Navigating high-cost medicines

Guiding principles for the governance of high-cost medicines in Australian hospitals

Version 1 – January 2022

CATAG
Council of Australian Therapeutic Advisory Groups

CATAG
Council of Australian
Therapeutic Advisory Groups

Address:
c/– NSW TAG
26 Leichhardt Street
Darlinghurst NSW 2010

Phone: (02) 8382 2852
Fax: (02) 8382 3529
Email: catag@stvincents.com.au
Web: www.catag.org.au

Version number

Version 1: January 2022

Recommended citation: Council of Australian Therapeutic Advisory Groups. Navigating high-cost medicines: Guiding principles for the governance of high-cost medicines in Australian hospitals. CATAG, 2022.

Disclosure

These Guiding Principles are funded by the Australian Government Department of Health through the Value in Prescribing – Biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) Program Grant. The author acknowledges the assistance provided by the Targeted Therapies Alliance in reviewing the Guiding Principles.

The views expressed are those of the authors and do not necessarily reflect those of the funder. No members of the project team or expert advisory group stand to gain financially from their involvement in these guidelines.

✦TARGETED THERAPIES ALLIANCE

Helping consumers and health professionals make safe and wise therapeutic decisions about biological disease-modifying antirheumatic drugs (bDMARDs) and other specialised medicines. Funded by the Australian Government Department of Health through the Value in Prescribing bDMARDs Program Grant.

The Alliance is led by NPS MedicineWise and includes Arthritis Australia, Australia and New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network, Australian Rheumatology Association, Cochrane Musculoskeletal, Council of Australian Therapeutic Advisory Groups, Pharmaceutical Society of Australia, Quality Use of Medicines and Pharmacy Research Centre (University of South Australia) and Society of Hospital Pharmacists of Australia.

Report production: Armstrong Communication Design

Contents

Executive summary

Good governance of high-cost medicines promotes consistent, evidence-based use of high-cost medicines in a fiscally responsible manner.

Hospitals play a significant and important role in funding high-cost medicines so that patients can access the treatments they need. This may include treatment of severe or rare diseases or where the choice of available treatments is limited. High-cost medicines are often specialty medicines, such as biologics, which contribute to a significant and increasing portion of the hospital medicine budget. It is thus imperative that the use of these expensive medicines is governed and managed with a fair, standardised evidence-based process. The implementation of a standardised review process for high-cost medicines, based on the best available evidence, fosters high-quality care through the appropriate and consistent use of high-cost medicines, when they provide a clinical benefit, while preventing their use when clinically effective and lower cost alternatives remain available.[1]

Decision makers for the governance of medicines, at the hospital, area health service or jurisdictional level, frequently receive requests for high-cost medicines. These medicines may have been approved for marketing in Australia via the Therapeutic Goods Administration or may be being used off-label or imported from overseas. Some of the medicines used in the public hospital system are not listed on the Pharmaceutical Benefits Scheme (PBS) and have never been, or may never be, evaluated by the Pharmaceutical Benefits Advisory Committee (PBAC) for national subsidy.[2] It may be appropriate for hospitals to approve these high-cost medicines given the local oversight that can be provided, as well as the ability to scrutinise outcomes. As decision making for access to medicines is fragmented across the various systems in use within Australia, local decision makers must determine whether they will fund these medicines. These decisions are made at the jurisdiction, area or hospital level and because this decision-making process is not part of a national process or policy framework, different decisions may be made with regard to the same high-cost medicine.[2] Variation in decision making may also be due to the heterogeneous capacity and expertise of decision makers, differing processes for assessment of evidence, and pressures to approve medicines for individual patient use that may result in inconsistent patient access to high-cost medicines. The management of accessibility of these medicines is challenging.

Several pathways exist for access to high-cost medicines in public hospitals. The medicine may be approved for addition to the formulary or may be approved for use by an individual patient (Individual Patient Use). See CATAG's *Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*. Other pathways include access to medicines on compassionate grounds or via Medicines Access Programs.

Prescriber familiarity with these high-cost medicines is best developed within appropriate governance frameworks, which facilitate the use of safe, appropriate and cost-effective medicines within hospitals. It is recognised that medicines are often prescribed initially in hospitals before subsidised outpatient accessibility commences or is expanded into the community.

There is also the pressure for decision makers in hospitals of balancing the constraints of the hospital budget and the provision of access to high-cost medicines.[3] A frequently encountered example of this balancing dilemma is the funding of one high-cost medicine for an individual patient potentially setting a precedent for a group of patients.

Good and effective governance of high-cost medicines requires compliance with one of the policy objectives of the National Medicines Policy – 'timely access to medicines that Australians need, and at cost the community and individuals can afford'. CATAG has developed these Guiding Principles to provide a framework to assist medicines governance committees* to assess and make good decisions about the quality use of high-cost medicines.

The guiding principles for the governance of high-cost medicines are:

Guiding principle 1. A definition of high-cost medicines should be determined and clearly articulated for use by each medicines governance committee.

Guiding principle 2. Review of high-cost medicines requires members with relevant expertise to facilitate good and effective decision making.

Guiding principle 3. The committee should engage directly with the applicant prior to review to ensure a full understanding of the rationale for the request.

Guiding principle 4. A consistent, robust and transparent procedure for the assessment of high-cost medicine applications should be defined and implemented for use by each medicines governance committee to ensure fair process.

Guiding principle 5. Ethical considerations fundamentally underpin deliberations around high-cost medicines.

Guiding principle 6. The decisions and outcomes of the decision making should be transparent and appropriately communicated to the various audiences.

Guiding principle 7. The high-quality assessment of high-cost medicines requires appropriate training and resourcing.

These Guiding Principles should be considered in conjunction with other resources for medicines governance committees (or equivalent committees) and medicine decision-making tools, such as CATAG's:

- *Rethinking medicines decision-making in Australian hospitals: Guiding principles for the quality use of off-label medicines*;
- *Achieving effective medicines governance: Guiding principles for the roles and responsibilities of drug and therapeutics committees in Australian public hospitals*;
- *Managing Medicines Access Programs: Guiding principles for the governance of Medicines Access Programs in Australian hospitals*; and
- *Biologics and biosimilars best practice: Guiding principles for the governance of biologics and their biosimilars in Australian hospitals.*

CATAG recommends that a method of sharing assessments and outcome data nationwide should be established. Access to this data will reduce duplication and enable efficient decision-making activity across Australia and provide feedback on the effectiveness and safety of specific drug treatments.

