eviQ Cancer Treatments Online

Program Governance

Version 1.3 | 14 November 2022

NSW GOVERNMENT

Cancer Institute NSW

Contents

Version 1.0 Released 10 December 2018.
Version 1.1 Released 11 January 2022.

1. Aim and structure of this manual

This document describes the processes and methods used to develop, maintain and update all eviQ information.

Its intended audiences are:

- internal eviQ staff involved in developing content
- eviQ reference committee chairs and members
- eviQ users including clinicians, nurses, pharmacists and allied health

It is also likely to be of interest to a broader audience, including other developers of policy, government bodies, stakeholders and users of eviQ content.

2. Introduction and overview

2.1. eviQ Cancer Treatments Online

eviQ is a freely available online resource of adult cancer treatment protocols and information developed by multidisciplinary teams of cancer specialists. With a goal to improve patient outcomes and reduce treatment variation, eviQ provides evidence-based best-practice treatment protocols and information to support health professionals in the delivery of cancer treatments at the point of care.

eviQ treatment protocols and information are intended to **provide guidance** on the optimal prescribing and administration of cancer treatments. eviQ guidance should be used in conjunction with a health professional's clinical judgment and expertise as well as individual patient factors to determine safe and effective cancer treatment. See section 7.1 for further detail on eviQ's intention of use.

While **not mandated**, eviQ has been nationally endorsed since 2012 as the preferred source of evidence-based cancer treatment information in Australia, and is embedded into clinical practice, policy and oncology information systems (OMIS) across the country.

2.2. eviQ and the Cancer Institute NSW

eviQ is part of the Cancer Institute NSW. The Institute is NSW's cancer control agency, established under the Cancer Institute NSW (2003) Act to lessen the impact of cancer across the state.

The Cancer Institute NSW is a pillar organisation of NSW Health, providing the strategic direction for cancer control in NSW. The Cancer Institute NSW is funded by the NSW State Government and governed by the Cancer Institute NSW Board. It reports directly to the Minister for Health and Medical Research.

2.3. eviQ structure

eviQ's founder Professor Robyn Ward, provides support and strategic leadership to the program within the Cancer Services and Information Division at the Cancer Institute NSW.

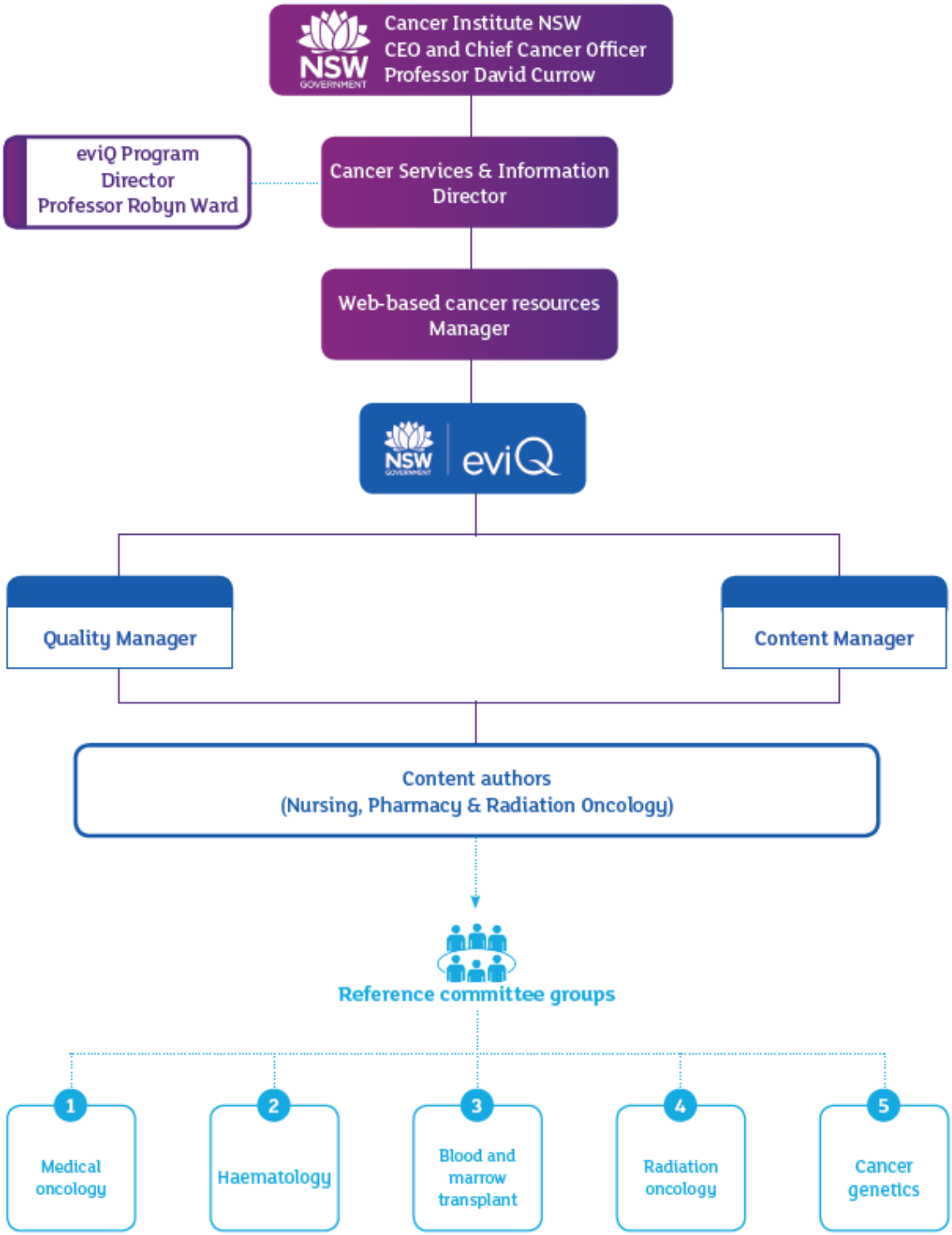


Figure 1: Overall structure of eviQ

2.4. National eviQ program

The program operates at a national level and holds Memorandums of Understanding (MOU) with all Australian states and territories (commenced in 2012) endorsing eviQ as the preferred provider of evidence-based cancer treatment information.

These agreements make a commitment to travel and attendance by interstate clinicians at eviQ reference committee meetings for protocol and content development and review. eviQ reference committees have wide representation from all Australian states and territories.

2.5 Funding of eviQ

eviQ is funded by the NSW state government and governed by the Cancer Institute NSW Board. In addition, eviQ receives a small amount of funding from each state and territory government health body to enable interstate travel by clinicians for the purpose of attendance at eviQ reference committee meetings.

eviQ does not receive sponsorship from any commercial or pharmaceutical industry, nor does it use advertising from any source.

This ensures that eviQ maintains editorial independence across all of its processes, and all content is presented free from bias.

3. eviQ Reference Committees

eviQ works with clinical expert groups (eviQ Reference Committees) to help develop and review the treatment protocols and clinical content available on eviQ.

There are five eviQ reference committee groups: cancer genetics, blood and marrow transplant, haematology, medical oncology and radiation oncology, each chaired by practising clinicians. Each group meets face-to face 2-3 times per year for 4-8 hours to review and discuss the content provided on eviQ, based on current literature available at the time. Meetings are generally focused on specific tumour groups or clinical topics.

Additional reference committee meetings either via teleconference or email may be conducted throughout the year, as required (see section 8.3 Out of session protocols).

Refer to eviQ Reference Committee Terms of Reference, for more detailed information.

3.1. Composition of the eviQ Reference Committee

Membership is open to all practising medical (consultant, fellow or trainee; minimum requirement is that clinicians must be in the Advanced Trainee program), nursing or allied health clinicians within Australia, in the area of blood and marrow transplant (BMT), cancer genetics, haematology, medical oncology or radiation oncology. For eviQ cancer genetics and paediatric cancer genetics reference committee membership eligibility criteria see Appendix A. All reference committee members play an important role in reviewing, developing and implementing eviQ treatment protocols. Membership is reviewed every two years.

