Technical Alert

Released - Permissible Ingredients Determination (No 4) 2019

Upcoming permissible ingredients changes - March 2020-2021

The *Therapeutic Goods (Permissible Ingredients) Determination (No. 4) 2019* has been published on the Federal Register of Legislation, for commencement on **1 Jan 2020**. It repeals and replaces *the Therapeutic Goods (Permissible Ingredients) Determination (No. 3) 2019*.

Notable changes are to ***Andrographis paniculata*** (new warning statement due **2 May 2020**), and a relaxation of the new restrictions to ingredients containing **menthol** and **methyl salicylate**, which were already due 1 Jan 2020, but now only apply if the medicine contains over 1% of the substances.

March 2020-2021 Changes – announced but not yet in the Determination

In addition, the TGA have released the outcomes of the "low-negligible" risk changes to permissible ingredients. These will be legislated in a new version of the Determination in March 2020, with a 12 month transition period to March 2021.

Proposed changes to the March 2020 Permissible Ingredients Determination were consulted upon in the Changes to Permissible Ingredients – Low-negligible risk consultation, which closed on 11 October 2019. A record of reasons for decisions, and consultation submissions received, can be viewed on the TGA website. CMA's submission resulted in a number of reductions in impact, including shorter warning statements and less restrictive changes to the ingredients Boron and Withania. The following ingredients will be amended within the Permissible Ingredients Determination **commencing March 2020 with a 12 month transition period to 2 March 2021**:

- Boron
- *Withania somnifora*
- *Vitex agnus-castus,*
- *Isphagula spp*, *Plantago spp*, and Psyllium husk
- *Cymbopogon spp* and
- *Malus pumila*

The March 2020 updates to the Permissible Ingredients Determination, will also include changes to the requirements for

- Coumarin (in topical preparations)

The reason for this decision is based on safety and toxicity data.

NEW Permissible Ingredients Determination (No 4) 2019 commencing 1 Jan 2020

Andrographis paniculata

More restrictive requirements - [NOTE CHANGES DUE BY 2 May 2020*]

If your medicine includes the ingredient,

- *Andrographis paniculata*

Then your medicine will be subject to the following specific requirements:

WARNING STATEMENT

- **'Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) stop use and seek immediate medical attention' (or words to that effect).'**

The statement is introduced due to pharmacovigilance reports of episodes of anaphylaxis and allergic reaction. These requirements apply for any purpose of the ingredient, ie active, excipient, homeopathic.

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW listings must comply from the date of commencement **1 January 2020**

Labels of EXISTING listings have **until 2 May 2020** to update product labels with the new requirements.

*The Determination provides that existing medicines supplied from 2 May 2020 must have the new warning statement. The TGA website for this decision clarifies that it means 'released for supply'. A saved copy of the website is available here on the CMA webpage.

Menthol and herbs containing menthol

Less restrictive amendment to the more restrictive changes due 1 January 2020

If your medicine includes any of the ingredients:

Mentha aquatica

Mentha arvensis

Mentha arvensis leaf oil

Mentha arvensis oil

Mentha haplocalyx

Mentha pulegium

Mentha spicata

Mentha x cardiaca

Mentha x piperita

menthol

mint oil dementholised

peppermint american ext.

peppermint leaf dry

peppermint leaf powder

peppermint oil

peppermint oil terpeneless

peppermint oil terpenes and terpenoids

spearmint oil

spearmint oil terpeneless

Then you should know that there have been less restrictive changes made to warning statements for menthol and methyl salicylate at less than 1%.

In 2017, the TGA reviewed the safety of menthol, methyl salicylate, and subsequently amended the requirements for menthol, methyl salicylate, and related ingredients in the Determination. Following these changes the TGA received multiple requests for exemption from the warning statement requirements for menthol and methyl salicylate when included in low concentrations in topical PIs.

Following reconsideration of the available data and the risk of skin irritation when menthol is present in very low concentrations, the TGA have determined that the label warning statements below are **not required when menthol is present in a medicine in concentrations of 1% or less, such as in PIs.**

The following warning statements are still applicable and still due on 1 Jan 2020, but will only be required on the label of topical listed medicines when the concentration of **menthol** in the medicine **is greater than 1%:**

- **(IRRIT) 'If irritation develops, discontinue use' and**
- **(SKTEST) 'If you have sensitive skin, test this product on a small area of skin before applying it to a large area'**

These requirements apply for any purpose of the ingredient, ie active, excipient, homeopathic.

ALL OTHER REQUIREMENTS FOR METHOL REMAIN APPLICABLE.