* Examples of medicines governance committees include drug and therapeutics committees, medicines advisory committees or equivalent, medication safety committees.

Overview

Purpose

The purpose of these Guiding Principles is to provide a principles based high level framework outlining national objectives to assist medicines governance committees, including Drugs and Therapeutics Committees (DTCs), to assess and make good decisions about the quality use of high-cost medicines. In addition, a recommendation for the future management of high-cost medicines by jurisdictions, area health service and local hospital and health service organisations has been made.

More specifically, the objectives of these Guiding Principles are to promote:

- a fair process and equity of access to high-cost medicines in public hospitals;
- the assessment of high-cost medicines using the best available evidence;
- the cost-effective utilisation of medicines within the public hospital system; and
- a reduction in the duplication of effort and fostering consistent and efficient decision making.

For the future, it is hoped that information sharing, including sharing of robust outcome data, occurs between governance committees responsible for assessing and approving high-cost medicines in Australian hospitals.

Background

DTCs have oversight of the medicines management system within a hospital, area health service or at a jurisdictional level. This oversight role includes decisions-making related to medicine listing on formulary or use of a medicine for an individual patient. As stated in CATAG's *Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*, criteria for DTC decision-making should be defined and implemented consistently across all formulary or individual patient use decisions. Often high-cost medicines are reviewed as applications for Individual Patient Use (IPU) (also known as Individual Patient Approval (IPA)).

High-cost medicines represent significant and increasing expenditures for hospitals. New high-cost medicines are generally commenced and utilised first within hospitals including specialist outpatient clinics. Optimal prescribing and usage of these medicines requires good governance frameworks that promote use of appropriate, affordable and cost-effective medicines. Having good governance frameworks in place at the outset supports appropriate practice being embedded as the routine, and the flow-on effects to community practice into the future.

The increasing cost of medicines has been described internationally and nationally and is a significant area of concern for entities funding medicines including governments, health insurers and individual patients.[4] The desire for increased access to medicines is driven by the ageing population and increasing consumer and clinician demands. In 2017–18, Australians spent an estimated $22.3 billion on medicines (including both prescribed and over-the-counter) – which includes spending by governments, non-government sources and individuals.[5] Currently eight of the ten most expensive medicines on the PBS (by cost to government, 2020–21) are biological medicines.[6] In the future, medicine costs are expected to substantially rise further with the availability of new biological medicines, immunotherapy and targeted therapies.

Decision making for access to medicines is fragmented across the country, with funding decisions being made at a federal PBS jurisdictional, area and hospital levels. Currently a uniform process for accessing medicines in Australia only exists for medicines accessed through the PBS.[7] In Australian hospitals, access to high-cost medicines is generally supported by jurisdictional funding (inpatient and outpatient) and funding from the national-based PBS (private hospitals and mainly outpatients in public hospitals depending on the jurisdiction). DTCs at a jurisdictional, area health service or hospital level are responsible for the decisions determining the availability of non-PBS high-cost medicines within hospital inpatient and outpatient settings. All new medicines, whether high-cost or not, require assessment by DTCs prior to introduction and funding. This involves complex safety, quality, cost-effectiveness and implementation considerations.

Variability in decision making exists between the jurisdictions, area health services and hospitals in this management process.[2,8] This variation may be due to differing processes for assessment of evidence, and quality parameters (examples include, but are not limited to effectiveness, acceptability, access and equity), available expertise and pressures to approve medicine access may result in some patients having access to certain high-cost medicines while others do not.

Scope

These Guiding Principles apply to decisions made by DTCs, whether they are hospital, area health service or jurisdictional committees. They may also be relevant to private hospitals and other health service organisations with a medicines use committee or equivalent, although these organisations have not been specifically consulted.

CATAG acknowledges that duplication exists between this document and the *Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*. However, it is particularly important to have good and effective medicines governance of high-cost medicines. The assessment of these high-cost medicines should be the most comprehensive and rigorous that the resourcing of the DTC allows. In addition, people accessing these high-cost medicines often have increasingly complex medical needs, are vulnerable as their treatment options are reduced and require specialist skills and monitoring. These medicines require governance processes that balance the needs of an individual (or group of people), in situations where evidence may be less clear, and/or there is significant resource impost in constrained budgetary environments. DTCs should allow for resourcing to be focused on those applications with the greatest budgetary impacts.

CATAG acknowledges that, while medicines governance committees are responsible for making recommendations regarding approval of high-cost medicines, the final approval often lies outside of the committee and other budgetary and political implications may be involved. The role of the financial delegate is beyond the scope of these Guiding Principles.

The guiding principles outlined in this document apply to applications for high-cost medicines, whether for formulary applications or for individual patient use applications.

This resource is applicable to all health service organisations and individuals wanting to deliver robust governance of medicines processes. These include:

- DTC chairs and members
- Area health services (also known as Local Health Networks, Local Health Districts, Health Service Networks, Local Hospital and Health Networks)
- Leads of corporate and clinical governance entities
- Hospital, area and jurisdictional quality and safety committees
- Any other individuals who are involved in the review, decision and evaluation of high-cost medicines applications
- Health professionals who are involved in implementing and preparing submissions
- Consumer and community representatives.

The guiding principles may need to be adapted in the future with the uptake of healthcare technologies and other advanced therapeutics. DTCs should also be aware that medicines are more rapidly transitioning from the ‘clinical trials phase’ to the ‘post marketing phase’, especially in ‘orphan’ conditions without current effective treatments.

Guiding principles

Governance

Guiding principle 1

A definition of high-cost medicines should be determined and clearly articulated for use by each medicines governance committee.

High-cost medicines contribute significantly to hospital expenditures and the higher the cost the greater the implication for the health system. A definition is required to ensure that access to high-cost medicines is managed consistently and fairly using a standardised evidenced-based process.[1] To achieve this, assessment of applications for medicines meeting the criteria for 'high-cost' should be the most comprehensive and rigorous that the resourcing of the DTC allows.

Numerous definitions have been used in Australian medicines governance groups and hospitals to describe a high-cost medicine. Definitions may be described as cost per patient per treatment course or episode of care or a cost per patient per year, or as a finite cost to the health system (whether at a jurisdiction, area or hospital level) per year. Each DTC should determine and approve their own definition of high-cost medicines, contextualised to their local environment for adoption and consistent use.