Prior to each content/tumour specific reference committee, the eviQ team aims to bring together a group of clinicians which fulfil the following parameters:

- have relevant clinical practice in the specific tumour groups or clinical topics
- contain expert members i.e. can co-opt members with specific expertise particularly when specialist clinical expertise in niche areas is required
- are multidisciplinary, with all relevant clinical specialties represented when required
- are geographically representative i.e. include clinicians from metro, regional and rural centres across all states and territories where possible
- broad range of experience – from registrar to senior consultant.

eviQ reference committee groups vary in size depending on the content/tumour area under consideration, but generally reference committee meetings comprise between 15 and 25 attendees in order to have a manageable group size for effective decision making. All members have equal status in the group.

3.2. Managing conflicts of interest

The participation of the eviQ reference committee chairs and members is voluntary and no compensation is provided for their involvement in the eviQ protocol development and update process. However, travel and expenses to attend reference committee meetings (generally held at the Cancer Institute NSW in Sydney) are covered by the eviQ program's allocated budget (both NSW and national funding supports these activities).

All contributors to eviQ are listed on the acknowledgements page on eviQ without attributing specific content to any particular individual.

All prospective members are sent an invitation to join the reference committee, along with the Terms of Reference. Invitees who accept are required to complete the eviQ code of conduct/conflict of interest form annually, which allows for:

- Disclosure of any potential conflicts of interest, including commitments that might be perceived as conflicts. A register of declared interests is kept by the Cancer Institute NSW and the degree and impact of conflict is reviewed and decided by eviQ and the relevant chairs.
- Observance of a strict policy of confidentiality i.e. protocols in draft or those pending publication; and a requirement to keep content of committee discussions confidential including, but not limited to, email, phone and other communications.

4. Terms of reference/responsibilities

Participation in the development and review of eviQ protocols involves a significant commitment of time and effort. Key to the success and sustainability of eviQ is its clinician engagement, ensuring the content remains practical, concise and reflects both the evidence and 'real world' experience of health care practitioners who deliver cancer treatments.

Meeting discussions are facilitated by the reference committee chair/s, and open disclosure and discussion is encouraged to ensure transparent and explicit reporting of the consensus view. The goal is to publish protocols based on the consensus of a broad range of experts in a transparent and systematic fashion, and to fully describe controversial areas where consensus cannot be reached. This ensures the eviQ's currency, applicability and validity.

All reference committee members should be aware that they represent both a geographical region and a specialty and must be prepared to consult with peers to ensure the widest possible range of views are considered.

Reference committee members are not expected to attend every meeting.

The responsibilities listed in section 4.1 aim to provide clarification around the expectations and scope of protocol development.

4.1. Reference Committee Chairs

The role of the eviQ reference committee chairs is crucial to the effective functioning of the reference committees, ensuring collaboration and a balanced contribution from all members.

For more detailed information on the process refer to eviQ Terms of reference

Each reference committee has at least two chairpersons who are practicing clinicians.

Responsibilities include:

- With the aid of the eviQ team, develop agendas, distribute materials prior to meetings and set and ensure reference committee members meet deadlines for submitting work.
- With the eviQ team, review protocol submission requests to identify and triage protocols for development.
- Provide a rapid response to time-sensitive issues identified by the eviQ team.
- Participate in the prioritisation of protocol review and development within each tumour area.
- Participate in the periodic review of protocols to identify potentially practice-changing data and help inform if a protocol needs to be updated.
- Monitor and negotiate through potential contentious issues/conflicts of interest in collaboration with eviQ leadership

- With the eviQ team, participate in the appointment of new chairs.
- Encourage younger members of the oncology community to participate in reference committee meetings for professional development.
- Advocate for eviQ and its role in best practice cancer care.

To facilitate the process of consensus at a meeting, the chair should:

- lay out the terms of reference/conflicts of interest under which the committee will operate (a member of the eviQ team can also do this);
- encourage all members to contribute to the discussion;
- be aware of and attentive to small group dynamics;
- keep the discussion unified and avoid dominance by any single member or subgroup;
- enable open and constructive debate; and
- summarise main points and key decisions.

Appointment and Term of the Chair

The appointment of chair and co-chair occurs via a formal process. When a new chair is due to be appointed, eviQ will call for nominations from members of the reference committee via an Expression of Interest (EOI) or Nomination Requests. Successful appointments are decided by the eviQ Program Director, current chairpersons and the eviQ leadership team.

The period of appointment of chair and co-chair is for 2 years. Ideally, the co-chair will then move into the chair position at the beginning of the following 2 years term, to ensure continuity. Therefore, the maximum combined term as co-chair and chair is 4 years.

4.2. Reference Committee Members

Responsibilities

- Attend face-to-face meetings and teleconferences as required.
- Review and edit drafts of the protocol, critically appraise and contribute to the interpretation of the evidence supporting protocol development – this is completed prior to a reference committee meeting via email
- Present the protocol at the face to face reference committee meeting -
- If identified as the lead clinician on a particular protocol/topic, make a full commitment to the tasks involved and be responsible for indicating areas of concern to eviQ. **Provide final sign off on behalf of the committee, for the document/protocol.**
- Check and respond to emails on a regular basis.
- Meet deadlines; if unable to adhere to the timeline for whatever reason, notify the eviQ team and reference committee chairs.
- Provide feedback or input into the development of eviQ clinical resources such as supporting documents, assessment tools etc. that have been developed to support the safe delivery of the treatment protocol.

4.3. eviQ content authors

eviQ content authors are employees of the Cancer Institute NSW who co-ordinate the development and review of eviQ content. eviQ content authors are health professionals with clinical experience in cancer care (nursing, pharmacy and radiation therapy).

Content authors support and facilitate the work of the reference committees to develop and review eviQ content, ensuring all governance processes are followed consistently and appropriately, and that quality assurance processes are followed for publishing content on the eviQ website.

Content authors plan and schedule content development and review, co-ordinate reference committee meetings, manage the committee membership and liaise with all stakeholders contributing to the development of protocols and clinical content.

Additional responsibilities include:

- conducting regular searches for new and updated evidence/guidelines
- continuous scanning of drug alerts
- daily monitoring and triaging of user feedback
- internal peer review and sign-off for all content.

4.4. Reference Committee documentation

All reference committee meetings are formally documented by the eviQ content authors. These documents are then approved by the reference committee chairs and published on the relevant reference committee homepage (accessed by authenticated users only). It is the responsibility of eviQ and the Cancer Institute NSW to maintain records throughout protocol development/review and ensure that record-keeping standards are appropriate for audit.

Reference committee documentation and email discussions are confidential and available only for reference committee members.

Available on the eviQ website are:

- upcoming dates for all reference committee meetings;
- details of all past and present reference committee chairs;
- a list of all contributors to eviQ since its inception and
- the processes for becoming a reference committee member.

5. Reference Committee Meetings

5.1. Overview of a Reference Committee Meeting

Face-to-face eviQ reference committee meetings provide an opportunity for critical appraisal of the evidence supporting the treatment protocols. During these meetings protocols are presented by a lead clinician, discussed by the committee and consensus agreement is reached by the reference committee.

All protocols that have been identified for development or review are assigned to a clinician (e.g. an advanced trainee or consultant). If an advanced trainee has been identified, then development will be under the guidance of a senior consultant/supervisor, who will be responsible for providing final sign off.

A content author supports the lead clinician in the protocol review or development process by conducting a preliminary search of the literature in addition to coordinating and providing:

- The development template.
- **For a protocol review**: a summary of the recommended potential changes e.g. drug status and any literature found during a preliminary search.
- **For a new protocol**: key evidence and any literature found during a preliminary search, data from submission requests and rationale for development.
- A link to the protocol specific literature search tab that is currently available within the eviQ protocol, which searches the PubMed database.
- The proposed timeline for completion.

5.2. Presenting and summarising evidence

A reference committee meeting provides clinicians with the opportunity to present a summary and analysis of all of the relevant evidence, including any limitations to their peers.

In order to ensure that the protocol is clinically relevant and applicable, the evidence must be contextualised (i.e. interpreted and extrapolated) to reflect everyday clinical situations.

During discussion, the lead clinician is expected to raise for discussion any other contentious parts of the protocol e.g. dose modifications or risk factors.

All discussions will be captured by the content authors in the meeting documentation and validated by the reference committee chairs.

