Australian Government
Department of Health
Therapeutic Goods Administration

Consultation: Proposed amendments to the Poisons Standard – ACMS, June 2021

27 April 2021

TGA Health Safety Regulation

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1.1 Amygdalin and hydrocyanic acid

Proposal

The applicant proposes to amend the Schedule 10 entry for amygdalin to allow for unscheduled oral use as a natural component in traditional Chinese medicines in adults, with a maximum daily dose not exceeding 5 mg of amygdalin.

A change to the Schedule 4 entry for hydrocyanic acid to allow for unscheduled oral use when present as a natural component in traditional Chinese medicines, in adults with a maximum daily dose not exceeding 0.3 mg of hydrocyanic acid.

A final decision was published on 22 April in relation to a previous proposal to amend the Poisons Standard entries for amygdalin and hydrocyanic acid

CAS number:

Amygdalin: 29883-15-6

Hydrocyanic acid: 74-90-8

Alternative names

Amygdalin: D-mandelonitrile-β-D-glucoside-6-β-glucoside; mandelonitrile-β-gentiobioside; Vitamin B17

Hydrocyanic acid: Hydrogen cyanide; formonitrile; prussic acid

Applicant

Private applicant

Current scheduling

Amygdalin

Schedule 10

AMYGDALIN for therapeutic use.

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AMYGDALIN

Schedule 10

Hydrocyanic acid

Schedule 7

HYDROCYANIC ACID **except**:

a) when included in Schedule 4; or

b) its salts and derivatives other than cyanides separately specified in this Schedule.

Schedule 4

HYDROCYANIC ACID for therapeutic use.

Appendix F, Part 3

POISON	WARNING STATEMENTS	SAFETY DIRECTION
HYDROCYANIC ACID when included in Schedule 7.	**13** (May be fatal if inhaled, swallowed or absorbed through skin)	**4** (Avoid contact with skin), **8** (Avoid breathing dust (or) vapour (or) spray mist)

Appendix G

POISON	CONCENTRATION (quantity per litre or kilogram)
HYDROCYANIC ACID	1 microgram

Appendix J, Part 2

POISONS	Authorisation Considerations
HYDROCYANIC ACID AND CYANIDES	P (additional restrictions on possession)

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HYDROCYANIC ACID
cross reference: CYANIDES

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Proposed scheduling

Amygdalin

Schedule 10 – Amend Entry

AMYGDALIN for therapeutic use **except** as a natural component in traditional Chinese medicines for oral use in adults with a maximum daily dose not exceeding 5 mg of amygdalin.

Hydrocyanic acid

Schedule 4 – Amend Entry

HYDROCYANIC ACID for therapeutic use **except** when present as a natural component of amygdalin in traditional Chinese medicines for oral use in adults with a maximum daily dose not exceeding 0.3 mg of hydrocyanic acid.

Key uses / expected use

Medicines

Summary of applicant's reasons for proposal

- Amygdalin is a cyanogenic glycoside found naturally in many plants including cassava, sorghum, lima beans, bitter almonds, apricot kernels and seeds of other plants in the *Prunus* genus.
- Many traditional Chinese medicines are formulated to include one or more of these plant ingredients, usually in combination with other traditional Chinese herbs. Under the current scheduling arrangements, products that contain amygdalin in any quantity cannot be used in therapeutic goods, which means that many formulated TCM products that are freely available in other countries are not available to Australian TCM practitioners.
- This application proposes excluding amygdalin from Schedule 10 when included as a natural component in traditional Chinese medicines for oral use in with a cut-off to unscheduled at a maximum daily adult dose of 5 mg or less.
- The selected cut-off of 5 mg per maximum daily dose is based on animal studies and assessment by a wide range of regulatory and expert committees that an oral intake of 5 to 20 µg/kg/d cyanide (equivalent to 5.1 to 20.3 mg/d amygdalin for a 60 kg adult) is considered to present no appreciable risk. It is substantially less than the legal limit in many foods for human consumption in Australia and New Zealand.
- By way of comparison, 100 g of confectionary could legally contain more than 8 times this proposed maximum daily dose and one standard drink of red wine could legally contain more than 4 times this dose.
- An associated change to exclude hydrocyanic acid from Schedule 4 when present as a natural component of amygdalin in traditional Chinese medicines for oral use in adults is also proposed.
- The effect of the changes would be to make traditional Chinese medicine products containing very low doses of amygdalin available without prescription