Definitions of high-cost medicines should be informed by review of local data to reflect their own circumstances. Different monetary thresholds may be adopted by DTCs depending on level of specialisation, bed numbers, budget, location and practicalities of management at a local level. The monetary threshold, triggering a high-cost medicine review, is selected to ensure that the most expensive treatments are prescribed in a clinically and fiscally responsible manner.[1]

It is not possible at this stage for CATAG to provide a meaningful and consistent national definition of a high-cost medicine, due to the varied systems that exist between the different jurisdictions in Australia, or between individual hospitals. We recommend that jurisdictions collaborate to decide on a threshold for high-cost medicines depending on the level of governance and decision-making such as a state-wide, area or hospital.

This would take into account the peer grouping of hospitals, level of specialty, size and budget so that medicines governance committees having oversight for equivalent types of patients have the same threshold.

When determining the definition(s), consider the following:

- Single time-limited course versus long-term or continuing therapy
- Potential high budgetary impact medicines such as lower cost/high volume of use for a single indication (e.g. zoledronic acid or neoadjuvant pertuzumab for early breast cancer)
- Administration-related costs (e.g. consumables required for medicines administration, infusion chair costs, staffing costs)
- Medicines funded by a pharmaceutical company as part of a Medicines Access Program (if life-long commitment to supply is not contracted with the pharmaceutical sponsor, there is a risk that the ongoing costs and supply remains with the initiating health service once the Medicines Access Program or compassionate access expires)
- High-cost medicines listed under the Pharmaceutical Benefits Scheme (section 85 or section 100) used in accordance with the PBS criteria for subsidy
- High-cost medicines funded under the Commonwealth's Life Saving Drugs Program.

In addition, exclusions to the high-cost medicine classification include:

- Medicines used in an approved clinical trial and paid for by the sponsor of the clinical trial
- Low unit cost medicines which represent a high cost due to high volumes of use (e.g. paracetamol).[9]

Table 1: Examples of monetary thresholds for high-cost medicine definitions

ORGANISATION	MONETARY THRESHOLDS
SA Health for high-cost medicine formulary[9]	• ≥$10,000 per patient per treatment course or per year; or • ≥$100,000 for an individual hospital per year; or • ≥$300,000 within the SA public health system per year.
QLD Health high-cost medicines which are not listed on the List of Approved Medicines[10]	• >$10,000 per patient per year/course; or • $100,000 per hospital per year.
NSW TAG[11]	Non-reimbursable acquisition costs equivalent to or more than: A. $1,000 per week per drug per patient, and are used as long-term therapy e.g. for 12 months or longer; or B. $50,000 per treatment course per patient.
Local hospital DTC definition (Sydney Children's Hospital Network)	$15,000 per patient per year, with consideration of impact at that particular hospital.

Guiding principle 2

Review of high-cost medicines requires members with relevant expertise to facilitate good and effective decision making.

A collaborative approach for the review and assessment of high-cost medicines, whether formulary or individual use applications, results in a more consistent, rigorous, evidence-based utilisation of these expensive medicines.[1] The review of high-cost medicine applications should involve the engagement of a multidisciplinary group of individuals who have an appropriate skill set and expertise including:

- Clinical specialties
- Medicine evaluation
- Health technology assessment
- Ethics
- Health economics
- Health finance
- Consumers.

It is recommended that a DTC or high-cost medicine subcommittee has a consumer representative as part of their membership to provide a consumer perspective wherever possible to allow for a better evaluation of the balance between potential benefits, costs and possible harms.[12,13] It is essential that the consumer representative understands the need for privacy and confidentiality and declares any conflict of interest as with any other member on the DTC. The patient for which the application is being made should not be the applicant, nor should they be associated in any way with the decision making.

For high-cost items where there is not a DTC member with the relevant expertise, committees should consider seeking other expertise and second opinions from within or outside the health network (e.g. from other states). This can be very beneficial, especially for regional and rural hospitals.

As per CATAG's *Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*, DTCs should have appropriate expertise for their decision-making and may appoint a subcommittee to manage specific projects or tasks, when appropriate. This may apply to the review of high-cost medicines. The purpose of such a review committee is to support appropriate governance and facilitate the process of assessment, ensuring consistency in decision-making and robustness of process. Some jurisdictions have implemented a high-cost medicine committee in concert with their state-wide formulary committee to undertake the assessment and monitoring of high-cost medicines for addition to the formulary. Alternatively, a DTC may review these formulary applications on a pre-determined basis e.g. be an agenda item every second month when expertise is available or refer the decision-making process to another DTC with the relevant expertise. The establishment of a separate committee may be dependent on the setting e.g. state-based versus district- or hospital-based, workload, budget assessment and resource availability.

IPUs may be handled separately to the formulary high-cost medicine committee, depending on the setting and the urgency. Non-urgent IPU applications may be reviewed by the high-cost medicine committee or local DTC.

If establishing a high-cost medicine committee, the goals and scope, governance and reporting arrangements need to be determined at establishment and included in the DTC terms of reference. Particularly important for high-cost medicines is the declaration of conflicts of interest (COI). Participants should declare perceived or actual COI, both pecuniary and non-pecuniary and document as part of routine procedure, with an agreed-upon process for managing these specific to the organisation. For medicines considered extremely high cost, extra care is required. At the meeting, it may be appropriate to ask a specific question in relation to a specific application. Each application should have COI applied to it. The degree of involvement in the decision-making process by those with perceived or actual conflicts of interest, should be determined prior to discussion. To ensure that relevant expertise is accessible, it may be necessary to engage with other peers, from within or outside the organisation, if COI arise. Regardless, individuals may have their own personal biases and beliefs around the use of high-cost medicines which may influence deliberations and outcomes. This highlights the importance of the use of an objective and fair process as outlined in guiding principle 4.

Application and assessment

Guiding principle 3

The committee should engage directly with the applicant prior to review to ensure a full understanding of the rationale for the request.