6. Advanced Trainee Program

eviQ encourages trainees to contribute to the development and review of content and currently has advanced trainee programs within the medical oncology and radiation oncology content areas. Partnership with the Medical Oncology Group of Australia (MOGA), Royal Australian and New Zealand College of Radiologists (RANZCR) and the Royal Australasian College of Physicians (RACP) advanced trainee committee, allows trainees to earn CPD points by developing and presenting eviQ protocols at reference committee meetings.

Advanced trainees are consistent users of eviQ and having them more formally involved in reference committees helps maintain the currency of the evidence base of the eviQ protocols. Additional key learning opportunities include conducting systematic reviews, critical appraisals and drawing from the experience of senior clinicians.

For more information and access to the registrars and advanced trainees' homepage contact eviQ.

7. eviQ treatment protocols and supporting documents

7.1. Intended use

eviQ treatment protocols and supporting documents are intended to **provide guidance** on the optimal prescribing (including dosing) and administration of a chosen cancer treatment. For this reason, eviQ is a point of care guidance resource rather than a clinical guideline. The latter takes the form of a document that guides decisions regarding diagnosis, management or treatment options.

eviQ protocols and supporting documents are based upon the best and most comprehensive evidence available at the time they are developed as per the consensus of the reference committee and contextualised for Australian clinical practice. Where the evidence is conflicting, lacking or controversial, the reference committee must come to consensus decision and the details of this decision and the rationale must be documented explicitly in the eviQ protocol.

eviQ recognises that treatment undertaken in the context of a clinical trial often does not reflect real-world practice. It is for this reason that eviQ reference committees use the published literature together with their own expertise to formulate and publish real-world treatment protocols on eviQ.

eviQ protocols provide an excellent starting point for treatment, however clinicians must apply their clinical judgement and consider the individual patient's situation e.g. patient performance status, disease extent, rate of progression, potential sensitivity to treatment and patient preferences. Variation from an eviQ protocol may be appropriate and in NSW the recommendation is that dose variations from documented protocols are clearly documented in the patient notes and informed consent is obtained from patients.[2]

eviQ provides safe and effective instructions on how to administer cancer treatments and recommendations for supportive treatments (antiemetics, premedications etc), however eviQ **does not provide every option** and there may be alternative ways to administer treatments, and alternative supportive treatments that are also appropriate.

Refer to Appendix B, detailing the scope of the eviQ paediatric cancer genetics content area.

7.2. Protocols not listed on eviQ

eviQ works within the bounds of the Commonwealth of Australia's regulatory and reimbursement process for drug marketing and subsidy and complies with the Therapeutic Goods Administration (TGA) and the Pharmaceutical Benefits Scheme (PBS). **A drug must be PBS listed and/or TGA registered for a particular indication in order for it to be included on the eviQ website for that indication.** For more information refer to the eviQ policy: eviQ compliance with TGA registration and PBS listing for drugs (Appendix C).

Therefore, some drugs and treatments will not appear on eviQ and other recognised evidence-based oncology resources may be useful e.g. National Comprehensive Cancer Network (NCCN), British Columbia Cancer Agency (BCCA), European Society for Medical Oncology (ESMO) or American Society of Haematology (ASH).

Facilities should consider establishing a local clinical governance process, whereby current and proposed protocols can be discussed within a multidisciplinary setting and the use of protocols not available on eviQ or from an alternative evidence-based source, are documented with consideration given to submitting these to eviQ where appropriate.

7.3. Information not aligned to Australian product information

On occasions, eviQ may publish drug administration information that is not directly in line with the approved Australian product information. The rationale for this being that if another jurisdictional registration authority, such as the FDA, approves changes in administration conditions or schedules (time, frequency, dose, reconstitution solutions, pre-meds etc.) then eviQ could adopt these changes – unless adopting such a change would promote poor practice in other ways – e.g. increasing costs, impacting on patient quality of life etc.

8. Protocol development

8.1. Protocol submission

Any individual or institution may submit a protocol for development/review consideration via the eviQ online submission form available for the eviQ homepage https://www.eviq.org.au/protocol-submission/submit-a-protocol. To reduce duplication,

prior to submission, all users are encouraged to review the following eviQ website pages, accessed via submission page or the eviQ FAQ:

- Protocols under development; and
- Protocols not endorsed (this lists protocols previously submitted, considered and rejected for development on eviQ by the reference committee)

8.2. Post submission - What happens to the request?

Protocol submission requests are first reviewed by the eviQ team. If it complies with the eviQ Content Development and Review Process (Appendix D), i.e. evidence for the protocol is NHMRC level I, II or III-1 evidence; and all drugs are PBS listed and/or TGA registered for the submitted indication then the protocol will be taken to the relevant reference committee chairs, +/- members, for consideration for development.

If the reference committee members agree that the protocol should be developed, then priority for development is based on the following criteria:

1. Practice changing e.g. newly registered drug; drug approved for a new indication; new published evidence available
2. Unmet need e.g. rare tumour groups where there are no protocols currently on eviQ
3. Safety concern with an existing eviQ protocol e.g. new data indicates excessive toxicity with specific drug and dose reduction is recommended

If the reference committee members decide the protocol should not be developed, then this is communicated on the website via the 'Protocols not endorsed' page, which lists protocols previously submitted and rejected by the reference committee.

Development of protocols following submission may happen during face-to-face reference committee meetings if an appropriate meeting is scheduled soon, or it may be developed 'out of session' (see 8.3) via email or teleconference to ensure timely development and publication on the website

During development, these protocols are listed on the 'Protocols under development page'.

8.3. Out of session protocols

To ensure eviQ reflects current practice, if the next relevant reference committee meeting is scheduled for > 6 months in the future then the protocol(s) may be developed out of session by teleconference or email. For example, when new drugs or new indications for existing drugs are approved by Australian regulatory authorities in accordance with the eviQ TGA/PBS policy, to reduce the time lag from approval to publication on eviQ, an out of session protocol development process is used.

8.4. Interim protocols

Interim protocols are intended to offer timely clinical information following the publication or presentation of potentially practice-changing data/new protocols from major studies. These protocols may be awaiting the final results of phase 3 randomised controlled trial (RCT) to be published. Once the data becomes available these protocols will be further developed/updated by teleconference/email.

Interim protocols contain all the standard sections of an eviQ protocol and are distinguishable from other eviQ protocols as they have 'INTERIM' in the protocol title and an alert (i.e. flag) at the top of the protocol such as:

CAUTION: This is an interim protocol based on preliminary data from a phase III trial that has only been presented in abstract form. The data has NOT yet been published in a peer-reviewed journal. This protocol may proceed to a full protocol once full data has been published.

The development and approval process for interim protocols is identical to that of all other eviQ protocols via a face-to-face reference committee meeting, with the additional option for approval via email/teleconference.

These protocols will be reviewed within 12 months of development, or sooner if further published data becomes available.

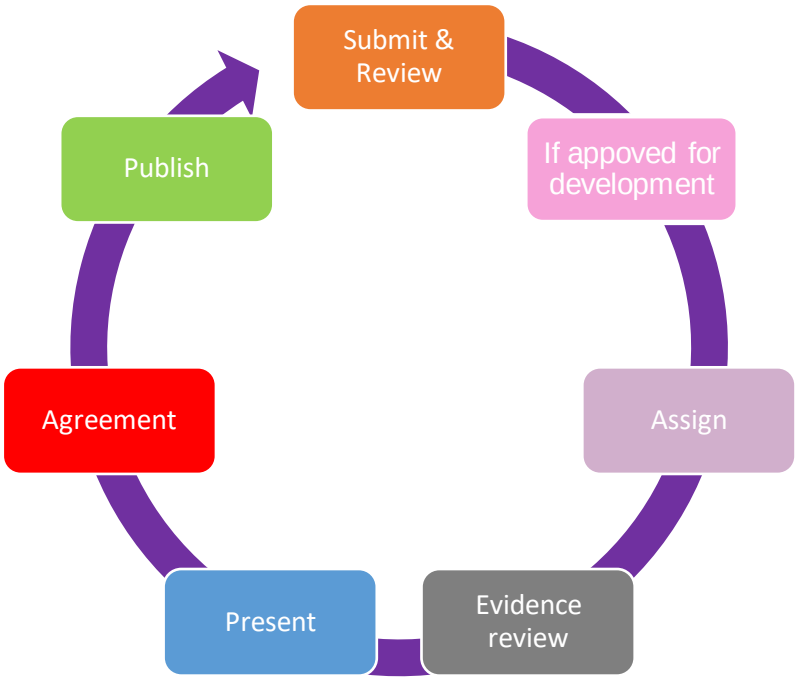


Figure 2: Protocol Development Process

9. Literature review

9.1. Review of evidence

eviQ protocols are based upon the best and most comprehensive evidence available at the time of their development and follow the NHMRC hierarchy of levels of evidence (Appendix E). Meta-analysis, or systematic review of randomised trials, of high methodological quality are ranked highest, while case studies are ranked lowest.

