Scope of vignette:
- authorised products (with marketing authorisation)
- decision process about routine use (and not named-patient individual requests for reimbursement)
- submissions for P&R made by manufacturers

Green = related to/any special considerations for rare disease and ultra-rare disease treatments

Australia	**Standard HTA process (non-orphan drugs)**	**Special process (RDTs) – Life Saving Drugs Program (LSDP)**
Overview of health system and P&R/HTA process	Tax based health system.[1] Medicines are regulated by the Therapeutic Goods Administration (TGA), which is part of the Health Products Regulation Group (HPRG) within the Australian Government Department of Health. The HPRG includes the TGA and the Office of Drug Control. [2] The Pharmaceutical Benefits Scheme (PBS) is part of the government's National Medicines Policy and lists all reimbursed medicines. [3] The Pharmaceutical Benefits Advisory Committee (PBAC) is comprised of medical practitioners, pharmacists, consumers, health economists and industry representatives. The PBAC meets three times per year, and recommends medicines to the Minister for Health (the Minister) for funding under the PBS. Two subcommittees provide advice to the PBAC: the Economics Sub-Committee (ESC) and the Drug Utilisation Sub-Committee (DUSC). [4,5] For drugs that do not meet the comparative cost-effectiveness criteria for funding through PBS, the Life Saving Drugs Program (LSDP) enables access for eligible patients to fully subsidized expensive treatments for life threatening and rare diseases. Recommendations for this program are made to the Minister by the Chief Medical Officer (CMO). An Expert Panel advises and assists the CMO in making recommendations. [6]	
Differentiation of rare disease treatments in the P&R system	Disease prevalence of 1:50,000 people or less in the Australian population. [6]	
Eligible medicines	Any drug with marketing authorization	Drugs for life threatening and rare diseases
Process	• There are four types of possible applications: major submission (new medicines/vaccines or indications), minor submission (changing current listings that do not alter population or cost-effectiveness), committee secretariat submissions (change requests that do not require PBAC),	• If a submission for a life threatening and rare disease is rejected by PBAC due to lack of cost-effectiveness but is considered clinically effective, a sponsor can apply for the medicine to be listed on the LSDP.

Australia	Standard HTA process (non-orphan drugs)	Special process (RDTs) – Life Saving Drugs Program (LSDP)
	application for new brand of existing drug [7] The evaluation process undergoes the following steps: • Manufacturer must send an intent to apply for submission by the deadline (which are provided online), followed by the actual submission approx. one month later • Pre-submission meetings occur to support applicants with their submissions. • PBAC engages external evaluation entities to assess major submissions on the principles of HTA, which provide an evaluation in a document called a 'commentary' and becomes part of the agenda papers of the PBAC and subcommittees. Evaluation entities are selected every four years • DUSC meeting occurs – the DUSC advises the PBAC and the applicant on important matters relating to use and cost, and reviews utilisation of currently listed PBS medicines. It provides its advice in a document called the DUSC Advice • ESC meeting occurs – the ESC reviews and interprets economic analyses and evaluations and advises on quality, validity and relevance of submissions in a document called the ESC Advice • PBAC meeting occurs • PBAC publishes its outcomes to inform the public about its advice to the Minister [4] For all major applications, applicants have two opportunities to provide written input: the pre-subcommittee response (following receipt of the commentary and included in the subcommittee and the PBAC agenda papers) and the pre-PBAC response (following receipt of the subcommittee advice and included in the PBAC agenda papers), and one opportunity to present comments to the PBAC in the form of a hearing	• Within two weeks of the application the LSDP secretariat prepares an overview of the application • The agenda for the Expert Panel is published four weeks before the next meeting • The Expert Panel meets and an optional stakeholder forum can occur at that meeting should it be requested • Two weeks after the meeting the Expert Panel provides its advice to the sponsor of the medicine being considered • The sponsor has one week to respond • The Panel advice and sponsor response is provided to the CMO for their consideration • After two to six weeks, the CMO makes a recommendation to the Minister [9] • Usage and financial costs of each drug are reviewed after 24 months to ensure these are aligned with the recommendations of the CMO and Expert Panel [6]

Australia	Standard HTA process (non-orphan drugs)	Special process (RDTs) – Life Saving Drugs Program (LSDP)
Disease specific expert input (e.g. clinicians or patients in any stage of the process)	Prior to the PBAC consideration, the department, the evaluators or members of the subcommittees can identify issues that would benefit from clarification or further information to improve the PBAC's deliberations. This information is usually received from representative organisations considered best to advise on the required input. In cases of a treatment that is not recommended or is deferred, PBAC can arrange stakeholder meetings (with both clinical and consumer representatives) to gain additional insights for: medicines for serious, disabling or life threatening conditions with not treatment alternative and that are not considered cost-effective; new and innovative treatments for diseases with high patient and public health burden; to inform issues such as proper target population, location for treatment administration, etc. Outcomes of such meetings are published on the PBS website. [4]	After the Expert Panel agenda is published, any interested patients, carers and clinicians can provide input to the secretariat via email. These comments will be made available to the Expert Panel and a summary of stakeholder input will be provided to the sponsor with the Expert Panel advice. [9]
Key domains in assessment	- Comparative clinical effectiveness - Comparative cost effectiveness - Net budget impact [3, 8]	• Whether application meets all listed criteria for applying to the LSDP: rare disease, identifiable with reasonable diagnostic precision, evidence of significant reduction of life expectancy, evidence of substantially increase life expectancy with use of drug in question, clinically effective but not cost effective, no medicinal alternatives, no non-drug alternatives, cost of drug would put unreasonable burden on patient/guardian, proposed drug price is comparable to overseas markets, proposed drug price is comparable to similar funded drugs (if existing) [9] • Applicant's proposal for collecting data to manage uncertainty
Evidentiary requirements	Evidence needs are the same for rare and non-rare disease treatments. It is recognised that there may be instances when RCTs are not feasible (e.g. rare diseases), and justification should be provided. [10]	