DTCs should engage with the applicant, whether for a formulary or individual patient use application, as the critical first step in understanding the application and reviewing any potential variations in practice. Where a comprehensive application has been made, this alone may be adequate engagement. Where the application is lacking in detail, the place in therapy of the requested medicine is unclear, or there is any other uncertainty regarding the application, early engagement with the applicant is essential to ensure that the DTC reaches an appropriate decision. This also results in applicants understanding the shared priorities of the organisation and being cognisant of practical realities. It also provides an opportunity for the applicant to revise and improve their application and provide their opinion and expertise within the context of the therapeutic environment.

Where possible, it may be appropriate for the applicant to be contacted when the application is being considered. This would allow the applicant to answer any questions and help promote efficiencies in the process. The applicant should not be present during any deliberation or discussion.

When possible, gaining the consumer perspective is encouraged, either at the first application or during the consultation process.

Guiding principle 4

A consistent, robust and transparent procedure for the assessment of high-cost medicine applications should be defined and implemented for use by each medicines governance committee to ensure fair process.

A key purpose of the DTC, as per CATAG's *Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals* is maintaining a formulary to ensure the judicious, appropriate, safe, clinically appropriate and cost-effective use of medicines. Without transparent fair process, legitimacy of the process may be undermined. Although this is important for all medicines, this is particularly important for high-cost medicines. People accessing these medicines often have increasingly complex medical needs, are vulnerable as their treatment options are reduced and require specialist skills and monitoring. Good and effective medicines governance of high-cost medicines require processes that balance the needs of an individual (or group of people), in situations where evidence may be less clear, and/or there is significant resource impost in constrained budgetary environments. Members should agree on the assessment process for high-cost medicines, including robust consideration of the essential information required. Members of the DTC should clearly establish which elements are relevant in assessing high-cost medicine use in their particular setting, and then consistently consider applications based on these agreed upon criteria. The members must have the expertise required to review the application adequately as per guiding principle 2.

See **Appendix 1** for a suggested algorithm for decision making.

a. As for all medicines, the decision-making process for high-cost medicines should be defined and transparent, and the grounds for decision making readily available and accessible, to applicants, stakeholders and the community.

The minimum criteria for approval should include safety, effectiveness, and cost effectiveness. The cost per patient per year and the number of patients likely to receive the treatment will be important in estimating the budgetary impact of any decision.[14] It should also include broader personal and social benefits to consumers e.g. increased capacity to self-care or to remain or participate in the workforce. Quality adjusted life years (QALYs) and next possible therapies should also be considered, as a single acute episode of access to, or denial of, a high-cost medicine can have significant lifelong consequences. These criteria, against which these applications will be measured, and these Guiding Principles should be readily available for viewing by applicants. The application for a high-cost medicine, should thus contain sufficient information to facilitate good decision making. The application form should mirror the required information for the decision-making process.

Table 2: Key elements of a high-cost medicine application

APPLICATION TYPE	APPLICATION DETAIL
For all applications	• Indication for therapy (including future use) • Reference to the uniqueness of therapy (no equally safe, effective and practical alternative therapeutic option) • Degree of clinical need of the patient or patient groups (severity/burden of disease/acute or chronic) • Outline previous therapy – is this the 1st/2nd/3rd option, and any alternative treatment pathways • Have all standard therapies been attempted and what are the options if the treatment is not approved? • Evidence to support effectiveness of the medicine • Evidence to support safety and comparative safety of the medicine • Goals of successful therapy and desired outcomes • Pre-defined measures to monitor effectiveness and safety outcomes (e.g. relevant biomarkers, surrogate endpoints or using a quantitative Quality of Life tool) (see section 4c) • Timeline for measurement of outcome(s) • Stopping criteria to indicate when treatment is no longer warranted for the patient • Evidence and approval by the departmental head or other relevant stakeholders with appropriate oversight • Economic evaluations including expected costs and ancillary costs and comparative costs against other available therapies or the current standard of care (see section 4b) • Clinician declaration for any perceived or actual conflicts of interest
For formulary applications	• Engagement with relevant clinicians • A defined patient cohort and criteria for initiating therapy • Anticipated number of patients • Outline if the proposed therapy will supersede other treatment options
For individual patient approval	• Treatment is discussed and agreed to with the patient or care giver (informed patient consent) • Urgency – is the patient's condition life threatening or are there other issues affecting the urgency of the application? • Are there likely to be other similar requests?

See **Appendix 2** for links to example application forms.

A wide range of evidence, implications and outcomes should be considered to facilitate good decision making. It is also necessary to compare with other therapies including medicines already available on the formulary for effectiveness, safety and cost and consider the implications for precedent setting for future potential patients or the need for repeat therapy.

All IPU/As should be assessed on the evidence in combination with patient specific factors. DTCs should be cognisant of past decisions made for clinically similar patients when assessing IPUs, however clinical nuances or differing patient circumstances may mean that two patients may receive different outcomes for similar IPU/As. DTCs must ensure that where any IPU decision is not perfectly consistent with previous decisions for the same treatment, that the reasons for this are articulated in DTC documentation, decision letters to the applicant, and any DTC reporting. To ensure transparency, the factors that led to an approval when a previous IPU/A had been rejected, or vice versa, should be identified and clearly communicated.

A standard set of criteria should be applied when reviewing any request, whether for formulary or IPU. These criteria include the strength of evidence supporting clinical effectiveness, superiority to less-expensive agents, safety concerns, and the risk for significant harm in delaying treatment.[1] The assessment should outline areas of uncertainty.

Table 3: Example criteria for assessment

EVIDENCE SOURCES	UTILISATION	COSTS
• Evaluations and experiences by other jurisdictions • Ongoing clinical trials/local experience • Guideline recommendations • Current usual care and prognosis • Efficacy and safety based on randomised controlled studies, non-comparative studies, observational studies • Quality appraisal of the strength of evidence	• Population epidemiology – national statistics • Medicine utilisation in own and other jurisdictions • Projected patient utilisation within the jurisdiction initiating and ceasing treatment (steady-state)	• Drug acquisition costs • Storage costs • Drug administration costs • Monitoring costs • Cost off-sets (e.g. reduced Emergency Department presentations) • Adverse event costs • Compounding costs

A wide variety of data sources including clinical studies (e.g. clinical trials, observational studies), national statistics, clinical practice guidelines, documents from other HTA groups (e.g. NICE, CADTH), registry data, surveys, expert opinion (national and/or international) and other evidence from pharmaceutical manufacturers can be used.[15,16]

b. The financial and economic consequences of funding high-cost medicines are an essential element in the assessment.