Australian regulations

- According to the TGA Ingredient Database[1] amygdalin and hydrocyanic acid are:
  - Not available for use as active ingredients in any application;
  - Not available for use as excipient ingredients in any application; and
  - Available for use as equivalent ingredients in Export Only and Listed medicines.
- As of April 2021, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[2] that contain amygdalin or hydrocyanic acid as an active ingredient.
- Amygdalin and hydrocyanic acid are captured as mandatory components of twenty ingredients in the Therapeutic Goods (Permissible Ingredients) Determination[3] No.1 of 2021.

Item	Ingredient name	Purpose	Specific requirements
451	Almond oil	A, E, H	• Amygdalin and hydrocyanic acid are mandatory components of Almond oil. • The concentration of Amygdalin in the medicine must be 0%. • The concentration of hydrocyanic acid in the medicine must be no more than 1 microgram/kg or 1 microgram/L or 0.0000001%.
A – active ingredient (for a medicine, has the same meaning as in the Regulations **E** – excipient (for a medicine, means an ingredient that is not an active ingredient or a homoeopathic preparation ingredient) **H** – homeopathic preparation ingredient (means an ingredient that is a constituent of a homoeopathic preparation)			

- Amygdalin and hydrocyanic acid are not included the TGA prescribing medicines in pregnancy database[4]
- There are no warning statements pertaining to amygdalin or hydrocyanic acid in the Therapeutic Goods (Medicines Advisory Statements) Specification 2019[5]

[1] TGA Ingredient Database https://www.ebs.tga.gov.au/
[2] ARTG database https://www.tga.gov.au/artg
[3] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[4] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[5] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213

- As of April 2021, there were no reports of adverse events for products containing amygdalin or hydrocyanic acid as an active ingredient in the Database of Adverse Event Notifications (DAEN)[6]

International regulations

As of April 2021:

- Amygdalin and hydrocyanic acid are not included in the WHO Model List of Essential Medicines 2019[7]
- There are no products containing amygdalin and hydrocyanic acid in the United States Food and Drug Administration Approved Drug Products database (Drugs@FDA) [8] or European Commission database for information on cosmetic substances and ingredients database[9]
- There are no products containing amygdalin and hydrocyanic acid in the Canadian (Health Canada) Drug Product Database[10] and Health Products Regulatory Authority of Ireland[11] database.
- Amygdalin and hydrocyanic acid were added to the New Zealand Inventory of Chemicals (NZIoC)[12] on 1 December 2006.
- Amygdalin and hydrocyanic acid are entered in the New Zealand Medicines and Medical Devices Safety Authority (MedSafe)[13] as follows:

Ingredient	Chemicals	Medicines
Amygdalin	At all strengths	Prescription
Hydrocyanic acid	**except** when specified elsewhere in this schedule; **except** in medicines containing 1 microgram or less per litre or per kilogram	Prescription

[6] Database of Adverse Event Notifications – medicines
https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[7] WHO model list of essential medicines – 21st list, 2019
www.who.int/publications/i/item/WHOMVPEMPIAU2019.06
[8] FDA Approved Drug Products Database https://www.accessdata.fda.gov/scripts/cder/daf/
[9] European Commission database for information on cosmetic substances and ingredients database
https://ec.europa.eu/growth/tools-databases/cosing/
[10] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp
[11] Health Products Regulatory Authority (HPRA)
https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=&field=
[12] New Zealand Inventory of Chemicals (NZIoC)
https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC
[13] New Zealand Medicines and Medical Devices Safety Authority (MedSafe)
https://www.medsafe.govt.nz/profs/class/classintro.asp