Australia	Standard HTA process (non-orphan drugs)	Special process (RDTs) – Life Saving Drugs Program (LSDP)
PROMs	Measures of quality of life, symptoms or function to include: • Generic PROM • Disease-specific PROM • Multi-attribute utility instruments (MAUIs). For some commonly used MAUIs, a detailed discussion of the validity and reliability is not required: Health Utility Indexes (HUI2, HUI3), Euroqol (EQ5D-3L, EQ5D-5L), Short Form (SF-6D, SF-36), Assessment of Quality of Life (AQoL), and Child Health Utility 9D (CHU9D) When PROMs are used or a MAUI not listed above, additional supporting references are requested (e.g. domains covered, scoring method, validity and reliability, responsiveness, clinical importance of differences detected). A description of how the PROM is used in the study is also requested, including characteristics of patients who missed or did not complete the PROM and methods used to adjust for response bias. [10]	
Appraisal framework	In addition to the key domains: • Overall confidence in the evidence and assumptions in the submission • Equity: implicit equity and ethical assumptions (e.g. age, or socioeconomic and geographical status) • Presence of effective therapeutic alternatives • Severity • Ability to target therapy with the proposed medicine precisely and effectively to patients likely to benefit most • Public health issues (e.g. development of resistance) [8]	
Reimbursement decision	Decisions can be: positive recommendation, deferral of a recommendation, not recommended [4]	
Pricing process	Applicant must submit an 'intent for pricing form' after receiving a positive recommendation. All post-PBAC negotiations for the PBS seek to reach agreement on price between the applicant and the Australian Government with reference to the recommendation by the PBAC. The different pricing pathways listed below reflect additional matters that may also need to be considered in order to reach overall agreement between the applicant and the Australian Government with reference to the recommendation by the PBAC.	Pricing arrangements are determined after sponsor is made aware that the CMO will make a positive recommendation. Price negotiation is based on any pricing parameters determined by the Expert Panel. Only the cost of the drug is funded through the LSDP, no additional costs (e.g. transport, storage, etc.) [9]

Australia	Standard HTA process (non-orphan drugs)	Special process (RDTs) – Life Saving Drugs Program (LSDP)
	There are five different pricing pathways: A) **'Facilitated'.** Can apply when the drug is expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over any alternative therapies; the medicine addresses a high and urgent unmet clinical need; it would be in the public interest for the submission to be recommended to follow this pathway B) **New Deed.** Applies for submissions which require negotiation and finalisation of a new deed of agreement where there are no similar arrangements in place. This could include an assessment of proposed risk-sharing, managed entry and/or special pricing arrangements C) **Existing deed.** Applies to submissions which require third-party responsible person notification of changes to an existing deed of agreement, and/or where an applicant has received a positive PBAC recommendation to list within the scope of existing arrangements, whether these relate to the new listing or to another existing listing. D) **No deed.** Applies to submissions which do not involve negotiation of a new or existing deed of agreement. E) **Secretariat pricing.** Applies to changes to listings of existing medicines which do not require a new price	
Managed entry agreements	• Discounts • Risk sharing agreement • Outcomes based agreements	
Main challenges in appraising medicines for rare diseases (tick all that apply)	X Lack of good quality clinical data X Lack of real world data X Introducing value for money X Monitoring treatment efficacy X Managing budget impact ☐ Lack of criteria/transparency of OMP P&R processes, ☐ Making arrangements to work for all stakeholders X Lack of long-term meaningful outcomes	

Australia	Standard HTA process (non-orphan drugs)	Special process (RDTs) – Life Saving Drugs Program (LSDP)
Impact of special processes	Improved transparency and rigour to medicine listing process, streamlining of the processes, delivering certainty to stakeholders and ensuring sustainability of LSDP.	
Proposed policy change	N/A	
Joint initiatives	N/A	
SOURCES		
1	https://www.bupa.com.au/healthcare-guide/what-is-australias-healthcare-system#:~:text=The%20Australian%20public%20accesses%20care,and%20allied%20health%2C%20and%20pharmacies.	
2	https://www.tga.gov.au/structure	
3	https://www.pbs.gov.au/info/about-the-pbs	
4	https://www.pbs.gov.au/industry/listing/procedure-guidance/files/Procedure-Guidance-for-Listing-Medicines-on-the-PBS-v1.8.pdf	
5	https://www.pbs.gov.au/info/industry/listing/participants/pbac	
6	https://www1.health.gov.au/internet/main/publishing.nsf/Content/lsdp-criteria	
7	https://www.pbs.gov.au/info/industry/listing/procedure-guidance/4-presubmission-requirements/4-1-types-of-submissions	
8	https://pbac.pbs.gov.au/information/about-the-guidelines.html	
9	https://www1.health.gov.au/internet/main/publishing.nsf/content/FD13E541FA14735CCA257BF0001B0AC0/$File/Procedure-guidance-for-medicines-funded-through-the-LSDP.pdf	
10	https://pbac.pbs.gov.au/content/information/files/pbac-guidelines-version-5.pdf	

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