Information about the effectiveness of high-cost medicines is necessary but not sufficient for decision-making about high-cost medicines. Explicit consideration of costs, both in terms of the financial impact on budgets and the economic impact, that is the opportunity costs or benefits foregone of different courses of action, should be considered. Assessments of the budgetary impact of high-cost medicines are usually undertaken to assess affordability. To be useful for decision makers, a budget impact analysis should consider the potential financial consequences over time based on costs and the projected size of the treated population (see **Table 4**). Economic evaluations such as cost-effectiveness analyses have been considered a 'desired' criterion but the expertise is either not available or not accessible, or there is little economic evidence relevant to the decision available. Additional resources are likely required for DTCs to translate economic evidence, when available, into the local context, or undertake *de novo* analysis or modelling.[3] This remains an area of substantial need across Australia.

Economic evaluation can be defined as a comparison of alternative options in terms of their costs and consequences.[17] Consequences are defined as the health effects (or occasionally other personal or societal benefits) of the high-cost medicines, and costs as the value of resources in providing the high-cost medicine which often extends beyond the cost of medicine to include the costs such as treating adverse events, pathology and storage costs). Several different types of economic evaluations exist (see **Table 4**).

Table 4: Different economic evaluations

ECONOMIC EVALUATION	DESCRIPTION
Budget impact analysis (BIA)	Used to estimate the financial consequences, over a period of time, of adding a healthcare intervention such as a medicine to a formulary or budget, based on cost and the likely population size to receive treatment as well as other inputs such as managing adverse consequences of the new medicine.[18,19]
Cost consequences analysis (CCA)	Presents a side-by-side comparison of the disaggregated costs and a range of outcomes for alternative treatments.[20]
Cost-minimisation analysis (CMA)	Compares the incremental costs of alternative treatments (including the costs of managing consequences of the treatment) that have equivalent clinical outcomes.[19,21,22]
Cost-effectiveness analysis (CEA)	Compares the incremental costs and benefits of alternative treatments that differ in the magnitude of their health outcomes; outcomes are expressed in natural terms such as life-years gained, or adverse events avoided. Results are expressed as an incremental cost-effectiveness ratio (ICER) – the difference in costs divided by the difference in benefits.[19,20,23]
Cost-utility analysis (CUA)	The same as CEA, except that health outcomes are expressed in quality-adjusted life-years (QALY) which allows for comparison across disease areas. CUAs are required by PBAC for their decision making.[19,20,24]

Cost-effectiveness analysis, where results are expressed in terms of 'incremental costs per incremental benefits' (i.e. an incremental cost-effectiveness ratio) is more useful for decision makers as it allows for a tangible 'weighing up' of costs and outcomes. Ideally final health outcomes such as lives saved, life-years gained or QALYs gained are presented to provide consistency and reference points for the committee over time. At the very least, a cost-consequences analysis should be presented.

The financial impact of the decision may require executive level governance and agreement.

c. There should be a standardised process for monitoring of decisions and subsequent outcomes.

When a high-cost medicine is approved for use in the health service organisation, certain monitoring criteria should be suggested in the application for approval and/or decided on as part of the approval process. The purpose of monitoring is to evaluate outcomes, which then strengthens future decision making i.e. to continue or stop therapy in an individual patient or to remove from formulary or to continue or extend a formulary listing. Other reasons to monitor approvals include safety, and compliance with formulary restrictions and support future funding. Consideration should be given to the feasibility of collecting the nominated outcome data. For example, collecting administrative data may aid in this process.

Examples of monitoring criteria may include use in specific indications, use by specific prescribers, cost of therapy (e.g. number of units/doses/patients and ancillary costs) and outcomes such as clinical effectiveness, adverse events and patient reported outcomes including improved quality of life, reduction in symptoms, days off work, hospitalisations. A nominated period should be attached to these criteria, although there appears to be difficulty in ensuring these are reported. Ideally, processes should be established that ensure real-time and/or automated data collection rather than reliance on retrospective data collection.

DTCs should provide oversight over the monitoring process while remaining as an independent decision-making body. For formulary listings, feedback to the applicant and the appropriate departments regarding outcomes of monitoring, and to the broader practice group should be routinely provided. This continues to build the body of evidence either for or against this therapy for the specified indication. Where extensive clinical trial evidence supports the treatment, this ongoing monitoring will be less important however even with strong evidence, new therapies without a long history of use may still benefit from such monitoring. Consumer reported outcomes should be collected and provided by applicants as ongoing evidence and be conditional on listing onto a formulary. For individual patient use approvals, the applicant should provide data within the timeframe as agreed during the application process.

Monitoring, evaluation and reporting is a shared responsibility between clinicians and governance committees. Research should be encouraged and supported to better understand the use of non-PBS funded high-cost medicines across public hospitals and to collect data on clinical outcomes associated with the use of high-cost medicines. These findings should be published, especially in the context of rare conditions, novel drugs or indications. Sharing results of outcomes (positive or otherwise) in the literature can help broaden the knowledge and understanding of decision makers for future high-cost medicine applications.

d. Applicants should be able to access an appeals process, and the established criteria should be open to revision based on new information including costs information.

The right to appeal the decision by the applicant is a component of a fair and transparent process. The criteria for appeal should be decided by the review committee and be available to all applicants. This should be a documented, structured and formal process that allows the applicant to appeal the results of decisions made as part of the assessment process, especially if a change in evidence or cost occurs. An advantage of the appeal process is that it can result in a better quality re-application.

Further, the broader DTC assessment process and agreed upon criteria should be regularly reviewed and updated and adjusted when new information or evidence is substantive.

Guiding principle 5

Ethical considerations fundamentally underpin deliberations around high-cost medicines.

Ethical considerations should be applied to all applications for a high-cost medicine and should consider both the specific individual and the broader community perspective.

Considerations regarding the 'judicious' use of medicines, or 'good' decision making around medicine approvals, are, to some extent, value-based. At the individual application level, the DTC is charged with deliberating on the proposed 'value' of the health outcome, and whether it is thought to be proportional to the cost. This involves the DTC considering, and to some extent agreeing upon, what goals and outcomes they think are worthwhile or important, and making some judgement as to whether the particular high-cost medicine can be considered 'value for money'. This consideration of 'value' must also take into consideration the likelihood of achieving that outcome in an individual patient, or for formulary applications, in a patient group.