To minimise bias and ensure adequate coverage of the literature, eviQ supporting evidence is derived from a number of resources, including but not limited to:

- Publications on databases including PubMed, Medline, The Cochrane Library.
- Proceedings of major national and international scientific meetings.
- Clinical guidelines and other recognised oncology resources such as National Comprehensive Cancer Network (NCCN), British Columbia Cancer Agency (BCCA), Cancer Care Ontario (CCO), European Society for Medical Oncology (ESMO) or the American Society of Haematology (ASH).
- eviQ Bibliometric literature search solution (provide link for more information).
- The clinical experience, judgement and consensus of eviQ reference committee members.

9.2. Achieving consensus

Regardless of the quality and quantity of the evidence available, the reference committee needs to critique, interpret, and reach consensus on the extrapolation of the evidence for practice in Australia.

When it is not possible to reach consensus, the committee may wish to identify wider views on best practice outside of the group i.e. further expert opinion. It then becomes the responsibility of the chairs to approach /engage other clinicians when further specialist clinical expertise is required. Consensus must be reached before a protocol or other content may be approved and published on the eviQ website.

9.3. Areas with conflicting, lacking or controversial evidence

Where the evidence is conflicting, lacking or controversial, the reference committee must come to a consensus decision and the details of this decision and its rationale must be documented explicitly in the eviQ protocol. i.e. by a flag at the top of the protocol and/or the inclusion of a limited evidence template (see below); or for more specific points within the protocol, then a statement in the relevant protocol section.

9.4. Levels of evidence on eviQ

To provide transparency of the level of evidence supporting each protocol there are two evidence templates used across the website - a **standard** and **limited** evidence template. This ensures that the supporting evidence displayed for each protocol is presented in a consistent format across the website.

The criteria for selecting which template will be used for the development of a protocol is determined by the level of evidence available, using the NHMRC Evidence Hierarchy table (Appendix E):

- Protocols based on Level I, II and III-1 will display the standard evidence template.
- Protocols based on Level III-2, III-3 and IV will display the limited evidence template

Standard template: The evidence section of an eviQ protocol is a succinct summary of the key evidence directly supporting the protocol. It is not a comprehensive meta-analysis, nor a literature review or a historical background of all of the available evidence for the protocol. Only directly relevant papers should be cited- in particular, multiple citations for the same statement should be avoided unless they are important to support the statement.

The evidence selected should address a key health outcome i.e. survival benefit; local control rates, quality of life; risk benefit, that justifies and supports the protocol.

The inclusion of tables/figures are incorporated into the protocol for easy access. The format is templated (Appendix F) and includes 3 sections; Evidence, Efficacy and Toxicity.

Limited evidence template: Protocols based on limited evidence must include a 'limited evidence table' summarising the literature to provide a basis for comparison and ensure transparency about the level of evidence available. Refer to Appendix G.

Reasons that may be considered for including a protocol on eviQ based on limited evidence (not exhaustive):

- Wide clinical acceptance that two agents have at least equivalent efficacy and may be substituted e.g.:
  - capecitabine for fluorouracil (5FU): capecitabine, the oral prodrug of fluorouracil is an effective and safe alternative to fluorouracil and therefore it is considered reasonable to substitute capecitabine for infusional 5FU

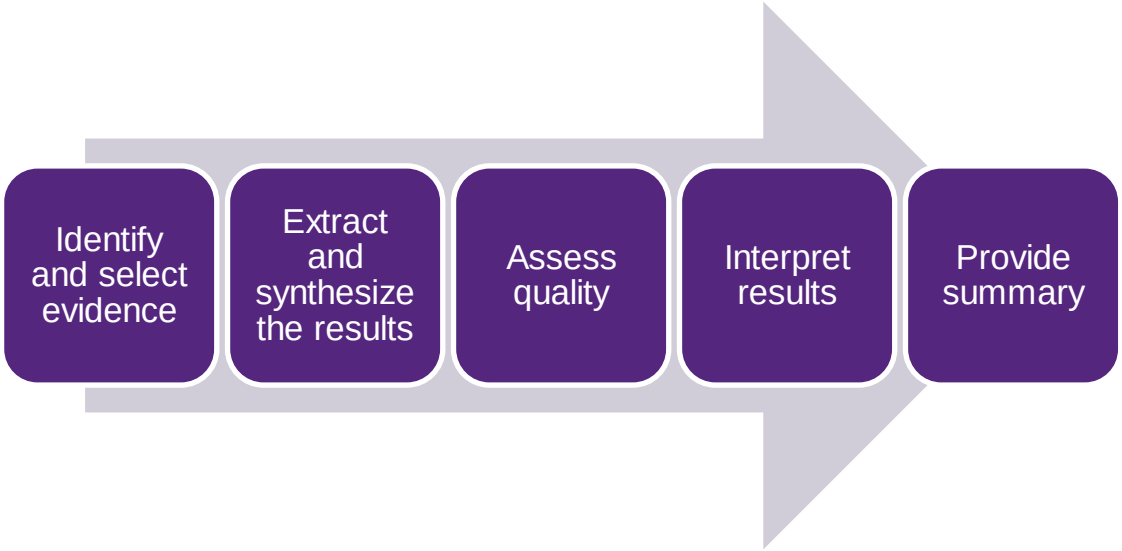
- Instances where there is limited or poor evidence and it is unlikely that good quality studies will be conducted in the future e.g.:
  - rare diseases/cancers
  - where the real-world treatment population varies considerably to the highly selected patients used in the clinical trials on which the evidence is based

- When the available literature is very limited, but recommendations are still necessary

9.5. Use of unpublished data/abstracts

Abstracts or unpublished data, which do not represent full results/analysis, should not generally be used in the development of eviQ protocols or as part of the supporting evidence, however abstract data may be included on a case-by-case basis after review by the reference committee. The rationale for inclusion of an abstract will be documented within the protocol. For example, an abstract could be used prior to the final results of a long-awaited phase 3 randomised controlled trial (RCT) and where study design, long term follow up, tumour response, toxicity and overall survival data is available e.g. an interim protocol - see section 8.4.

The process used to inform evidence involves 5 main steps (Figure 3):



10. Protocol review/update

The currency of the eviQ protocols is maintained according to a review schedule with appropriate intervals. Each protocol is stratified into one of three review groups; yearly (1 year), biennial (2 year) or quinquennial (5 year) review.

A protocol may be reviewed prior to a scheduled review if new evidence or information is identified that is considered relevant to be included. Example: safety concerns, new data from published studies indicating a change in evidence, or changes in the regulatory status of certain drugs within the protocol.

10.1. Protocol stratification

Protocols are stratified into three groups according the following criteria:

Group 1: Annual review *

Protocols that at the time of publishing, the committee felt the evidence supporting the protocol or its place in therapy may change i.e. newly registered drug with limited toxicity experience, limited evidence protocol, some uncertainty or controversy about relative effectiveness or a superior new treatment is expected to become available.

Group 2: 2-yearly Review *

Protocols in which there have been significant changes or updates in the literature and/or in clinical practice. Includes protocols with, new evidence, an expansion of patient population through changes to the PBS/TGA or safety alerts.

Group 3: 5-yearly Review*

Only current published protocols can be assigned a 5 yearly review date. These include protocols in which there have been no changes or updates in the literature or in clinical practice. For example, protocols that have been prescribed for many years where a dose change is unlikely or where the evidence is supported by systematic reviews without safety alerts.

The literature still needs to be reviewed for these protocols at 5 years as there may be:

- important changes in effectiveness, but not opposing findings that may translate to the protocol being superseded or discontinued OR
- a systematic review or meta-analysis that is confirmative of current supporting evidence. In such cases, a note will be added to the evidence section, but the original supporting evidence does NOT need to be re-written.