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW listings must carry the warning statement from commencement of the new Determination, **1 January 2020**

Labels of EXISTING listings: As these changes are less restrictive there is no specific date by which labels must be updated.

For those products with **1% OR MORE OF MENTHOL** labels must be updated **by 1 January 2020.**

Methyl salicylate and herbs containing methyl salicylate

Less restrictive requirements – changes due 1 January 2020

If your medicine includes any of the ingredients:

Betula lenta

Betula nigra

Betula pendula

birch leaf dry

Filipendula ulmaria

Gaultheria procumbens

meadowsweet herb dry

methyl salicylate

Nyctanthes arbor-tristis

wintergreen oil

Then you should know that there have been less restrictive changes made to warning statements for menthol and methyl salicylate.

In 2017, the TGA reviewed the safety of menthol, methyl salicylate, and subsequently amended the requirements for menthol, methyl salicylate, and related ingredients in the Determination. Following these changes the TGA received multiple requests for exemption from the warning statement requirements for menthol and methyl salicylate when included in low concentrations in topical PIs.

Following reconsideration of the available data and the risk of skin irritation when methyl salicylate is present in very low concentrations, the TGA have determined that the label warning statement below is **not required when menthol is present in a medicine in concentrations of 1% or less, such as in PIs.**

WARNING STATEMENT

The following warning statements will only be required on the label of topical listed medicines when the concentration of **methyl salicylate** in the medicine **is greater than 1%:**

- **(IRRIT) 'If irritation develops, discontinue use**

These requirements apply for any purpose of the ingredient, ie active, excipient, homeopathic ingredient.

ALL OTHER REQUIREMENTS FOR METHYL SAICYLATE REMAIN APPLICABLE.

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW listings must carry the warning statement from commencement of the new determination, **1 January 2020**

Labels of EXISTING listings: As these changes are less restrictive there is not specific date by which labels must be updated.

For those products with **1% OR MORE** of methyl salicylate, labels must be updated **by 1 January 2020 .**

Boron

More restrictive requirements - [NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine contains any of the ingredients

Borax

Borax pentahydrate

Boric Acid

Sodium Perborate

Then your medicine will be subject to the following specific requirements:

MANDATORY COMPONENTS

Boron is a MANDATORY component of borax, borax pentahydrate, boric acid, and sodium perborate.

NEW REQUIRED WARNING STATEMENTS and CONTENT RESTRICTIONS

1. The percentage of boron in these ingredients should be calculated according to molecular weight.

2. The maximum recommended daily dose must provide no more than 6mg of Boron.

3. In preparations for **dermal use**, which are not for paediatric or antifungal use, the concentration of boron in the medicine must be **no more than 3500 mg/kg or 3500 mg/L or 0.35%**.

4. When the maximum recommended daily dose of the medicine provides **more than 3 mg*** of boron and the medicine is for **internal use and/or oral application**, the following warning statement is required on the label:

   - **(NOTUND12) 'Not to be taken by children under 12 years old' (or words to that effect); or**
   - **(ADULT) 'Adults only' (or words to that effect).**

5. When the maximum recommended daily dose of the medicine provides **more than 1 mg of boron but less than 3mg** of boron and the medicine is for **internal use and/or oral application**, the following warning statement is required on the label:

   - **(NOTUND2) 'Not to be taken by children under 2 years old' (or words to that effect); or**
   - **(ADULT) 'Adults only' (or words to that effect).**

6. When the maximum recommended daily dose of the medicine provides **more than 1 mg of boron and the medicine is for internal use and/or oral application**, the label of the medicine, the following warning statement is required on the label:

   - **(BORON) 'Contains boron' (or words to that effect).**

7. When the medicine is **for topical use for dermal application**, the following warning statement is required on the label:

- **(BROKEN) 'Use on unbroken skin only' (or words to that effect).**

*If your medicine contains exactly 3mg of boron it is not currently covered – this is being amended but the Determination will need to be checked to see if the requirement for the '12 year olds' or '2 year olds' apply. If in doubt, apply the more restrictive statement (12 year olds statement).

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW listings must comply from commencement of the new Determination, 2 March 2020.

Labels of EXISTING listings have **until 2 March 2021** to update product labels with the new requirements

Withania somnifera

More restrictive requirements – [NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine includes the ingredient, *Withania somnifera*

Then your medicine will be subject to the following specific requirements:
When

1. The maximum recommended daily dose of the medicine contains **more than 1200* mg** of *Withania somnifera*; or
2. The plant part is **other than root**; or
3. Any extraction solvents used are **NOT water, ethanol or methanol**

*Clarification is being sought to confirm that this means the amount of equivalent herb.