Broader ethical considerations relating to fairness are also relevant and include:

- Facilitating access where appropriate, according to due process
- Promoting equity, by considering valid claims for special or differential treatment based on social or economic vulnerability, or those at particular risk of discrimination
- Having an awareness of obligations to resource stewardship, including consideration of sustainability in light of consistency in dealing with subsequent applications
- Considering opportunity cost, and the appropriateness of allocating resources in the high-cost medicine domain as opposed to other areas of healthcare delivery.

Importantly, the DTC should be aware of other broader interests or influences that may affect due process. Examples include political pressures from powerful individuals or advocacy groups, media exposure and framing, personal relationships and connections, and conflicts of interest in both pecuniary and non-pecuniary domains. Explicit consideration and awareness of these potential influences should be acknowledged, with practices incorporated in the DTC processes to eliminate where possible any undue influence.

Communication

Guiding principle 6

The decisions and outcomes of the decision making should be transparent and appropriately communicated to the various audiences.

There are many potential audiences for the process and outcomes of DTC deliberations. In settings where this decision is centralised, the audience may be relatively clear, however this is not always the case. It is important to share the decision with all key stakeholders, including the consumers.

Communication of the decision to the clinician should include:

- Why the particular decision was made, including a statement that the decision was based on cost-effectiveness, safety, budget and equity.
- Feedback that can be provided to the patient(s), which does not damage the relationship between clinician and patient.

The decision (whether for or against) and rationale should also be communicated to the consumers in a timely manner, and be undertaken by an appropriate person (preferably a senior clinician), who can competently explain the complexities of the information in terms the consumer or carer can understand.[13]

The decision should also be documented in medical notes (for individual patient use applications), by the treating clinician, whether approved or rejected.

Training and resourcing

Guiding principle 7

The high quality assessment of high-cost medicines requires appropriate training and resourcing.

A challenge for the assessment of high-cost medicines is the availability of individuals with appropriate expertise. To facilitate best practice, there is an ongoing need to provide investment in the development of both capacity building and expertise by training those participating in these reviews. When expertise is not available, health service organisations may need to contract external expertise.

Currently there is no standardised training available for DTC members, nor is there a minimum competency criterion required. CATAG recommends all DTC members undertake similar training to assist in 'good decision making', and also work towards a consistent training approach throughout Australia, further contributing to the goal of equitable access. For those reviewing high-cost medicine applications, further training for example in health technology assessment and budget impact analysis is required. It is noted in the report *The New Frontier – Delivering better health for all Australians* recommends that the Australian Government develop a labour market and skills strategy to expand the number of health economists in Australia. This could include encouraging training within Australia as well as seeking expertise from overseas.[25] Mentoring of new members of review panels should be considered. Training also extends to the secretariat of the DTC. Training of DTC members is identified as an area for future development.

It is essential that health service organisations appropriately fund and support DTCs to enable them to fulfil their roles and responsibilities as per CATAG's *Guiding principles for the roles and responsibilities of Drug and Therapeutics Committees in Australian public hospitals*. Positions on DTCs, including the functions of the secretariat, should be funded to account for the expertise, time and effort required to review these applications. CATAG acknowledges that increased resourcing is required to implement these principles.

For the future

Promote equity of access by having a national definition for jurisdictions and hospitals to use for high-cost medicines

One of CATAG's stated objectives is to promote fair process and equity of access for all patients. This requires transparency and standardisation in decision making, evaluation and review between jurisdictions to improve patient centrality within this process.

Medicine access equity means that everyone should have a fair opportunity to access funded medicines to attain their full health potential, and that no one should be disadvantaged from achieving this potential.[26] There are many barriers to equity which include personal and health system barriers. Equitable access is determined by five drivers: medicine availability, accessibility, affordability, acceptability and appropriateness. Medicine availability includes how a medicine is funded and the implementation of those decisions so that everyone who is eligible can access the medicine.[26]

Promote the sharing of assessments and outcome data and the development of a national high-cost medicine formulary

It is important to acknowledge the current duplication of work evaluating medicines, especially high-cost medicines, for availability at Australian public hospitals. This duplication of effort would be increased if budget impact analysis and health technology assessment are introduced for each individual DTC. Along with duplication, this time-intensive process potentially increases time to access of medicines for patients. In situations where patients may be transitioned from one health service to another, for example from a paediatric hospital to adults or metropolitan to regional, the sharing of the assessment and decision making for the high-cost medicine is especially important.

Establishment of national processes is recommended. This could be achieved by formalising and promoting the already established network for sharing resources, through CATAG, whereby anonymised information is shared, rather than the informal process currently in use. The information would ideally include supporting information used to inform decisions, the resultant decisions (whether positive or negative), outcome data, and medicine use evaluations. This would require resourcing for infrastructure such as interoperable electronic IPUs and DTC tools, in addition to resourcing to maintain and analyse data. Further supporting information could then be developed including high-cost medicine evaluation resources, standardised templates and nationally consistent guidance to support cost effectiveness reviews. This would facilitate 'network learning' between DTCs and allow sharing of information between sites to reduce duplication of effort and improve transparency and consistency based on the latest research evidence. It could be used to inform the possible development of a national hospital high-cost medicine formulary.

Appendices

APPENDIX 1: High-cost medicines decision-making algorithm

This algorithm (see **Figure 1**) provides a simplified summary of the decision-making process for the governance of high-cost medicines, acknowledging that the actual process is far more complex than this algorithm. This algorithm provides a guide for medicines governance committees, to illustrate the process and place of the guiding principles.

For formulary and IPU applications, the algorithm provides a proposed process for submission and decision making. Each hospital or health service should have governance arrangements in place for the consideration of high-cost urgent IPU requests.

Individual hospitals or health services will need to decide how many IPUs trigger a formulary application. If this a repeated IPU request (e.g. more than three applications within a 12-month period for the same indication in different patients), then the medicine should be reviewed for either formulary application or a streamlined approval process.

This algorithm has been adapted from the NSW Therapeutic Advisory Group Decision Algorithms for evaluation of medicines for formulary listing in public hospitals and for individual patient use (IPU) approval (2009), and South Australian Medicines Evaluation Panel (SAMEP) process for high-cost medicines. [Lambert R, Burgess N, Hillock N, Gailer J, Hissaria P, Merlin T, et al. South Australian Medicines Evaluation Panel in review: providing evidence-based guidance on the use of high-cost medicines in the South Australian public health system. Aust Health Rev. 2021;45(2):207–13.]