*Note that unscheduled updates/review may occur at any time if information becomes available indicating a review.

10.2. Review process: Internal and External

The review process maintains the currency and accuracy of the protocols.

The process is designed to:

- identify protocols that contain evidence that may have been invalidated by new evidence
- identify protocols that are no longer relevant and therefore do not need to be maintained i.e. supersede or discontinue protocols (see section 12)
- prioritise protocols/documents for a full review, if required

Internal review

eviQ content authors maintain the review schedule and work with the reference committee chairs to assess and prioritise the review process.

The wider reference committee group +/- additional experts if applicable, participate in an electronic review process, which may include an online survey, to gather the requisite information relevant to the review. eviQ content authors then collate and summarise the responses for the reference committee chairs. Protocols are triaged with review to be completed either electronically or through face-to-face discussion at a reference committee meeting.

eviQ content authors coordinate and provide:

- a summary of recommended potential changes e.g. drug status or new supporting document developed

- gathered evidence and link to protocol specific Literature search tab, which searches the PubMed database.

External review

Clinicians are expected to conduct their own comprehensive literature search (in addition to information provided by eviQ), to identify areas where new data/evidence have changed either the standard of care or the way in which existing data are interpreted or areas where there is variance in practice and notify eviQ if they believe evidence for a protocol needs to be updated/discussed.

In appraising the literature for validity and applicability, clinicians should consider the quality of the evidence and if it is applicable/generalisable to the Australian population. Also, what the potential impact will be and whether the existing evidence in the eviQ protocol needs to be updated.

Documentation of protocol review

The protocol history section will be modified to reflect changes (if any) and the review date amended accordingly. If consensus has reasoned that the protocol is to be superseded or discontinued the relevant flag/rationale will added to the protocol.

11. Protocol approval

Following the reference committee meeting, a summary of comments are formally documented and circulated to the chairs for approval, prior to dissemination to rest of the reference committee.

In finalising the protocol, eviQ content authors ensure that each point raised at the meeting has been addressed and any changes to the protocol as a result noted or, if no change is made, the reasons for this recorded. eviQ content authors will maintain an audit trail of all the changes.

Clinicians are required to submit a formal sign off on protocols (Appendix H), which can occur on the day of the reference committee or by email after the meeting. Sign off articulates that consensus has been reached amongst the committee and that the protocol has been developed following a thorough consideration of the best available evidence and clinical experience.

If sign off cannot be achieved in a timely manner, then it is the responsibility of the chair to negotiate sign off from other reference committee members.

12. Protocol status/categorisation

The protocol status is noted on each page e.g. under development, endorsed, under review, superseded and discontinued. Below is an explanation of each status:

Endorsed:

Protocol has been presented to and endorsed by the reference committee members and is published and available on the eviQ website.

Under review:

The protocol is being assessed for currency or a full update is in progress. The status of the protocol may change as a result.

If the decision has been made not to proceed with the development of a protocol, this information will be available on the "protocols not endorsed page" with one of the following rationale:

- Insufficient evidence
- Unacceptable toxicity
- Superior alternatives available
- Dose or treatment schedule not justified
- Patient population impossible to define
- No clinical need

From time to time it may be necessary to supersede or discontinue protocols. Proposals to supersede or discontinue a protocol are discussed at relevant reference committee meetings. Once consensus has been reached, all changes are made and rationale for the decision noted in the protocol and reference to any alternative sources of advice.

Superseded:

- Following discussion and consensus at a reference committee meeting, a protocol may be superseded if there is evidence demonstrating other treatment options to be superior.
- 'SUPERSEDED' appears in the protocol title and the reason for superseding appears at the top of the protocol. All protocol information is still available, as they may still be appropriate for use in certain populations and certain clinical scenarios.

Discontinued:

- When a protocol is no longer in regular clinical use, deemed less efficacious or excessively toxic than alternative treatments, it may be discontinued following discussion and consensus decision by the relevant eviQ reference committee.
- 'DISCONTINUED' will appear in the title of the protocol and an **abbreviated version** with only the rationale for discontinuation noted, the treatment schedule

and references being available. All previous protocol versions shall be maintained by eviQ and are available on request.

12.1. Protocol version

A protocol version number increases when a notable change to a protocol section is carried out that affects clinical practice. e.g.:

- update to the evidence
- expansion of the indication/patient population
- change to the treatment schedule i.e. the way the treatment is prescribed or administered or; **a change to a dose of an antineoplastic drug constitutes a new protocol**
- updated or additional information added to Clinical Information section e.g. update in the management of immune related adverse events; or update recommended blood tests

Instances that do NOT constitute a new protocol version include:

- refreshing a protocol to ensure that it remains in line with current editorial standards (e.g. updating or fixing broken links, formatting or fixing spelling errors)
- updates to enhance clarity or eliminate ambiguity (generally addressing user feedback)
- when changes are made reflecting a modification in the availability/status of a drug e.g. from TGA approved only to PBS reimbursed.
- if a protocol has been reviewed in-line with its review cycle and no changes or updates were made; a note will be made in the History section of the protocol that review occurred, but no changes required.

Details of all changes and updates are noted in the protocol's history section.

13. Protocol publication

Once external sign off has been received, as a final quality control check, the protocol undergoes internal sign off i.e. editorial review. Once completed, the protocol is published and made freely available on the eviQ website.

The final protocol is the result of detailed scrutiny, collaboration and revision by the entire reference group and not attributed to eviQ or an individual clinician.

13.1 Notification of content updates

eviQ notifies its users of newly published content (as a result of new development or review) in a number of ways:

- The History section of each protocol or document on eviQ details the changes made throughout the lifespan of the protocol. This section can be accessed via the

History icon available at the top right of each protocol or document.

- Each content area landing page accessed by clicking on the content area in the main menu i.e. haematology and BMT; medical oncology, radiation oncology and clinical resources; automatically lists all protocols that have been recently added, recently updated or recently superseded/discontinued within the past 90 days.

- Users may subscribe to receive monthly email updates for each content area that they choose. These email updates list all protocols, patient information and other documents relevant to the content area that have been newly published or recently reviewed in additional to information about site-wide content updates and changes.

- eviQ is currently working on additional options to further enhance its notification of content changes to its users.

14. eviQ protocol data into electronic systems

eviQ protocol data is routinely utilised within electronic systems used in Australian cancer centres. For any information on the use of eviQ protocols within these electronic systems please contact the eviQ team.

When labelling a treatment protocol in an electronic system with an eviQ unique ID, the protocol's antineoplastic drugs and doses, the days they are administered, and the number of cycles must match that of the eviQ protocol**.**

The supportive medication including antiemetics and premedications are NOT included in this match as there are a range of different medications within each class that are appropriate, and each facility will vary as to what they use. The supportive medication within an eviQ protocols are defaults only, as stated within the disclaimer at the top of the treatment schedule in eviQ protocol.

eviQ currently provides an XML file format for most of its medical oncology and haematology treatment protocols to facilitate upload into electronic systems. Access is available by request.

15. References

eviQ would like to acknowledge the benefit gained from the websites of recognised guideline development groups, for example, National Institute for Clinical Excellence (NICE), Scottish Intercollegiate Guideline Network (SIGN), the National Comprehensive Cancer Network (NCCN), and the American Society of Clinical Oncology (ASCO), in the development of this document.

1. National Comprehensive Cancer Network (NCCN) Development and Update of the NCCN Guidelines® https://www.nccn.org/professionals/development.aspx
2. Inquiry under section 122 of the Health Services Act 1997. Off-protocol prescribing of chemotherapy for head and neck cancers. Final report 31 July 2016 http://www.health.nsw.gov.au/patients/cancertreatment/Documents/section-122-final-report.pdf
3. National Institute for Health and Care Excellence - Developing NICE guidelines: the manual [PMG20] 31 October 2014
4. https://www.nice.org.uk/process/pmg20/chapter/introduction
5. Scottish Intercollegiate Guidelines Network. SIGN 50: A guideline developer's handbook. Edinburgh: Scottish Intercollegiate Guidelines Network; 2008 (Revised edition 2019) [cited 2009 Jul 29]. Available from: http://www.sign.ac.uk/media/2038/sign50_2019.pdf
6. Cancer Care Ontario (CCO), The Program in Evidence-based Care (PEBC) Handbook 2012 https://www.cancercareontario.ca/sites/ccocancercare/files/assets/CCOPEBCHandbook.pdf
7. The American Society of Clinical Oncology (ASCO) Guideline Procedures Manual - Guideline Development Process 2018 https://old-prod.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/2021-Guidelines-Methodology-Manual.pdf

16. Appendices

Appendix A - eviQ cancer genetics reference committee eligibility criteria

These criteria are in place to ensure diverse and national representation of healthcare experts working in the field of cancer genetics. These criteria apply to 1 May 2022 and will be reviewed at that time.

eviQ cancer genetics reference committee (RC) members are expected to attend at least one virtual meeting per year **AND/OR** to actively participate in eviQ cancer genetics document review and/or development.