Hydrocyanic acid	for oral use in packs containing 5 milligrams or less and more than 0.5 milligrams; **except** in medicines containing 1 microgram or less per litre or per kilogram	Pharmacy Only
Hydrocyanic acid	for oral use in packs containing 0.5 milligrams or less; in medicines containing 1microgram or less per litre or per kilogram	General Sale

1.1 Bufexamac

Proposal

The Delegate of the Secretary of the Commonwealth Department of Health (the Delegate) proposes to amend the Schedule 4 entry for bufexamac to include all products.

CAS number:

2438-72-4

Alternative names

4-Butoxy-*N*-hydroxybenzeneacetamide; 2-(*p*-butoxyphenyl)acetohydroxamic acid; 2-[*p*-(butyloxy)phenyl]acetohydroxamic acid

Applicant

Delegate of the Secretary of the Commonwealth Department of Health

Current scheduling

Bufexamac is currently listed in Schedule 4 of the Poisons Standard, as follows:

Schedule 4

BUFEXAMAC **except**:

c) in preparations for dermal use containing 5 per cent or less of bufexamac; or

d) in suppositories.

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BUFEXAMAC

Schedule 4

Proposed scheduling

Schedule 4 – Amend Entry

BUFEXAMAC ~~**except:**~~

a) ~~in preparations for dermal use containing 5 per cent or less of bufexamac; or~~

b) ~~in suppositories.~~

Key uses / expected use

Medicines

Summary of applicant's reasons for proposal

- Bufexamac is an over-the-counter non-steroidal anti-inflammatory drug (also known as an NSAID), which is used in combination with chlorhexidine and lidocaine (lignocaine) in first aid creams that are applied to the skin.
- A recent TGA investigation determined that, based on the assessment and independent advice from the Advisory Committee on Medicines (ACM), the safety and effectiveness of bufexamac-containing products are unacceptable. Bufexamac is associated with a risk of serious skin reactions (also known as allergic contact dermatitis). The TGA has also determined that there is inadequate evidence that the bufexamac ingredient in these products is effective. As a result, the registration of all bufexamac-containing products was cancelled, effective 18 September 2020.
- Bufexamac is currently included in Schedule 4, with exceptions for dermal use and in suppositories. Since there are no longer any preparations for dermal use, nor suppositories, containing bufexamac on the ARTG, it may be appropriate to remove these from the Schedule 4 entry.

Australian regulations

- According to the TGA Ingredient Database[14] bufexamac is:
  - Available for use as an active ingredient in biologicals, export only, over the counter and prescription medicines
  - Available for use as an excipient ingredient in biologicals, devices and prescription medicines
  - Not available as an equivalent ingredient in any application
- As of March 2021, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[15] that contain bufexamac as an active ingredient.
- Bufexamac is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[16] No.1 of 2021.

[14] TGA Ingredient Database https://www.ebs.tga.gov.au/
[15] ARTG database https://www.tga.gov.au/artg
[16] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination

- Bufexamac is not listed in the TGA prescribing medicines in pregnancy database[17]
- There are no warning statements pertaining to bufexamac in the Therapeutic Goods (Medicines Advisory Statements) Specification 2019[18]
- Since January 2010, there were 21 reports of adverse events for products containing bufexamac as an active ingredient on the Database of Adverse Event Notifications (DAEN)[19] with 20 reports where norethisterone was the single suspected medicine. There were no reports of deaths associated with bufexamac use.
- As of March 2021, there were no products containing bufexamac listed on the Public Chemical Registration Information System Search (PubCRIS)[20]

