Medicines Australia | Better health through research and innovation

HTA comparators

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Evaluations of innovative medical technologies should compare their benefits and costs against standard clinical practice in Australia

- In Australia, a new medicine or treatment must go through a Health Technology Assessment (HTA) to determine its efficacy, safety and benefit before it can be listed on the Pharmaceutical Benefits Scheme (PBS).
- The comparator in HTA compares the new medicine to other existing, similar medicines to determine if the new technology provides any additional benefits to what is already reimbursed.
- International best practice HTA principles and the Pharmaceutical Benefits Advisory Committee (PBAC) guidelines state that the comparator used as a benchmark should be the medicine which is the most likely to be replaced in practice by the new medicine.
- However, Australian HTA policy has adopted the "lowest cost comparator" as a standard approach, even when this is not widely used in clinical practice, which provides an excessively low-price benchmark and frequently results in sponsors being unable to continue pursuing listing for new medicines onto the PBS.
- The Strategic Agreement between Medicines Australia and the Australian Government states the PBAC can determine whether a particular therapy is an alternative therapy, regardless of whether it is the lowest cost comparator.

Possible policy outcomes

1. The comparator should be the treatment most likely to be replaced in practice by the proposed medicine. An appropriate approach to comparator selection would be to reinstate the intent of the original PBAC guidelines in policy. This would mean that the comparator would be the medicine most likely to be replaced in clinical practice, which would be consistent with the original interpretation of the National Health Act (pre-2016) and the practice of other international HTA organisations.

Please note, this is a discussion paper that has been developed with the intention to start the conversation. It is not a final position paper.

2. If a new medicine is non-inferior to multiple comparators that it could replace, and a cost-minimisation approach is appropriate, the cost-minimised price of the new medicine should be the average price of the other alternative medicines weighted by market share, rather than the price of the lowest priced alternative. The weighted comparator pricing approach is a fair and balanced solution that achieves a comparator price which more accurately represents the average cost to the PBS of current treatment.

What is a comparator?

The comparator is used to establish the benchmark upon which comparative efficacy, safety and cost-effectiveness analyses are conducted. The comparator is instrumental in determining the price and budget impact of a new medicine.

The original definition and intent of the PBAC Guidelines was for the comparator to be the *most likely medicine(s) to be replaced in clinical practice.* This approach is consistent with HTA best-practice principles and comparable international HTA organisations. International HTA organisations continue to reference the comparator specific to use in clinical practice. No international organisation mandates that a comparator reference *must* be the lowest priced comparator (Table 1). While Canada requests a comparison with 'minimum practice', the requirement for this approach alone to inform reimbursement decisions is not as rigid as in Australia.

Why do comparators matter?

One key aspect outlined for consideration in the 2022 Independent HTA Review is the approach to comparator selection. If the current use of the of lowest cost comparator and reference pricing policy continues, it will delay and prevent sponsors from bringing new, innovative therapies to Australia and threaten the supply of existing medicines.

In the current system, if a sponsor cannot demonstrate a statistically significant and clinically meaningful improvement in efficacy or safety over an alternative medicine, the PBAC is unwilling to recommend a new medicine at a higher cost than the lowest cost alternatives (irrespective of their market shares and likelihood of being replaced in practice).

Patient preferences – which can lead to higher medicine compliance – are not accepted as a justification for superiority by the PBAC unless these outcomes are supported by direct evidence of improved clinical effectiveness or safety. The default position, in the absence of evidence of an improvement in efficacy or safety, is for the PBAC to assume no clinical difference. The PBAC's preference for randomised controlled trial (RCT) data, and unwillingness to accept a claim of therapeutic superiority using indirect comparison methodology, often sets an unattainable evidence threshold. Therefore, sponsors are required to accept cost-minimisation to the least costly alternative for a recommendation and PBS listing to proceed.

Determining a price on new, innovative medicines and technologies to match the reduced price of old medicines, penalises innovation and creates a race to the bottom. This is a growing disincentive for innovation to be brought to Australia and disadvantages patients

who will not benefit from new medical and scientific advances other countries will be getting earlier.

Recognising the value of innovative medical technologies

The Strategic Agreement between the Australian Government and Medicines Australia outlines a shared commitment to "ensure access for Australian patients to the rapid advances in modern, and emerging, technologies, therapies and vaccines, and to address the complexities of enabling access for therapies to treat rare diseases".

The Strategic Agreement also makes a commitment to review HTA policy and methods, which is the first comprehensive review of Australian HTA in 30 years. This is an important opportunity to introduce bold reforms and comparators are in specific focus of the review. Addressing these issues will aim to ensure innovative medical technologies are appropriately valued and ensure Australian patients have fast access to the latest, innovations in medicines and medical technology.