As paediatric cancer genetics is a subspecialty, exceptions to these eligibility rules may be made when considering membership of the eviQ cancer genetics paediatric RC at the discretion of that committee's chair and co-chair.

Genetic counsellors

To be eligible to join the eviQ cancer genetics RC, genetic counsellors must:

- Possess FHGSA Certification in genetic counselling AND be registered with the HGSA AND have a minimum of two (2) years full-time equivalent (FTE) experience working as a genetic counsellor where a substantial component of work done is cancer genetics OR
- Possess FHGSA Certification in genetic counselling AND be registered with the HGSA AND have a minimum of one (1) year FTE experience working as a genetic counsellor where a substantial component of work done is cancer genetics WITH a reference from their Head of Department OR
- Possess MHGSA in genetic counselling AND be Provisionally Registered with the HGSA AND have a minimum of five (5) years' FTE experience working as a genetic counsellor where a substantial component of work done is cancer genetics WITH a reference from their Head of Department OR
- Provide evidence of other genetics or cancer genetics experience deemed suitable at the discretion of the eviQ cancer genetics RC chair and co-chair (including but not limited to overseas-qualified genetic counsellors with appropriate experience working as a cancer genetic counsellor, genetic counsellor working in Australia or New Zealand with substantial evidence of cancer genetics research, including PhD).

Geneticists/other specialists/medical

To be eligible to join the eviQ cancer genetics RC, medically qualified individuals must:

- Have six (6) months' FTE advanced training in cancer genetics OR
- Have 12 months' FTE advanced training in medical oncology OR

- Have completed FRACP or FRACS in a relevant specialty at the discretion of the eviQ cancer genetics RC chair and co-chair OR
- Provide evidence of other genetics or cancer genetics experience deemed suitable at the discretion of the eviQ cancer genetics RC chair and co-chair (including but not limited to substantial evidence of cancer genetics research).

Cancer genetics researchers

To be eligible to join the eviQ cancer genetics RC, researchers must provide evidence of cancer genetics experience deemed suitable at the discretion of the eviQ cancer genetics RC chair and co-chair (including but not limited to substantial evidence of cancer genetics research).

Non-member observers

At the discretion of the eviQ cancer genetics RC chair and co-chair, an individual not eligible for membership of the eviQ cancer genetics RC may be granted permission to attend via teleconference one (1) reference committee meeting as an observer.

Individuals applying to observe an eviQ cancer genetics RC must provide in writing details of:

- Their cancer genetics experience AND
- Their reason for applying to observe the RC AND
- Their current position AND
- A reference from their Head of Department OR an introduction from a member of their service who is a current or past member of the eviQ cancer genetics RC.

Where an individual's application to observe an eviQ cancer genetics RC is approved, the non- member must be referred to eviQ to provide registration details for governance-required agreement to the code of conduct and terms of reference and to declare any potential conflict(s) of interest.

Non-reference committee members' expert input into eviQ documents

Where an eviQ cancer genetics RC member engages an expert non-member to provide input into eviQ content, the non-member expert must be referred to eviQ to provide registration details for governance-required agreement to the code of conduct and terms of reference and to declare any potential conflict(s) of interest.

Appendix B - eviQ paediatric cancer genetics scope

The eviQ paediatric cancer genetics reference committee ('paediatric CG RC') is a subcommittee of the eviQ cancer genetics reference committee ('main CG RC').

Protocol development
The paediatric CG RC will develop and maintain **risk management and genetic testing protocols** for paediatric populations (age less than 18 years).

Protocol development **inclusion criteria**:

- gene pathogenic variants for which there is no adult phenotype OR
- where the paediatric phenotype is distinct from the adult phenotype

Protocol development **potential inclusion criteria** (considered on a case by case bases):

- syndromic/dysmorphic paediatric onset disorders where the dominant feature of the phenotype is predisposition to malignant neoplasms.

Protocol development **exclusion criteria**:

- gene pathogenic variants that have a paediatric phenotype which IS NOT distinct from the adult phenotype (these protocols will be reviewed by the main CG RC)
- treatment-related documents/protocols
- syndromic/dysmorphic paediatric onset disorders where the dominant features of the phenotype are non-cancer features, and/or the absolute risk of cancer is small, and/or there is insufficient data to develop evidence-based cancer management guidelines

Other document development and review
The paediatric CG RC may develop and review, at times with the main CG RC, other documents deemed to be useful to paediatric cancer genetics clinicians and that fall within eviQ governance criteria.

Membership
Membership will be open to the members of the main CG RC, as well as clinicians who have an interest and expertise in paediatric cancer, cancer genetics and specific paediatric syndromes.

Terms of Reference and Code of Conduct
Members of the paediatric CG RC will abide by the eviQ Terms of Reference and Code of Conduct.

Chair and Co-chair
Paediatric CG RC chair and co-chairs will be appointed and serve two-year terms per the eviQ Terms of Reference.

Appendix C - eviQ compliance with TGA/PBS listing for drugs

This document is to be read in conjunction with the Flow Diagram for eviQ compliance with TGA registration and PBS listing for drugs. Together they explain eviQ's process for inclusion of drugs on the eviQ website.

eviQ provides evidence-based, best practice cancer treatment protocols and works within the bounds of the Commonwealth of Australia's regulatory and reimbursement process for drug marketing (TGA) and subsidy (PBS). A drug must be PBS listed and/or TGA registered for a particular indication in order for it to be included on the eviQ website for that particular indication.

The Therapeutics Goods Administration (TGA) is the government body responsible for registering a drug for a specific indication, formulation and route of administration, for sale in Australia at a point in time. The registered indications are described in the product information of the drug. The TGA is unable to change the product information as this document is the legal property of the pharmaceutical company or drug sponsor. Changes in the product information can only be made at the request of the drug sponsor. For this reason, the TGA registered indication for many older drugs may no longer be wholly valid in the context of clinical practice. Once a drug is registered it may be prescribed, however no government subsidy will be provided until it has been recommended for subsidy by the PBAC and the Health Minister has added it to the pharmaceutical schedule.

The Pharmaceutical Benefits Advisory Committee (PBAC) is an independent expert body comprising of clinicians, health economists and pharmacists. It has a statutory role to decide whether to recommend listing of a drug and the circumstances of listing. It has a statutory requirement under Section 101 (3A) of the National Health Act 1953 to consider comparative effectiveness and cost of therapy. The PBAC can only consider a drug for government funding provided the proposed restriction, dose and formulation falls within the TGA registered indications. In making recommendations the PBAC necessarily interprets the initial TGA registered indications and in doing so the restrictions sometimes provide subsidy for drugs to a broader group of patients than encompassed within the initial TGA registered indications. The PBAC cannot directly contradict a statement made by the TGA registered indication of a drug (e.g. if initial TGA registration says drug A must not be used for XXXX, the PBAC cannot go against this).

The PBS listed indication is always the most up-to-date version of the restrictions as the TGA registered indication for a drug is rarely, if ever updated.

The Pharmaceutical Benefits Schedule (PBS)

Drugs listed on the Pharmaceutical Benefits Schedule (PBS) fall into three broad categories of Section 85:

- **Unrestricted benefits** - have no restrictions on their therapeutic uses
- **Restricted benefits** - can only be prescribed for specific therapeutic uses (noted as restricted benefit)
- **Authority required benefits** – The PBAC has decided, based on current evidence, the drug will only be subsidised if prescriptions comply with the listed restrictions. These restrictions are based on matters of efficacy, safety, and economic analyses.