International regulations

- Bufexamac is not included in the WHO Model List of Essential Medicines 2019[21]
- The Health Products Regulatory Authority of Ireland[22] have not approved use of bufexamac.
- The United States Food and Drug Administration[23] have not approved use of bufexamac.
- Bufexamac was previously approved for use as an over the counter medicine in Canada, according to the Canadian (Health Canada) Drug Product Database[24], but all products containing bufexamac have since been cancelled.
- According to the New Zealand Medicines and Medical Devices Safety Authority (MedSafe)[25] bufexamac is available in New Zealand as follows:

Ingredient	Conditions	Classification
Bufexamac	**except** in suppositories or for dermal use in medicines containing 5% or less	Prescription
Bufexamac	in suppositories; for dermal use in medicines containing 5% or less	General Sale

[17] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[18] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213
[19] Database of Adverse Event Notifications – medicines https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[20] Database of Adverse Event Notifications – medicines https://portal.apvma.gov.au/pubcris
[21] WHO model list of essential medicines – 21st list, 2019 www.who.int/publications/i/item/WHOMVPEMPIAU2019.06
[22] Health Products Regulatory Authority (HPRA) https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=&field=
[23] FDA Approved Drug Products Database https://www.accessdata.fda.gov/scripts/cder/daf/
[24] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp
[25] New Zealand Medicines and Medical Devices Safety Authority (MedSafe) https://www.medsafe.govt.nz/profs/class/classintro.asp

1.2 Ibuprofen

Proposal

The applicant proposes to amend the Schedule 2 entry for ibuprofen to include a modified release dosage form, each containing 600 mg (specifically) of ibuprofen in a primary pack containing not more than 16 dosage units, when labelled:

i) with a recommended daily dose of 1200 mg or less of ibuprofen; and

ii) not for the treatment of children under 12 years of age.

CAS number:

15687-27-1

Alternative names

p-isobutylhydratropic acid; (±)-2-(4-isobutylphenyl)propionic acid

Applicant

Private applicant

Current scheduling

Ibuprofen is currently listed in Schedules 2, 3 and 4 of the Poisons Standard as follows:

Schedule 4

IBUPROFEN **except**:

a) when included in or expressly excluded from Schedule 2 or 3; or

b) in preparations for dermal use.

Schedule 3

IBUPROFEN:

a) in divided preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 50 dosage units, when labelled:

i) with a recommended daily dose of 1200 mg or less of ibuprofen; and

ii) not for the treatment of children under 12 years of age; or

b) in a modified release dosage form, each containing 600 mg of ibuprofen in a primary pack containing not more than 32 dosage units, when labelled:

i) with a recommended daily dose of 1200 mg or less of ibuprofen; and

ii) not for the treatment of children under 12 years of age;

except when included in or expressly excluded from Schedule 2.

Schedule 2

IBUPROFEN in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen:

a) in liquid preparations when sold in the manufacturer's original pack containing 8 g or less of ibuprofen; or

b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:

i) as the only therapeutically active constituent (other than phenylephrine or when combined with an effervescent agent);

ii) packed in blister or strip packaging or in a container with a child-resistant closure;

iii) in a primary pack containing not more than 25 dosage units;

iv) compliant with the requirements of the Required Advisory Statements for Medicine Labels;

v) not labelled for the treatment of children 6 years of age or less; and

vi) not labelled for the treatment of children under 12 years of age when combined with phenylephrine; or

c) in divided immediate release preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 12 dosage units, when labelled not for the treatment of children under 12 years of age.

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IBUPROFEN

Schedule 4
Schedule 3
Schedule 2
Appendix F, Part 3
Appendix H

It is also included under the entry IBUPROFEN in Appendix F as follows:

Schedule F, Part 3

Warning Statements:

101. Don't use [*this product/name of the product*]:

If you have a stomach ulcer.

In the last 3 months of pregnancy. [*This statement may be omitted in preparations used exclusively for the treatment of dysmenorrhoea.*]

If you are allergic to (name of substance) or anti-inflammatory medicines.

104. Unless a doctor has told you to, don't use [*this product/name of the product*]:

For more than a few days at a time.

