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eviQ compliance with TGA registration and 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's Program Governance document*** should also be read to provide further context.
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 (Therapeutic Goods Administration (TGA)) and subsidy (Pharmaceutical Benefits Schedule (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.

Rationale for eviQ's compliance with TGA registration and PBS listing for drugs

eviQ does not have the authority, expertise or resources to decide whether a drug meets the safety and efficacy standards for use and marketing for a particular indication in Australia. This is the role of the TGA. Thus, the TGA registration for a drug is set as the threshold for a drug's inclusion on eviQ.

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. TGA registration is defined as drug's inclusion on the Australian Register of Therapeutic Goods (ARTG). 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 (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.

Non-TGA registered drugs and non-TGA registered indications on eviQ

The conditions discussed below do not apply to drugs which are listed on the PBS Unrestricted Benefits category. These are covered above.

On occasion eviQ will consider inclusion of a drug for an indication that it is not registered with the TGA i.e. off-label indications, or a drug that is not registered at all with the TGA. These are exceptional circumstances and there must be clear and compelling reasons to include a drug for a non-TGA registered indication on eviQ. These situations are generally related to older, off-patent drugs where there is little incentive for the pharmaceutical company or drug sponsor to update the product information, make a submission for an additional indication or sponsor the drug for marketing in Australia at all.

The following criteria are necessary but not sufficient for publishing a non-TGA registered drug on eviQ:

- it is registered for this indication by other jurisdictions including both EMA and FDA
  and
- it is recognised as standard of care internationally and supported by evidence of efficacy and safety
  and
- where safe prescribing is compromised by the paucity of publicly available information
  and
- where non-expert health professionals require a reference source to understand dosing, toxicities
  and
- no registered or PBS listed alternatives are available.

If the above criteria are met, eviQ will embark on best endeavours to contact the pharmaceutical companies, the TGA and the PBAC (and cc any other relevant organisations e.g. MOGA, Rare Cancers Australia) requesting commentary on the reasons for not registering the drug in Australia, any information about safety concerns (even if not in the public domain), and any other information relevant to a consideration for publishing a protocol containing this drug. Experts familiar with use of the particular drug will also be consulted.

After due consideration of the above criteria, the response from the authorities and sponsors and additional factors (such as the cost of the medicine), a decision will be made as to whether to publish the drug.

eviQ reserves the right to not include a drug even if it fulfils all the criteria. The final decision to include a drug for a non-TGA registered indication on eviQ is at the discretion of the eviQ Scientific Director.

Should publication proceed, protocols on eviQ that include drugs for non-TGA registered indications will include a ‘flag’ at the top of the protocol clearly stating the rationale for inclusion, that the potential liability is increased when prescribing off-label and that this liability lies with the prescriber.

Example 1:
Mitotane is an older drug and is not registered for use in any indication in Australia. Mitotane is an established drug used in the management of adreno-cortical carcinoma for decades and is registered for this indication by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

Metastatic adreno-cortical carcinoma is a rare cancer and patients are disadvantaged because mitotane is not registered for use in Australia. As a result of not being registered in Australia, mitotane is not widely available and there is a safety risk due limited availability of information on dosing, monitoring and toxicities plus required supportive treatments. Experts are aware of how to safely and effectively use this drug, but other health professionals involved in these patients' care may not be familiar and require easy access to Australian resources.

While mitotane is available via Special Access Scheme (SAS) or via the Authorised Prescriber Scheme in Australia, the above issues are not addressed by this mode of supply. Therefore, including a protocol and administration information on eviQ for mitotane is important for patient safety.

eviQ formally wrote to the TGA notifying them of these issues and requesting a company to supply and support the conditions of registration be sought out.

Access to drugs that are not TGA registered in Australia
This paragraph is provided for context and is not part of the eviQ policy.
Unapproved drugs may be accessed in Australia via the Special Access Scheme (SAS) or via the Authorised Prescriber Scheme.
The Special Access Scheme allows certain prescribers to access unapproved drugs for a single patient on a case-by-case basis.
The Authorised Prescriber Scheme allows authorised prescribers to access unapproved drugs for a class of patients with a particular medical condition. In July 2020, the TGA streamlined the application process for drugs considered to have an established history of use. Drugs on the List of medicines with an established history of use according to subregulation 12B(1B), do not require Human Research Ethics Committee (HREC) approval or specialist college endorsement.