In addition to the drugs listed under the normal PBS arrangements, a number of drugs are also available as pharmaceutical benefits but are distributed under alternative arrangements via Section 100. These drugs are accessed through a hospital and a S100 form must be completed. Supply of drugs through S100 does not attract a patient co-payment whereas supply under Section 85 attracts a patient co-payment.

TGA registered drugs, if accepted for PBS subsidy, will usually enter the PBS as an authority item.

Drugs listed as Authority Required Benefits will only be subsidised if prescriptions comply with the listed restrictions. Then, as time passes, allowing for more experience with the drug (and expiration of the patent), the drug may be reclassified as a restricted benefit, often coinciding with its use in a broader group of patients. The restrictions may remain listed on the PBS as a guide for the prescriber however restrictions may not be updated as evidence broadens the accepted use of a drug. This process ensures that PBS listings of drugs more closely reflect contemporary practice rather than outdated information contained in the product information. This is true for many older drugs:

Example 1:

Idarubicin is currently listed on the PBS in the Restricted Benefits category, with the restriction listed as acute myelogenous leukaemia. There is now good evidence for its use in multiple myeloma, in the CID protocol. The restriction is a guide and so for the purposes of eviQ, idarubicin may be included on eviQ as the drug is in practice prescribed and reimbursed on the PBS for multiple myeloma.

Example 2:

Dexamethasone is an old drug, registered many years ago. The original TGA registered indication does not include it as an antiemetic. Dexamethasone is listed on the PBS as an Unrestricted Benefit and therefore may be used for whichever therapeutic use deemed appropriate by the prescriber. There is sufficient evidence to show dexamethasone is an effective antiemetic, and therefore it may be prescribed as such and reimbursed via the PBS.

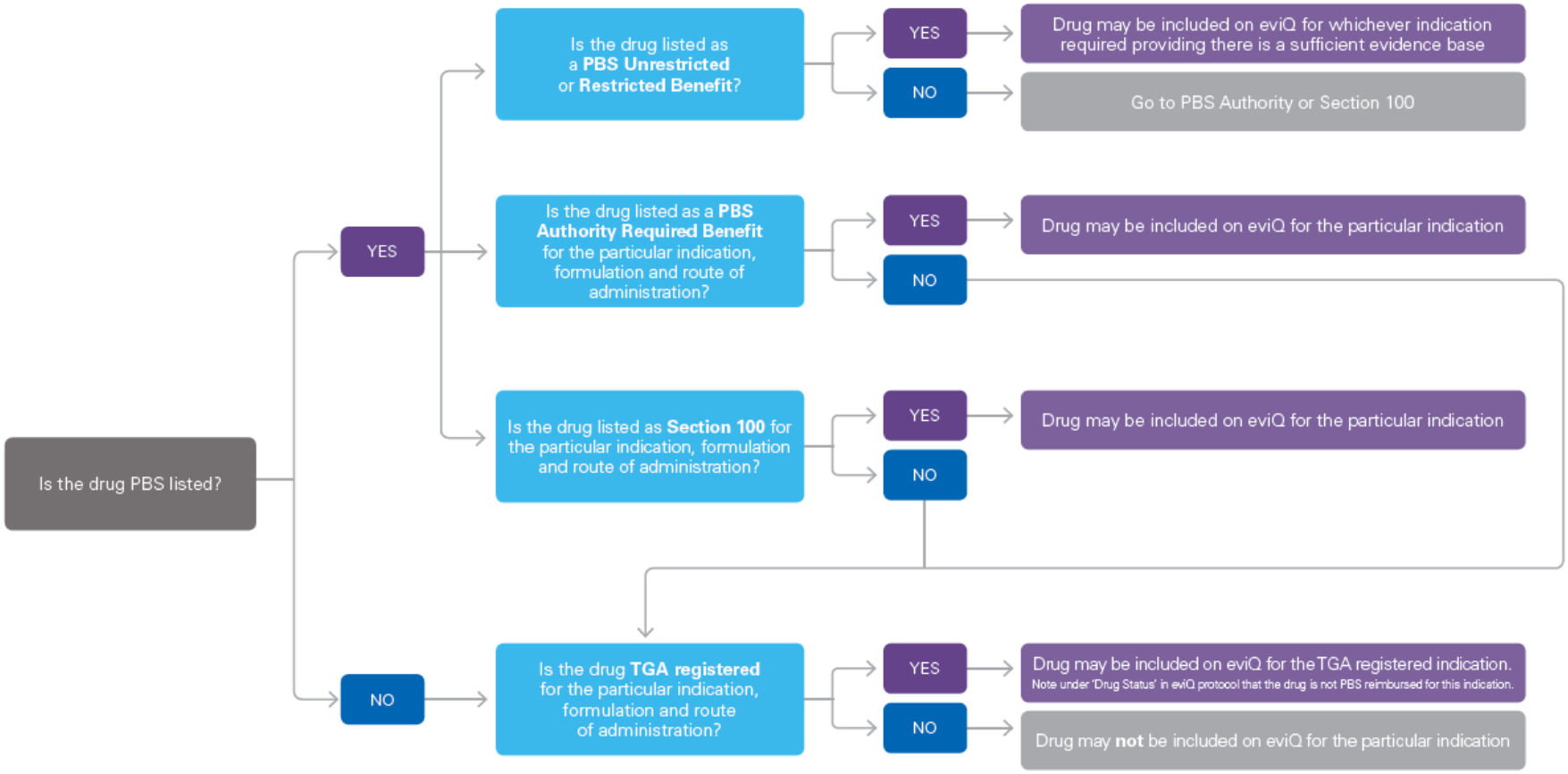
References:

- The Schedule of Pharmaceutical Benefits (PBS), Department of Health and Ageing, Australian Government, accessed 20 December 2010 https://www.pbs.gov.au/pbs/home
- Pharmaceutical Benefits Advisory Committee (PBAC), Department of Health and Ageing, Australian Government, accessed 20 December 2010 <http://www.health.gov.au/internet/main/publishing/nsf/
- Therapeutics Goods Administration (TGA), Department of Health and Ageing, Australian Government, accessed 20 December 2010 http://www.tga.gov.au/

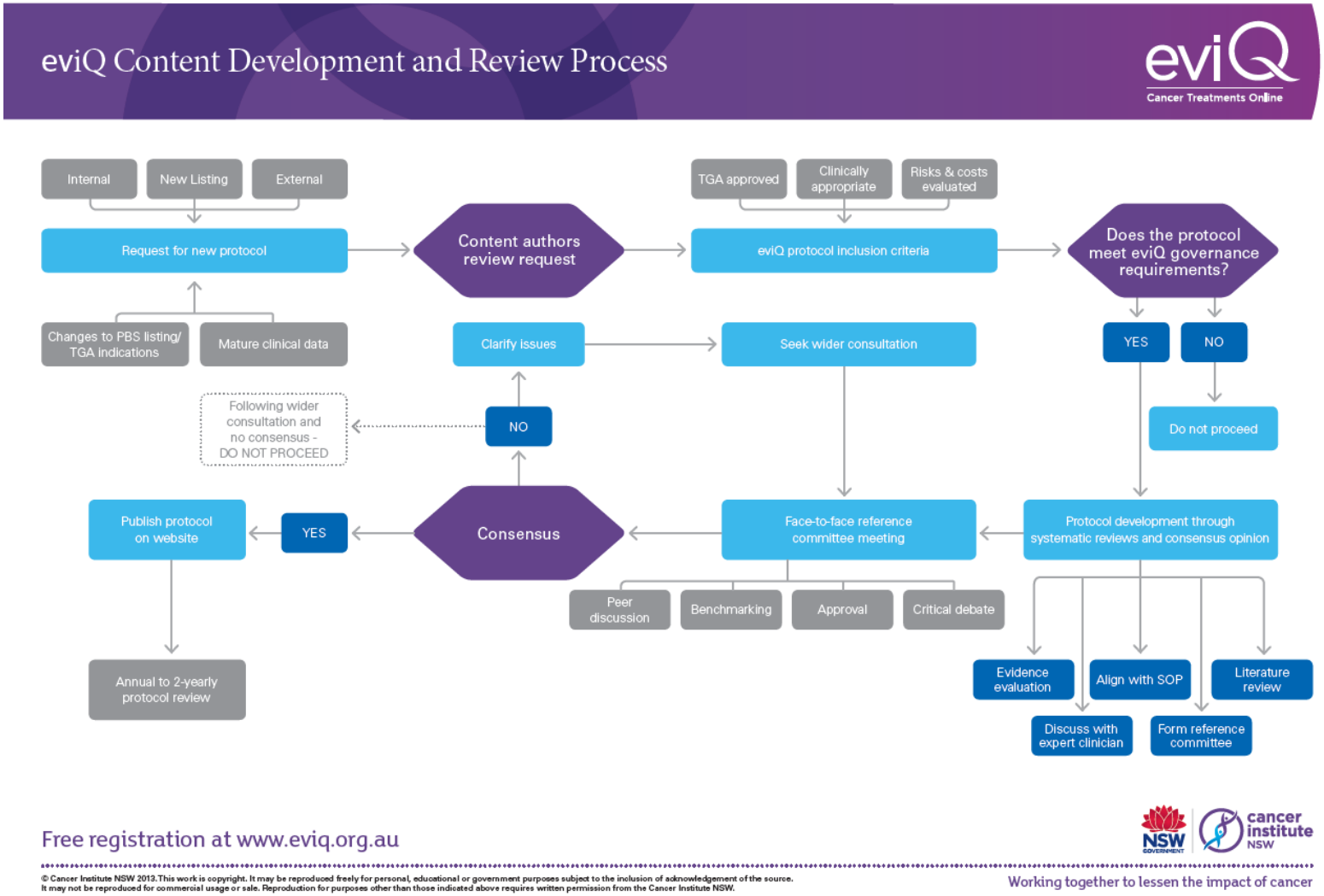
eviQ compliance with TGA registration and PBS listing for drugs

