Pharmaceutical Benefits Advisory Committee. *Lucentis® - Public Summary Document - March 2014 PBAC Meeting* 2014; Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2014-03/ranibizumab.

56. Pharmaceutical Benefits Advisory Committee. *Lucentis®(DME) - Public Summary Document - July 2014 PBAC Meeting* 2014; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2014-07/ranibizumab-dme-psd-07-2014.pdf.

57. Pharmaceutical Benefits Advisory Committee. *Lucentis®(RVO) - Public Summary Document - July 2014 PBAC Meeting* 2014; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2014-07/ranibizumab-rvo-psd-07-2014.pdf.

58. Pharmaceutical Benefits Scheme. *Ministerial Discretion to reduce or not apply Statutory Price Reductions*. 2025; Available from: https://www.pbs.gov.au/info/industry/pricing/ministerial-discretion.

59. Pharmaceutical Benefits Advisory Committee. *Price Disclosure Reductions for 2017 October Cycle*. 2017; Available from: https://www.pbs.gov.au/info/industry/pricing/price-disclosure-spd/price-disclosure-reductions-2017-october-cycle.

60. Pharmaceutical Benefits Advisory Committee. *Price Disclosure Reductions for 2018 October Cycle*. 2018; Available from: https://www.pbs.gov.au/info/industry/pricing/price-disclosure-spd/price-disclosure-reductions-for-2018-october-cycle.

61. Pharmaceutical Benefits Advisory Committee. *Price Disclosure Reductions for 2019 October Cycle*. 2019; Available from: https://www.pbs.gov.au/info/industry/pricing/price-disclosure-spd/price-disclosure-reductions-for-2019-october-cycle.

62. Pharmaceutical Benefits Advisory Committee. *Price Disclosure Reductions for 2022 October Cycle*. 2022; Available from: https://www.pbs.gov.au/info/industry/pricing/price-disclosure-spd/Price-Disclosure-Reductions-for-2022-October-Cycle.

63. Pharmaceutical Benefits Advisory Committee. *Price Disclosure Reductions for 2024 October Cycle*. 2024; Available from: https://www.pbs.gov.au/info/industry/pricing/price-disclosure-spd/Price-Disclosure-Reductions-for-2024-April-Cycle.

64. Pharmaceutical Benefits Advisory Committee. *Infliximab, 100 mg injection, 1 x 100 mg vial, Remicade® - Match 2014*. 2014; Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2014-03/infliximab-psd-03-2014.

65. Pharmaceutical Benefits Advisory Committee. *VEDOLIZUMAB 300mg vial; Entyvio®, Takeda Pharmaceutical Australia.* 2015; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2015-03/Files/vedolizumab-2-psd-march-2015.pdf.

66. Pharmaceutical Benefits Advisory Committee. *GOLIMUMAB, Injection 50 mg in 0.5 mL single use pre-filled syringe and injection 50 mg in 0.5 mL single use pre-filled pen, Simponi® and Simponi Smartject®, Janssen-Cilag Pty Ltd*. 2018; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2018-07/files/golimumab-psd-july-2018.pdf.

67. Pharmaceutical Benefits Advisory Committee. *TOFACITINIB, Tablet 5mg, tablet 10mg, Xeljanz®, Pfizer Australia Pty Ltd*. 2020; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2020-11/files/tofacitinib-psd-nov-2020.pdf.

68. Pharmaceutical Benefits Advisory Committee. *OZANIMOD, Pack containing 28 capsules 920 micrograms; Pack containing 4 capsules 230 micrograms and 3 capsules 460 micrograms Zeposia®, Celgene Pty Ltd*. 2022; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2022-11/files/ozanimod-psd-11-2022.pdf.

69. Pharmaceutical Benefits Advisory Committee. *USTEKINUMAB Injection 130mg in 26mL vial, injection 45mg in 0.5mL vial, Stelara®, Janssen Cilag Australia Pty Ltd*. 2017; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2017-03/files/ustekinumab-psd-march-2017.pdf.