Notes to Figure 1

A. If this application is a request for a non-urgent IPU the following needs to be considered:

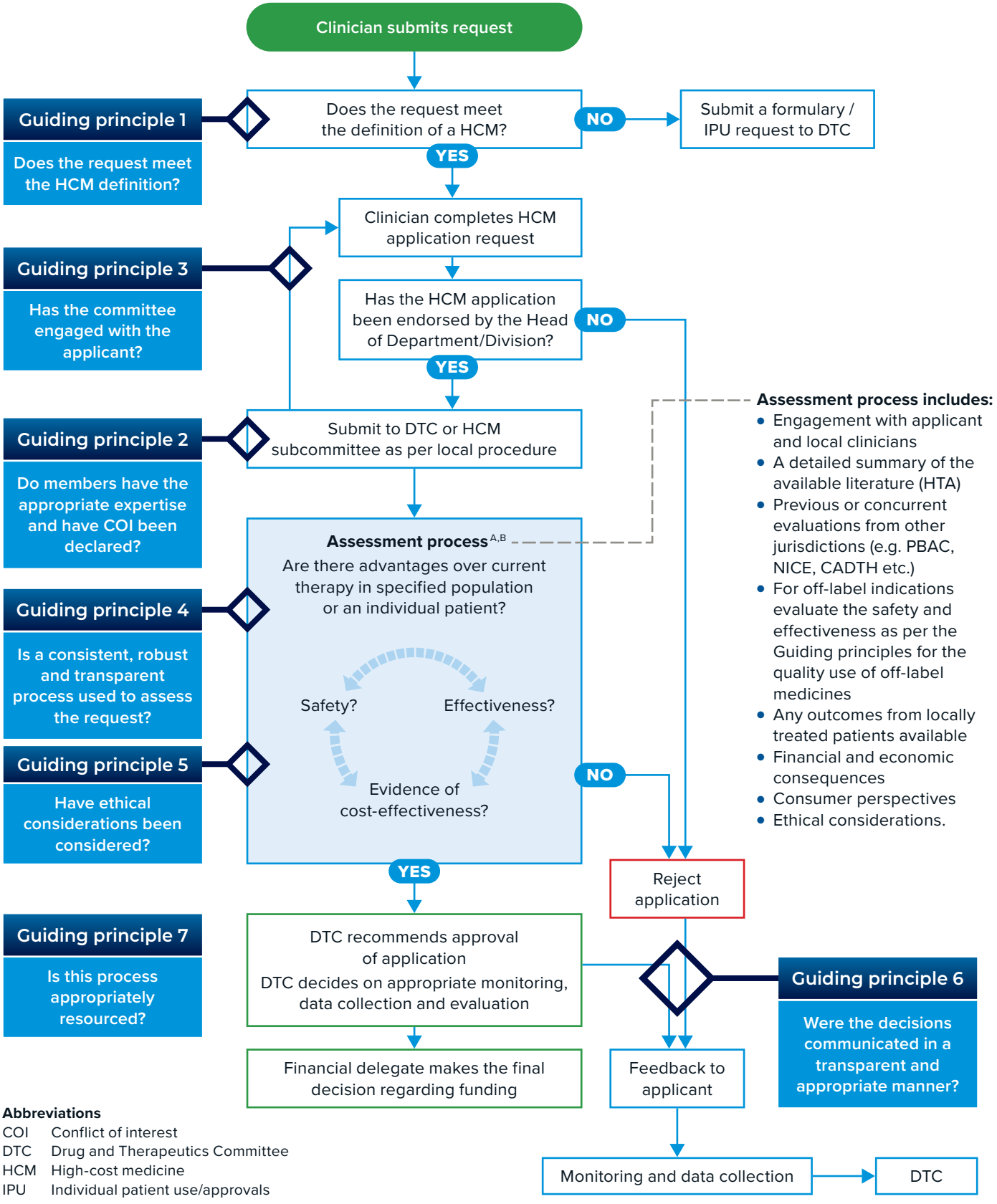
   Is there justification for exceptional use?

   - serious underlying disease or condition; and
   - some evidence to support beneficial effect; and
   - potential benefits outweigh potential risks and
   - standard therapy has been trialled or is inappropriate; and
   - there is written informed consent for medicines that are newly developed, experimental or have known high risk complications or being used off-label or unlicensed use.[27]

   If there is no high quality evidence supporting use of a particular medicine, and it is not suitable for 'exceptional indications' or for the purpose of research, use of the medicine is generally not recommended.[28]

B. Consider requests for off-label use using CATAG's *Rethinking Medicines Decision Making: Guiding Principles for the quality use of off-label medicines*, during consideration as a high-cost medicine.

Figure 1: High-cost medicines decision-making algorithm



Abbreviations

COI Conflict of interest
DTC Drug and Therapeutics Committee
HCM High-cost medicine
IPU Individual patient use/approvals

APPENDIX 2: Examples of formulary and individual patient use application documents

- SA Health Statewide Formulary for High Cost Medicines Submission Form
- SA Health Individual Patient Use (IPU) Medicine Request Form
- Western Australian Drug Evaluation Panel (WADEP) Statewide medicines formulary – submission form – non-pharmaceutical benefits scheme (non-pbs) listed medications
- Queensland Health Management and governance of individual patient approvals for medicines and other therapeutic goods (including high-cost medicines)
- NSW TAG DTC Formulary Submission and IPU Application Templates

