Technical Alert

IMPORTANT REMINDER: Permitted Indications - Transition period ends 5 March 2021

- **The last day that sponsors will have to submit their application to re-list their medicine with permitted indications is 5 March 2021.**
- **Changes to indications only are free until 5 March 2021 and any products that do not have updated records by this date *will be cancelled from the ARTG and sponsors will no longer be able to supply these medicines*.**

→ **There will not be any letters proposing to cancel the listing issued prior to the cancellation.**

→ **Any cancellations that occur are not associated with any appeal rights.**

→ **Cancelled products that sponsors desire to retain would therefore need to be re-listed as new products.**

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Permitted Indications - Transition period ends 5 March 2021

The end of the three-year phase in period to amend ARTG records to permissible indications is approaching. It is important for sponsors to update the ARTG entries of listed medicines before **5 March 2021**.

Listed medicines that have not been updated to include permitted indications will be **cancelled** and removed from the ARTG under transitional provisions in Part 2 of Schedule 2 to the *Therapeutic Goods Amendment (2017 Measures No.1) Act 2018* (the 2018 Amendment Act).

The TGA have advised that this cancellation process will be **automatic**, and there are no exemptions or extensions possible for listed medicines that have not transitioned to permitted indications, nor any appeal rights for cancelled listings. If sponsors do not have evidence of submitting their application to transition to permitted indications on or before **5 March 2021**, then the medicine is likely to be captured in the automatic cancellation process.

The TGA have advised that, as of 30 September 2020, approximately 2,500 (24%) medicines listed under section 26A of the Act (spanning 540 sponsors) did not have permitted indications included on their ARTG entry. This does not include medicine kits or 'Export only' medicines. These medicines, if not updated via a grouping application submitted through the listed medicine application portal, are expected to be cancelled after 5 March 2021.

The TGA have further identified more than 1,500 medicines where the ARTG entry has not been varied or updated since 2016 and believe that these medicines are more likely to have information that requires updating on the ARTG entry.

From commencement of the *Permissible Indications Determination*:

- There is no 'free-text field' for sponsors to enter their medicine indications when they apply to list their medicine in the ARTG using the Electronic Listing Facility.
- Sponsors who apply to list a new medicine will be required to select the indications for their medicine from the list of permitted indications.
- Sponsors can apply to have new indications considered for inclusion in the *Permissible Indication Determination*. The application form is available after logging in to your sponsor portal via the TGA Business Services website. An application fee applies.

Medicines that have not yet transitioned to permitted indications

The TGA are advising sponsors to transition their listed medicines at soon as possible. If sponsors wish to delay their transition to permitted indications until closer to the transition end date, they are encouraged to log into the TBS portal **now** to prepare and validate draft applications. This will assist sponsors in identifying whether any other regulatory changes have occurred, which may need to be addressed before a listed medicine can be transitioned to permitted indications.
Draft applications for listed medicines can remain in the portal for up to one year therefore, previously drafted applications may still exist in the portal. Further information on validating applications to change an ARTG entry can be found on Listed and assessed listed medicines: Application and submission user guide.

Considerations for sponsors when choosing permitted indications

The TGA webpage FAQs on issues raised by industry in relation to permitted indications provides information on some issues of key importance when deciding on the types of indications that can be used for a medicine. There are twenty-one questions addressed in total, and CMA recommends vested stakeholders read through the each of the detailed explanations. Questions related to multiple targets and to pregnancy medicines are highlighted below.

Q 4. What evidence do I need to hold to support indications that have multiple targets?

The TGA response indicates that where a permitted indication may contain more than one target, that sponsors do not need to use each of the targets and accordingly the evidence held needs to be relevant to the target(s) included on the presentation of the medicine.

Q5. How can I make my indication more specific?

Permitted indications can be made more specific using the qualifiers in the Code Tables and allows for aligning the evidence with a specific indication. This can be achieved directly by including in the listing the appropriate qualifier from the Code Tables, and that the meaning is consistent across ARTG, label and advertising materials. Or, the specificity can be implied in the overall presentation of the goods, for example, Men's multivitamin, providing the qualifier is permitted (is included in the Code Tables.)