APPENDIX: Examples of comparator case studies

Product /date of consideration	Condition	Context	Implication
Price referencing to lowest cost comparator			
Beclomethasone with formoterol – March 22	Treatment of Asthma	Reference priced to lowest cost comparator ICS/LABA despite superior clinical evidence	Failure to adequately value innovative medicine
Diroximel fumarate – March 22	Treatment of relapsing-remitting multiple sclerosis (RRMS)	Reference priced to lowest cost comparator dimethyl fumarate / interferon beta despite superior clinical evidence	Failure to adequately value innovative medicine
Upadacitinib – Nov 19	Severe active rheumatoid arthritis	Reference priced to lowest cost comparator in rheumatoid arthritis despite superior clinical evidence	Failure to adequately value innovative medicine
Guselkumab – March and July 18 Guselkumab – July 20 and March 21	Severe chronic plaque psoriasis (CPP)	Reference priced to lowest cost comparator in severe chronic plaque psoriasis despite superior clinical evidence. New form was price referenced to lowest cost comparator despite being unlikely to replace this treatment option in clinical practice	Failure to adequately value innovative medicine and new dose form referenced to lowest price comparator despite low likelihood of substitution

Guselkumab – Nov 20	Severe psoriatic arthritis (PsA)	Referenced priced to lowest cost comparator in psoriatic arthritis despite the pricing reference having minimal market share and will not be most replaced in practice	Failure to adequately value innovative medicine and referenced to lowest price comparator despite low likelihood of substitution
Risankizumab – July 19 and November 21	Severe chronic plaque psoriasis (CPP)	Reference priced to lowest cost comparator in severe chronic plaque psoriasis despite superior clinical evidence	Failure to adequately value innovative medicine and new dose form referenced to lowest price comparator despite low likelihood of substitution
Carmellose and Hypromellose – July 19	Severe dry eye syndrome in patients who are sensitive to preservatives in multi-dose eye drops.	Reference priced to lowest cost comparator preservative free eyedrops	Referenced to lowest price comparator despite likelihood of substitution for higher priced comparators in clinical practice
Tocilizumab subcutaneous administration form – March 16	Severe active rheumatoid arthritis	Reference priced to lowest cost comparator IV infliximab in rheumatoid arthritis despite being unlikely to replace this treatment option in clinical practice	Referenced to lowest price comparator despite likelihood of substitution for higher priced comparators in clinical practice
Delay to patient access			
Ustekinumab – July 22	Severe chronic plaque psoriasis	Submission made 2 years after registration due to high chance of lowest cost comparator (strong precedence for bDMARDs)	Delay to Australian patients of innovative medicine
Risankizumab new dose form – November 2021	Sever chronic plaque psoriasis (CPP)	Inability of a new dosage form to list due to lowest cost comparator recommendation	Delay to Australian patients of innovative administration form
Guselkumab Pre-filled Pen (PFP) new dose form – July 2020	Severe chronic plaque psoriasis (CPP)	Inability of a new dosage form to list due to lowest cost comparator recommendation	Delay to Australian patients of innovative/new medicine form

APPENDIX: Comparators around the world

Jurisdiction	Legislation/Guidelines	Reference to comparator	Reference to price/cost
Australia	PBAC guidelines	Guidelines state that the main comparator is/are the therapy(ies) most likely to be replaced by prescribers in practice.	PBAC guidelines do *not* specify/require the main comparator to be the lowest price.
Australia	National Health Act 1953 legislation *Described further in Appendix 1*	Sect. 101 (3B) Without limiting the generality of subsection (3A), where therapy involving the use of a particular drug or medicinal preparation, or a class of drugs and medicinal preparations, is substantially more costly than an alternative therapy or alternative therapies, whether or not involving the use of other drugs or preparations, the Committee: (a) shall not recommend to the Minister that the drug, preparation or class be made available as pharmaceutical benefits under this Part unless the Committee is satisfied that the first-mentioned therapy, for some patients, provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies;	Legislation requires more costly medicines to provide a significant improvement in efficacy or reduction in toxicity. Cost is not defined as price. *Department of Health and PBAC frequently interpret this legislation to require the comparator to be the lowest price.*
Canada	CADTH guidelines	The drug treatment should be compared with both existing practice and minimum practice. Existing practice is defined as the most prevalent clinical practice, minimum practice is defined as the lowest cost comparator, or no treatment.	Lowest cost comparator is referenced. Therapeutic reference pricing is not applied. However this is not required to be the only comparator elected.
England	NICE guidance	Guidelines state that when establishing the most appropriate comparator, the committee will consider: established NHS practice in England, natural history of the condition without suitable treatment, existing NICE guidance,	Guidelines reference cost-effectiveness and do not require specific reference/comparison to lower/lowest price therapies.

		cost effectiveness and the licensing status of the comparator.	
Germany	IQWIG General Methods guidance	All healthcare-relevant interventions in a therapeutic area should be considered in a health economic evaluation	Price of comparator is not referenced
ICER* group (USA)	2020-2023 Value Assessment Framework	Appropriate comparators represent alternative therapies used among the populations and settings of focus. Relevant comparators are selected through a survey of clinical guidelines from professional societies, consultation with clinical experts and patients, and review of clinical trial designs.	Price of comparator is not referenced
New Zealand	PHARMAC Prescription for Pharmacoeconomic Analysis guidelines	Guideline recommends that the nominated comparator is either: 1. the funded treatment that most prescribers or clinicians would replace in clinical practice; and/or 2. the treatment given to the largest number of patients, if this differs from the treatment most prescribers or clinicians would replace.	Price of comparator is not referenced

*Institute for Clinical and Economic Review

Feedback

Do you have any thoughts on the policy ideas in these papers? We'd love to hear your feedback! Please let us know at this email address: HTA-Reform@medicinesaustralia.com.au.