With other medicines containing (name of substance) or other anti-inflammatory medicines.

If you have asthma.

If you are pregnant. [*This statement may be omitted in preparations used exclusively for the treatment of dysmenorrhoea*.]

Proposed scheduling

Schedule 2 – Amend Entry

IBUPROFEN in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen:

a) in liquid preparations when sold in the manufacturer's original pack containing 8 g or less of ibuprofen; or

b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:

i) as the only therapeutically active constituent (other than phenylephrine or when combined with an effervescent agent);

ii) packed in blister or strip packaging or in a container with a child-resistant closure;

iii) in a primary pack containing not more than 25 dosage units;

iv) compliant with the requirements of the Required Advisory Statements for Medicine Labels;

v) not labelled for the treatment of children 6 years of age or less; and

vi) not labelled for the treatment of children under 12 years of age when combined with phenylephrine.

c) in divided immediate release preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 12 dosage units, when labelled not for the treatment of children under 12 years of age.

d) in a modified release dosage form, each containing 600 mg of ibuprofen in a primary pack containing not more than 16 dosage units, when labelled not for the treatment of children under 12 years of age.

Key uses / expected use

Medicines

Summary of applicant's reasons for proposal

- Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) used as an analgesic, antipyretic, and anti-inflammatory. It decreases synthesis of pain- and inflammation-promoting prostaglandins via non-selective inhibition of both cyclo-oxygenase (COX), COX-1 and COX-2 enzymes. It has been extensively studied, and its efficacy and safety profile in humans following oral administration is well-established.
- The approved indications for non-prescription modified release 600 mg ibuprofen available in Australia are the same as those approved for standard, immediate release non-prescription 200 mg and 400 mg ibuprofen solid dose preparations and other Schedule 2 analgesics such as naproxen and ibuprofen/paracetamol combination formulations. Such

preparations are approved for providing temporary relief of pain from mild conditions including body pain, back pain, neck and shoulder pain, muscle pain, sprains and strains, osteoarthritis, arthritic, joint and rheumatic conditions, period pain, dental pain, sinus pain, cold and flu.

- These conditions are accepted as being able to be self-identified and self-managed by the consumer, without need for medical intervention. The only significant differentiating feature is the duration of action, with modified release 600 mg ibuprofen providing extended relief so is suitable and approved in situations where pain is likely to last more than 6 hours. The approved indications for non-prescription 600 mg modified release ibuprofen **do not** extend to chronic pain states.
- The currently available 600 mg ibuprofen modified release formulation is bioequivalent to ibuprofen 200 mg immediate release tablets and has an equivalent safety profile, with both products having the same warning and precaution statements and an identical maximum daily dose of 1200 mg.
- Given there is no material difference in safety, and purpose of use for 600 mg modified release ibuprofen compared with existing Schedule 2 analgesics including paracetamol, naproxen and standard ibuprofen, the same Schedule 2 classification is appropriate and provides consistency in scheduling decisions.
- Consumer access to 600 mg modified release ibuprofen as a Schedule 2 medicine would also align with Canada, where this formulation has been available for consumer self-selection in pharmacies for over 5 years.
- As noted by the TGA delegate in making their interim decision for inclusion of 400 mg ibuprofen in Schedule 2 "*ibuprofen has a wide therapeutic index and the risk from harm from overdose is minimal…….the risk profile of ibuprofen* [is considered] *to be superior to that of other nonsteroidal anti-inflammatory drugs (NSAIDs) and compared to combination paracetamol+ibuprofen formulations currently available in Schedule 2… very large doses of ibuprofen are required for moderate to severe toxicity (>/= 400mg/kg or 28 g for a 70 kg person) .... There is unlikely to be any increased safety risk when taken according to directions, noting the availability of 20 g ibuprofen in the 100 pack of 200 mg tabs (with a maximum dose of 1200mg/day) is currently available under Schedule 2*." These reasons equally apply when considering suitable scheduling of non-prescription 600 mg ibuprofen.