70. Pharmaceutical Benefits Scheme. *Medicine Status Website: OZANIMOD*. 2026; Available from: https://www.pbs.gov.au/medicinestatus/document/846.html.
71. The Pharmaceutical Benefits Scheme. *Fact sheet – Setting an approved ex-manufacturer price for new or extended listings*. 2017; Available from: https://www.pbs.gov.au/info/industry/pricing/pbs-items/fact-sheet-setting-an-approved-ex-manufacturer-price.
72. Pharmaceutical Benefits Advisory Committee. *Public Summary Document - USTEKINUMAB, Injection 90 mg in 1 mL pre-filled syringe, Solution concentrate for I.V. infusion 130 mg in 26 mL Stelara®, Janssen-Cilag Pty Ltd.* 2022; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2022-07/files/ustekinumab-uc-psd-july-2022.pdf.
73. Pharmaceutical Benefits Scheme. *Medicine Status Website: USTEKINUMAB*. 2025; Available from: https://www.pbs.gov.au/medicinestatus/document/808.html.
74. Pfizer Australia. *Health Technology Assessment Review Submission* 2023; Available from: https://www.pfizer.com.au/files/Pfizer-Australia_HTA-Review_submission.pdf.
75. Pharmaceutical Benefits Advisory Committee. *Prevenar 20® - Public Summary Document -November 2022 PBAC Meeting* 2022; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2023-11/files/20-valent-pneumococcal-conjugate-vaccine-psd-nov-2023.pdf.
76. Pharmaceutical Benefits Advisory Committee. *Prevenar 20® - Public Summary Document - November 2023 PBAC Meeting* 2023; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2023-11/files/20-valent-pneumococcal-conjugate-vaccine-psd-nov-2023.pdf.
77. National Immunisation Program. *Childhood pneumococcal vaccine Program advice for health professionals*. 2025; Available from: https://www.phnimmunise.org.au/assets/Provider-advice.pdf.
78. Pharmaceutical Benefits Advisory Committee. *Kevzara® - Public Summary Document - November 2018 PBAC Meeting*. 2018; Available from: https://m.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2018-11/files/sarilumab-psd-november-2018.pdf.
79. Therapeutics Goods Administration. *KEVZARA sarilumab (rch) 150 mg (131.6 mg/mL) solution for injection pre-filled pen Cancelled under Section 30(1)(c) of the Act*. 2021; Available from: https://www.tga.gov.au/resources/cancellations-by-sponsors/kevzara-sarilumab-rch-150-mg-1316-mgml-solution-injection-pre-filled-pen-cancelled-under-section-301c-act.
80. Pharmaceutical Benefits Scheme. *PBS Arrangements for tocilizumab shortage*. 2021; Available from: https://www.pbs.gov.au/info/news/2021/08/pbs-arrangements-for-tocilizumab-shortage.
81. Janetzki, J.L., et al., *Impact of medicine shortages on Australian pharmacists' professional practice and patient care: a nationwide survey.* Journal of Pharmacy Practice and Research, 2025. **55**(2): p. 146-153.
82. IQVIA. *Evolving Beyond the PBS: Exploring Australia's Private Medicines Market*. 2025; Available from: https://www.iqvia.com/-/media/iqvia/pdfs/australia-and-new-zealand/white-papers/iqvia-anz-evolving-beyond-the-pbs-whitepaper.pdf.
83. The Pharmacy Guild of Australia. *1 in 5 Australians have delayed or forgone medicines due to cost*. 2025; Available from: https://www.guild.org.au/news-events/news/forefront/v16n02/2-amn.
84. Department of Health Disability and Ageing. *Ninth National HIV Strategy*. 2024; Available from: https://www.health.gov.au/sites/default/files/2024-12/ninth-national-hiv-strategy-2024-2030.pdf.
85. Pharmaceutical Benefits Advisory Committee. *Vocabria® and Cabenuva® - Public Summary Document - March 2021 PBAC Meeting* 2021; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-03/files/cabotegravir-rilpivirine-psd-mar-2021.pdf.
86. Pharmaceutical Benefits Advisory Committee. *Vocabria® and Cabenuva® - Public Summary Document - November 2021 PBAC Meeting* 2021; Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-11/files/cabotegravir-rilpivirine-psd-nov-2021.pdf.
87. Evohealth, *Survey of patient advocates: Impact of comparator choice on medicines access*. 2025.
88. Australian Clinical Trials. *National reforms in health and medical research*. 2025; Available from: https://www.australianclinicaltrials.gov.au/resources/national-reforms-health-and-medical-research.
89. The Hon Mark Butler MP. *$13.6 million to cement Australia's status in world-class clinical trials - 2 October 2025*. 2025; Available from: https://www.health.gov.au/ministers/the-hon-mark-butler-mp/media/136-million-to-cement-australias-status-in-world-class-clinical-trials?language=en.
90. Medical Services Advisory Committee. *PICO confirmation development*. 2024; Available from: https://www.msac.gov.au/apply/pre-assessment/pico-confirmation-development.
91. GOV.UK. *Life Sciences Sector Plan to grow economy and transform NHS*. 2025; Available from: https://www.gov.uk/government/news/life-sciences-sector-plan-to-grow-economy-and-transform-nhs.

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Authors: Renae Beardmore, Deanna Mill, Madeline Wilson, James Taylor

Report design: Adam Sorgini

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+61 2 6198 3440

www.evohealth.com.au

Level 1, 18 National Circuit,
Barton ACT, Australia 2600