APPENDIX 3: Glossary

TERM	DEFINITION
Affordability	The ability to purchase a necessary quantity of a product or level of a service without suffering undue financial hardship.[29]
Drug and Therapeutics Committee (DTC)	The group assigned responsibility for governance of the medication management system, and for ensuring the safe and effective use of medicines in the health service organisation.[30] These may also be known as a medicines advisory committee, pharmacy and therapeutics committee, drug committee, drug and therapeutics advisory committee, formulary committee or quality use of medicines committee.
Effectiveness	How beneficial a test or treatment is under usual or everyday conditions, compared with doing nothing or opting for another type of care.[31]
Efficacy	The extent to which an intervention is effective when studied under controlled research conditions.[31]
Equity	The fair allocation of resources or treatments among different individuals or groups, such that they each get what they are owed or what they are entitled to.[32]
Health professional	For the purpose of this guidance, health professional includes nurses, midwives, medical practitioners, pharmacists and other individuals deliver health care.[33]
Health technology assessment	This systematically evaluates the direct and intended effects of a health technology, as well as its indirect and unintended consequences. An HTA is generally undertaken to help others make a decision on a technology's use or purchase.[19]
Individual patient use/ approvals (IPU/IPA)	A request to or approval by the DTC for the use of a medicine by an individual patient outside the formulary regulations.[13]
Medicine	A chemical substance given with the intention of preventing, diagnosing curing, controlling or alleviating disease or otherwise enhancing the physical or mental welfare of people. Includes prescription and non-prescription medicines, including complementary health care products, irrespective of the administered route.[34]
Pharmaceutical Benefits Scheme (PBS)	A national, government-funded scheme that subsidises the cost of a wide range of pharmaceutical medicines, and that covers all Australians to help them afford standard medicines.[35]
Public Hospital	A hospital controlled by a state or territory health authority. In Australia public hospitals offer free diagnostic services, treatment, care and accommodation to all who need it.[35]

APPENDIX 4: How these Guiding Principles were developed

This document was prepared by the CATAG Project Team in consultation with an Expert Advisory Group (EAG). The EAG was comprised of individuals with recognised expertise in a range of areas, such as therapeutics/quality use of medicines, evidence-based medicine use, medicines governance and patient issues. All feedback was discussed and agreed upon for incorporation into these Guiding Principles. During the development the document, CATAG member organisations undertook consultation, at various stages, with their wider constituents, including hospital drug and therapeutics committees, hospital pharmacy departments and clinicians. External consultation with key national organisations was also undertaken. A final version was approved by the EAG.

These Guiding Principles have been funded by the Australian Government Department of Health through the Value in Prescribing – Biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) Program Grant. The author acknowledges the assistance provided by the Targeted Therapies Alliance in reviewing the document.

These Guiding Principles were developed in consultation with and endorsed by representatives from the CATAG member organisations listed below:

- Canberra Health Services
- NSW Therapeutic Advisory Group (NSW TAG)
- Northern Territory Drug and Therapeutics Committee
- Queensland Health Medicines Advisory Committee (QHMAC)
- South Australian Medicines Advisory Committee (SAMAC)
- The Tasmanian Medication Access and Advisory Committee (TMAAC)
- Victorian Therapeutics Advisory Group (VicTAG)
- Western Australian Therapeutics Advisory Group (WATAG).

Acknowledgement

We are grateful for the contributions and feedback from the following individuals who assisted us in developing and reviewing the Guiding Principles:

- **Lisa Pulver** – CATAG Project Officer
- **Jane Donnelly** – National Coordinator, Council of Australian Therapeutic Advisory Groups
- **Camille Schubert** – Team Leader – Health Economics, Adelaide Health Technology Assessment, School of Public Health, The University of Adelaide.

Expert Advisory Group

- **Professor Catherine Hill (Chair of EAG)** – Director, Rheumatology Unit, The Queen Elizabeth Hospital. Staff Specialist, Royal Adelaide Hospital. Clinical Professor, University of Adelaide, SA.
- **Peter Barclay** – Director of Pharmacy, The Children's Hospital at Westmead, NSW.
- **Dr Sasha Bennett** – Executive Officer, NSW TAG, NSW.
- **Naomi Burgess** – Director, Medicines and Technology Programs (MTP), System Leadership and Design Division, Department for Health and Wellbeing, SA Health, SA.
- **Dr Jonathan Dartnell** – Programs and Clinical Services Manager, NPS MedicineWise, VIC.
- **Catherine Drake** – Society of Hospital Pharmacists of Australia.
- **Associate Professor Tracey-Lea Laba** – NHMRC Early Career (Sidney Sax) Fellow, Centre for Health Economics Research and Evaluation, UTS NSW.
- **Dr David Liew** – Consultant Rheumatologist and Clinical Pharmacologist, Project Lead, Medicines Optimisation Service, Austin Health, VIC.
- **Dr Kylie Mason** – Haematologist, Peter MacCallum Cancer Centre, Melbourne, VIC
- **Terry Melocco** – Director of Pharmacy, St Vincent's Hospital Sydney, NSW.
- **Dr Mary O'Reilly** – Medical Director, Patient Safety & Clinical Excellence, Deputy CMO, Infectious Diseases physician, Austin Health, VIC.
- **Dr Linda Sheahan** – Staff Specialist Palliative Medicine, Clinical Ethics Consultant, Honorary Associate, Centre for Values, Ethics, and the Law in Medicine, University of Sydney, NSW.
- **Dr Kavitha Subramaniam** – Senior Staff Specialist, Gastroenterology and Hepatology Unit, Canberra Hospital, ACT.

External consultation

- Arthritis Australia
- Australian College of Nursing
- Australian Digital Health Agency
- Australian Medical Association
- Australian Rheumatology Association
- Children's Healthcare Australasia
- Gastroenterological Society of Australia
- Medicines Australia
- Medical Oncology Group of Australia Incorporated (MOGA)
- Northern Territory Government Department of Health
- Pharmaceutical Defence Limited
- Pharmaceutical Society of Australia
- Pricing & PBS Policy Branch, Australian Government Department of Health
- Queensland Government, Department of Health
- Rare Voices Australia
- Royal Australasian College of Medical Administrators
- Society of Hospital Pharmacists Australia
- Tasmanian Government, Department of Health
- Government of South Australia, SA Health
- Therapeutic Goods Administration
- Therapeutic Guidelines
- Western Australia Government, Department of Health.

Conflicts of interest

- Professor Catherine Hill: Member of Pharmaceutical Benefits Advisory Committee (PBAC); Chair, South Australian Medicines Evaluation Panel.
- Dr Tracey-Lea Laba: Member of Drug Utilisation and Economics Sub Committees of PBAC, Member of NSW Statewide Formulary and High Cost Drug Committees.
- Dr David Liew: Member of Drug Utilisation Sub Committee of PBAC.
- Dr Kylie Mason: Member of PBAC; Member of Economics Sub Committee of PBAC.

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