References:

• The Pharmaceutical Benefits Scheme (PBS), Australian Government Department of Health accessed 1 June 2021 <https://www.pbs.gov.au/pbs/home>
• Pharmaceutical Benefits Advisory Committee (PBAC), Australian Government Department of Health accessed 1 June 2021 <https://pbac.pbs.gov.au/home.html>
• Therapeutics Goods Administration (TGA), Australian Government Department of Health, accessed 1 June 2021 <https://www.tga.gov.au/>

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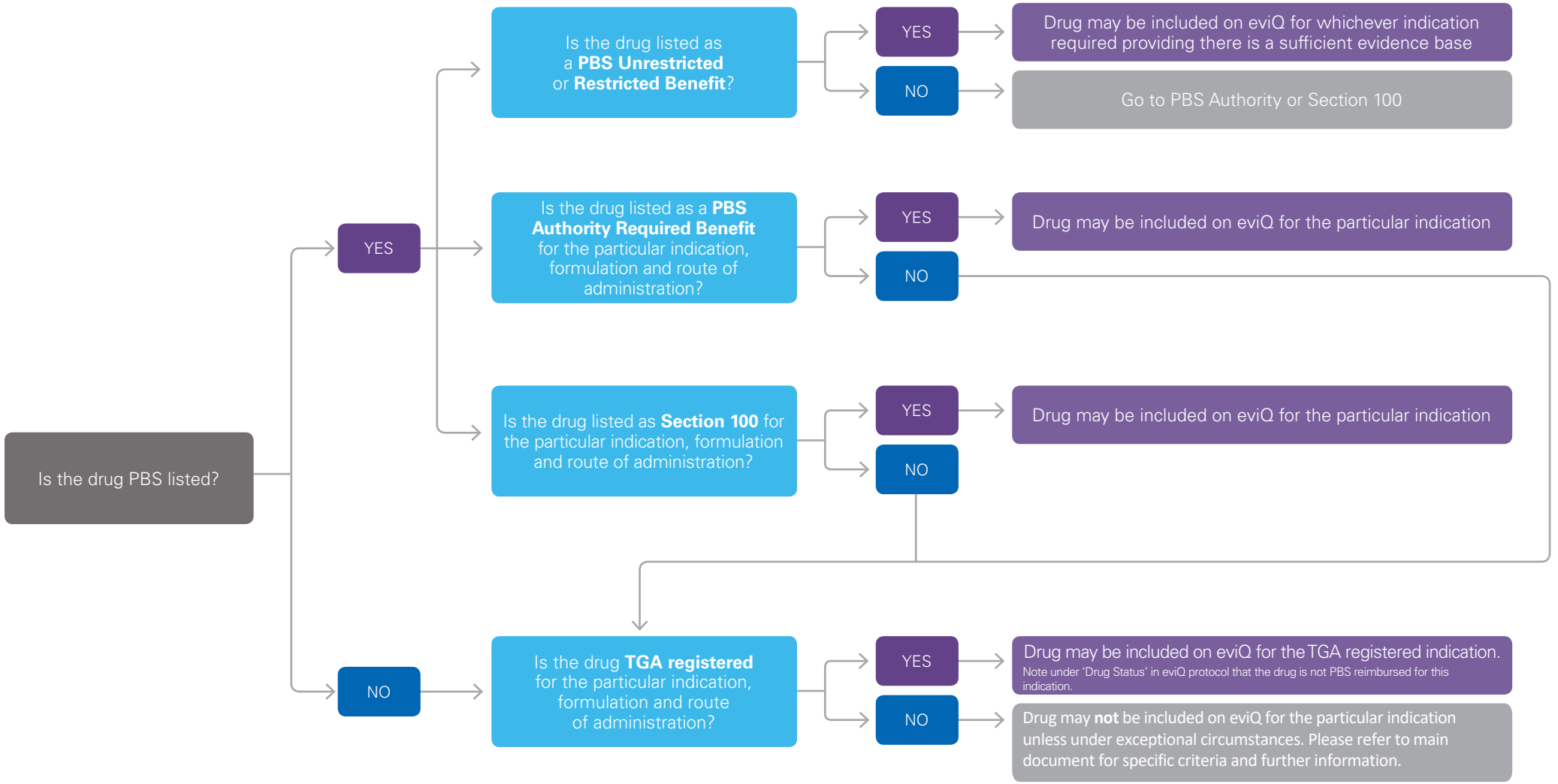
This process excludes the access of unapproved drugs via the Special Access Scheme (SAS) or Authorised Prescriber Scheme. Further information about these processes is available at: https://www.tga.gov.au/accessing-unapproved-products



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