This process excludes the access of unapproved drugs via the Special Access Scheme (SAS). Further information about this process including application forms is available at: www.tga.gov.au/hp/access-sas.htm

eviQ Cancer Treatments Online



Appendix D - eviQ content development and review process



Appendix E - NHMRC evidence hierarchy table

NHMRC Evidence Hierarchy: designations of 'levels of evidence' according to type of research question

Level	Intervention [1]	Diagnostic accuracy [2]	Prognosis	Aetiology [3]	Screening Intervention
I [4]	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among consecutive persons with a defined clinical presentation[6]	A prospective cohort study[7]	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among non-consecutive persons with a	All or none[8]	All or none[8]	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)

Level	Intervention [1]	Diagnostic accuracy [2]	Prognosis	Aetiology [3]	Screening Intervention
		defined clinical presentation[6]			
III-2	A comparative study with concurrent controls: • Non-randomised, experimental trial[9] • Cohort study • Case-control study • Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: • Non-randomised, experimental trial • Cohort study • Case-control study
III-3	A comparative study without concurrent controls: • Historical control study • Two or more single arm study[10] • Interrupted time series without a parallel control group	Diagnostic case-control study[6]	A retrospective cohort study	A case-control study	A comparative study with concurrent controls: • Historical control study • Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)[11]	Case series, or cohort study of persons at different stages of disease	A cross-sectional study or case series	Case series

For explanatory notes, as referenced in above table (superscript 1 to 11) please refer to NHMRC: https://www.nhmrc.gov.au/sites/default/files/images/NHMRC%20Levels%20and%20Grades%20(2009).pdf Source: Hierarchies adapted and modified from: NHMRC 1999; Bandolier 1999; Lijmer et al. 1999; Phillips et al. 2001.

Appendix F - Standard evidence template

Evidence

The evidence supporting this protocol is provided by a phase XX multicentre international randomised trial (XXX) involving [n] patients comparing XXX with XXX alone in patients with Stage XXX and YY [insert site] cancer.

Between XXX and XXX, [n] patients were randomised to receive XXX (include drugs, dose and frequency, no. of cycles etc.) and [n] patients were randomised to receive XXX (include drugs, dose and frequency, no. of cycles etc.)

The primary end point was XXX and secondary end points were XXX

Provide a summary statement of the comparative effectiveness

Efficacy

After a median follow up of XXX, the median [OS] was XXX in XXX vs XXX in XXX group (HR=X; CI 95% X to X ; p=X).

Insert a tabulated and/or graphical summary of the efficacy results including: overall survival, disease free survival, time to progression, complete or partial remission rates as appropriate.

The presentation of Kaplan-Meier survival curves is appropriate. These curves should include numbers of patients at risk at various time points. Where results are available from more than one trial, consideration should be given to the graphical presentation of results e.g. forest plots.

Present efficacy results for relevant sub-groups if these are relevant to clinical prescribing (i.e. it coincides with PBS/TGA restrictions or it has significant differences in risk/benefit profiles) (In this case, include only a brief sentence relating to the overall results).

State whether quality of life (QOL) data was collected in the key evidence. If it is present, assess the robustness of the results, and summarise this in a sentence (e.g. QOL data was collected but was unreliable since only 20% of patients completed the questionnaires, or, it did not capture the patient relevant factors etc.). If the QOL results are useful, then summarise them, emphasising particularly their relation to adverse events, rather than disease effects. (E.g. QOL data was collected on 40% of patients. Despite the unfavourable adverse event profile of the drug, global functioning scores were unchanged.)

Toxicity

Provide a tabulated summary of the safety results. Include the following if available: number of deaths, number of patients discontinuing treatment due to adverse events,

grade 3 & 4 toxicities. If no mention is made of comparative toxicities in the reference, a note should be made of this.

Appendix G - Limited evidence template

Steps:

- Search the literature for any phase II studies, case series and observational studies
- Check if protocol is available on NCCN, BCCA and CCO guidelines
- List all the studies found and choose top 2-5 at RC meeting and summarise search results as per headings in the table below

Text to include:

A search of the literature did not find strong evidence to support the use of XXX in the treatment of XXX cancer. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by [phase II/observational study/CCO guideline/expert opinion-should be explicit].

(If the protocol is an old one e.g. Cisplatin/VP16 but the indication is new then state)

"The protocol has been used extensively for the treatment of "

Source	**Study & Year Published**	**Supports Use Yes/No/NA**	**Is the dose and regimen consistent with the protocol?** Yes/No	**Comments**
Phase II trials		Yes	No.	
Case series	-	NA		
Observational studies	-	NA		
Guidelines	**Date published/revised**	**Supports Use** Yes/No/NA	**Is the dose and regimen consistent with the protocol?**	
NCCN	-	Yes	Yes.	
BCCA	-	NA	-	
CCO	v.2 2009	No	-	

Efficacy

Steps:

- Pick the best efficacy results from all the studies identified in the evidence section. Different studies can be listed for each efficacy result, i.e. 1 study may have the best OS and another may have a better PFS.
- Control arm (where relevant): Include what the control was for that particular study, including BSC.
- Effect (where relevant): Include in this column one of the following - HR, 95% CI, p-value, not reported

Text to include:

A summary of the evidence supporting the effect of this protocol is below:

Outcome	Study	No. of patients	Control arm	Effect
Overall survival	Mitry et al	53	2 (BSC)	HR 077
Median survival				Not reported
Progression free survival				
Response rate (partial)				

Toxicity

Steps:

- If there is more than one study available, choose the study that has toxicity data most representative of this treatment and patient group.
- Pick out the two most clinically significant toxicities and list them. This is required because the toxicity data may not be indicative of the most clinically significant toxicities as study numbers are generally small and thus data may be skewed. State this in the toxicity section if appropriate.
- Importance for prescribing: Given that toxicity gradings may not be available, this column gives an idea of how influential the toxicity (or lack of it) is for pushing prescribing. Options to use : critical/important/not important

Text to include:

A summary of the toxicities associated with this protocol are included in the table below. The most clinically significant toxicities for this treatment are [toxicity 1] and [toxicity 2].

Toxicity	Study	Incidence of event	Importance for prescribing

Nausea	Mitry et al	3/50	Critical/Important/Not important
Diarrhoea			

References

Appendix H - Clinician sign off

Protocol Name: (add in protocol title and direct hyperlink)			ID:
Section of Protocol	**Check**	**Approve YES/NO**	**Comment**
Treatment Schedule Summary			
Indications			
Clinical Information			
Dose modifications			
Evidence/References			
Clinician Name (on behalf of reference committee):			
Date:			