Q 10. When do I need to use population qualifiers?

Consistent with question 5, where the evidence held relates to a specific population, if the evidence held for an indication relates to a specific population (not the general adult population), a qualifier is required to be linked to the indication, such that indication and evidence are aligned.

Q. 18 Why aren't 'population' and 'time of use' qualifiers available for pregnancy and foetuses?

The TGA maintain that indications related to pregnancy and foetal development, be limited to those prescribed indications in the Code Tables. The rationale provided is that pregnant women are a "vulnerable population group who may be susceptible to being persuaded that a medicine imperative for the optimal health of their unborn child."

Q. 19 Can I use product names that refer to pregnancy?

The FAQ states that if the overall presentation of a medicine, including its name, states or implies pregnancy, it will be inferred that any indication included on the product label or in advertising materials will be considered to be indicated in that population. Accordingly, any representations/indications for use, must be aligned with the existing indications for pregnancy and foetal development.

Q 20. Can I combine indications for pregnancy/foetal development with other permitted indications?

The FAQ response discourages combining other indications with pregnancy and foetal development indications, as collectively they have the probability of changing the intent or meaning of the permitted indication. However concurrent indications could be used on a label, separately, providing evidence is held to support each indication. However, the TGA cautions this practice as any indication

related to pregnancy and maternal health will limit the types of other indications that are permitted to be used alongside those indications.

For further information relating to pregnancy indications, we encourage sponsors to read the July 2020 CMA technical alert on Pregnancy Indications and Pregnancy Products.

Evidence requirements for permitted indications

At the time of listing a medicine in the ARTG, sponsors must certify that they hold evidence to support any indications and claims made about their medicine. Information on the types of evidence required to support scientific and traditional indications for listed medicines can be found in the Evidence guidelines: Guidelines on the evidence required to support indications for listed complementary medicines. There are four categories of permitted indications based on the type of evidence required to support their use:

Table 2 - Evidence requirements

Type of indication	Type of evidence
Scientific indications	Must be supported by scientific evidence, such as clinical studies or systematic reviews, for example: '*Help maintain/support bone mineralisation*'.
Traditional indications*	Must be supported by evidence of traditional use in a recognised paradigm outside modern conventional medicine. These include indications that can be used across different traditional paradigms, for example: '*Blood cleanser/purifier*'.
Traditional Chinese medicine indications	Must be supported by evidence of traditional use within traditional Chinese medicine (TCM). These indications use specific terminology used in TCM, for example: '*Traditionally used in Chinese medicine to disseminate Lung Qi*'.
Traditional Ayurvedic indication	Must be supported by evidence of traditional use within Ayurvedic medicine. These indications use specific terminology used in Ayurvedic medicine, for example: '*Traditionally used in Ayurvedic medicine to relieve aggravated Vata*'.

***** Sponsors should be aware of evidence requirements for using permitted indications. Of particular importance is the use of **traditional indications**, as The TGA announced in July 2020 that they will be initiating targeted compliance reviews of a selection of listed medicines that use traditional indications in the second half of 2020. The July 2020 CMA technical alert provides important information on the traditional indications review and provides a basic evidence self-assessment section which includes further key considerations for sponsors.

Applications to transition to permitted indications

In order to submit an application to transition to permitted indications, all aspects of the medicine will need to be up-to-date and comply with current requirements (even if this has changed since they listed), including (but not limited to):

- Formulation and ingredient details
- Manufacturer's details such as overseas GMP clearances

For assistance in transitioning listed medicines, sponsors can access specialised learning modules provided by the TGA designed to help sponsors to transition provided by the TGA, and available on TGA's website, under Guidance materials for permitted indications for listed medicines. A list of available permitted indications can be accessed via the *Permissible Indications Determination* (the Determination) or via the TGA Business Services (TBS) website.

Application Fees

Changes to indications before **5 March 2021 are free** however, where other changes are made at the same time the applicable variation fee will apply. Changes to indications after **5 March 2021** will be subject to standard listing application fees.