The medicine requires the following warning statement on the label:

- **'If you are pregnant, or considering becoming pregnant, do not take without consulting a health professional' (or words to that effect).**

These requirements apply for any purpose of the ingredient, ie active, excipient, homeopathic ingredient.

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW LISTINGS must carry the revised label changes from commencement of the new Determination, **2 March 2020**

Labels of EXISTING LISTINGS have **until 2 March 2021** to update product labels with the new requirements

Vitex agnus-castus

More restrictive requirements - [NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine includes the ingredient, *Vitex agnus-castus*

When for **internal use**, the medicine requires the following warning statement on the label:

- **(VAC) 'Vitex agnus-castus may affect hormones and medicines such as oral contraceptives. Consult your health professional before use' (or words to that effect).**

These requirements apply for any purpose of the ingredient, ie active, excipient, homeopathic ingredient.

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW LISTINGS must carry the revised label changes from commencement of the new Determination, **2 March 2020**

Labels of EXISTING LISTINGS have **until 2 March 2021** to update product labels with the new requirements

Isphagula spp, Plantago spp, psyllium husk

More restrictive requirements - [NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine includes any of the ingredients:

Ispaghula husk dry

Ispaghula husk powder

Plantago afra

Plantago arenaria

Plantago asiatica

Plantago lanceolata

Plantago major

Plantago ovata

Plantago seed dry

Psyllium husk dry

Psyllium husk powder

Psyllium seed dry

When a **dose for children is stated**, the medicine requires the following **warning statement** on the label:

- **(PSYLL) 'Should only be used for children on medical advice' (or words to that effect).**

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW LISTINGS must carry the revised label changes from commencement of the new determination, **2 March 2020**

Labels of EXISTING LISTINGS have **until 2 March 2021** to update product labels with the new requirements

Cymbopogen spp

More restrictive requirements - [NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine includes any of the ingredients:

Cymbopogon flexuosus

Cymbopogon martini

Cymbopogon nardus

Cymbopogon nardus

Then your medicine will be subject to the following requirements.

When for **topical use**:

1. Aldehydes calculated as citral is a mandatory component of Cymbopogon nardus.
2. The concentration of Aldehydes calculated as citral in the medicine must not be more than 5%.

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

ARTG: relevant listings must be updated, and all product in supply must comply with this content limit by **2 March 2021**

Labels of NEW LISTINGS must carry the revised label changes from commencement of the new determination, **2 March 2020**

Labels of EXISTING LISTINGS have **until 2 March 2021** to update product labels with the new requirements

Malus pumila

[NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine includes the ingredient, *Malus pumila*

Then your medicine:

Needs to change to *Malus domestica* (the synonym).

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

ARTG: Request TGA to update ARTG listings by 2 March 2021 with the synonym *M.domestica*

Labels of NEW LISTINGS: no label changes are required.

Labels of EXISTING LISTING: no label changes are required.

Coumarin

More restrictive requirements - [NOTE CHANGES DUE BY 2 MARCH 2021]

If your medicine includes the ingredient, Coumarin

Then your medicine will be subject to the following restrictions:

1. Only for use as an active homeopathic ingredient or excipient ingredient

2. When used as an **active homoeopathic ingredient**, the concentration of coumarin in the medicine must be **no more than 0.001%.**

3. When used as an **excipient,** must only be used in **topical medicines for dermal application.**

4. **When used as an excipient,**

   - the concentration of coumarin in the medicine **must not be more than 0.001%;** and
   - the label of the medicine should carry the WARNING STATEMENT to the effect that it **should only be used by adults.**

Always check the Determination's specific requirements to ensure compliance when making a product decision. "How to use legislation" tips are included on the CMA webpage: http://www.cmaustralia.org.au/TGA-Timeline

Labels of NEW LISTINGS where coumarin is an excipient, medicines must carry the label warning statement from the date of commencement, **2 March 2020**

Labels of existing listings have **until 2 March 2021** to update product labels with the new requirements

Next Steps for affected companies

Sponsors should review the relevant product labels, packing and ARTG entries for compliance with the relevant determination and schedule the required changes.

Resources

Outcomes to the Low – Negligible risk consultation
Andrographis paniculata
Menthol and methyl salicylate
Coumarin in topical medicines
Permissible ingredient determination

Members are encouraged to forward any identified issues to technical@cmaustralia.org.au for attention by the Committee Secretariat.

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