Variations to existing listings within the first 18 months of the transition period			
Type of change	**Fee payable**	**New ARTG number issued**	**Must transition to permitted indications**
New	Standard listing fee	Yes	Yes
Grouping (changes to indications only)	Nil	No	Yes
Variation	Standard variation fee only	No	No
Correction to ARTG record	Nil	No	No

What if a sponsor does not wish to transition a medicine to permitted indications?

If a sponsor does not wish to transition listed medicines to permitted indications, the ARTG entry for that medicine can be cancelled at any time **on or before 5 March 2021** through the TBS portal. Further information can be found on Request to cancel an ARTG entry.

Sponsors are encouraged to cancel all listed medicines that will not be transitioning to permitted indications **on or prior to 5 March 2021** which provides sponsors with the opportunity to control the narrative around the delisting process, as cancellations conducted by the TGA due to non-transitioned

medicines will mean that the medicine will no longer eligible for listing, and this information will be published on the TGA website (Cancellations from the ARTG).

TGA communication with sponsors in the lead up to the end transition date

The TGA have advised that they intend to communicate broadly through various channels and directly with sponsors in the lead up to the end transition date, using the primary 'organisation email address' listed in TGA's client database for these sponsors. Please ensure your organisation's details are updated in TBS to ensure you are receiving these important regulatory notices.

The organisation's TBS administrator can update the organisation's email address, see TGA Business Services: Questions and answers for administrators or an authorised representative can contact the TGA Business Services team for assistance at ebs@health.gov.au.

TGA communication in relation to the transition is expected to include:

During October and November 2020:

- An Update TGA's website
- Email directed to sponsors with medicines that have not transitioned from our Complementary Medicines inbox
- Addition of a reminder to the tagline on outgoing emails from Complementary Medicines inbox.
- TBS News Item
- Social media campaign

In January to February 2021:

- Email directed to sponsors with medicines that have not transitioned
- Publish a revised TBS News Item
- Continue social media campaign

Resources

- TGA web page Permitted Indications for Listed Medicines
- TGA Permitted indications for listed medicines guidance
- TGA Guidance materials for permitted indications for listed medicines
- Therapeutic Goods (Permissible Indications) Determination (No. 2) 2019
- TGA FAQ's on issues raised by industry in relation to permitted indications
- TGA TBS portal
- TGA Evidence guidelines: Guidelines on the evidence required to support indications for listed complementary medicines
- Request to cancel an ARTG entry.
- TGA Review of listed medicines with traditional indications

Permitted Indications Transition Timeline

2021 6 March

The transition period for existing listed medicines ends.

All listed medicines must only contain permitted indications. ARTG entries that have not transitioned to Permitted Indications will be cancelled.

2019 Dec

A new Therapeutic Goods (Permissible Indications) Determination (No. 2) 2019 commences and includes 8 new indications, as well as more restrictive changes to current indications, and some more permissive changes to existing indication requirements.

2019 Sep

The 'fee free' period for transitioning ARTG listings to permitted indications is formally extended for 18 months to 6 March 2021.

The initial 'fee-free' period for sponsors to transition existing listed products was set to end and applications to transition existing products would be required to pay listing application fee in accordance with the TGA's Schedule of fees and charges from this date. However, in response to CMA's advocacy, the fee free period for transitioning ARTG listings to permitted indications was formally extended for 18 months to **6 March 2021.**

2019 August

Changes to the Permitted Indications Determination

The TGA updates the Permissible Indications Determination to add 4 new indications and make minor changes/clarifications to 32 existing indications.

2019 Feb

Changes made to the Therapeutic Goods (Permissible Indications) Determination No. 1 of 2018 (the 2018 Determination).

Following the implementation of the 2018 Determination in March 2018, stakeholders identified issues that sponsors were having when selecting indications for their listed medicines. Based on stakeholder and subject matter expert feedback, the Determination was amended and renamed Therapeutic Goods (Permissible Indications) Determination No. 1 of 2019.

2018 March

Implementation of a list of permitted indications

The TGA implemented a list of permitted indications for medicines listed under section 26A of the *Therapeutic Goods Act 1989* (the Act), with a 3-year transition period, ending on the 5 March 2021.