Australian regulations

- According to the TGA Ingredient Database[26] ibuprofen is:
  - Available for use as an Active Ingredient in: Biologicals, Export Only, Over the Counter, Prescription Medicines
  - Available for use as an Excipient Ingredient in: Biologicals, Devices, Prescription Medicines
  - Available for use as an Equivalent Ingredient in: Biologicals, Export Only, Prescription Medicines
- As of March 2021, there were 262 medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[27] that contain ibuprofen (as base, lysine or sodium dihydrate) as

[26] TGA Ingredient Database https://www.ebs.tga.gov.au/
[27] ARTG database https://www.tga.gov.au/artg

an active ingredient. These include 17 prescription and 240 non-prescription medicines, 3 medicines for export only, and 2 medical devices.

- Ibuprofen is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[28] No.1 of 2021.
- The TGA prescribing medicines in pregnancy database[29] classifies ibuprofen as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
IBUPROFEN	C	Musculoskeletal system	Non-steroidal anti-inflammatory drugs (NSAIDS)	
Category C – Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.				

- The Therapeutic Goods (Medicines Advisory Statements) Specification 2019[30] requires the following warning statements pertaining to ibuprofen to be included on the labelling:

Substance	Conditions	Required Statement(s)
Ibuprofen (1 of 6)	For the purpose of exclusion from the schedules to the SUSMP, when the preparation is for oral use in adults and children aged 12 years and over.	• Do not use if you have a stomach ulcer. • Do not use if you have impaired kidney function. • Do not use if you have heart failure. • Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. • If you get an allergic reaction, stop taking and see your doctor immediately. • Unless a doctor has told you to, do not use if you have asthma. • Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.

[28] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination

[29] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database

[30] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213

		• Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy. • Unless a doctor has told you to, do not use if you are aged 65 years or over.
Ibuprofen (2 of 6)	When included in a schedule to the SUSMP for oral use in adults and children aged 12 years and over	• Do not use if you have a stomach ulcer. • Do not use if you have impaired kidney function. • Do not use if you have heart failure. • Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. • If you get an allergic reaction, stop taking and see your doctor immediately. • Unless a doctor has told you to, do not use if you have asthma. • Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy.
Ibuprofen (3 of 6)	For the purpose of exclusion from the schedules to the SUSMP, for oral use in children under 12 years of age	• Do not use if you have a stomach ulcer. • Do not use if you have impaired kidney function. • Do not use if you have heart failure. • Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. • If you get an allergic reaction, stop taking and see your doctor immediately. • Unless a doctor has told you to, do not use if you have asthma. • Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy. • Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting.

		• Unless a doctor has told you to, do not use if you are aged 65 years or over. • Unless a doctor has told you to, do not use in children 6 years of age or less.
Ibuprofen (4 of 6)	When included in a schedule to the SUSMP for oral use in children under 12 years of age	• Do not use if you have a stomach ulcer. • Do not use if you have impaired kidney function. • Do not use if you have heart failure. • Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. • If you get an allergic reaction, stop taking and see your doctor immediately. • Unless a doctor has told you to, do not use if you have asthma. • Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy. • Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting.
Ibuprofen (5 of 6)	In combination with paracetamol, in medicines for oral use	• Do not give to children under 12 years of age. • Adults: Keep to the recommended dose. Do not take this medicine for longer than a few days at a time unless advised to by a doctor. • Children and adolescents: Keep to the recommended dose. Do not give this medicine for longer than 48 hours at a time unless advised to by a doctor. • Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • Do not use if pregnant or trying to become pregnant. • Do not use if you have a stomach ulcer. • Do not use if you have impaired kidney function. • Do not use if you have heart failure. • Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. • If you get an allergic reaction, stop taking and see your doctor immediately. • Unless a doctor has told you to, do not use if you have asthma. • Unless a doctor has told you to, do not use if you are aged 65 years or over. • Do not take with other products containing paracetamol, ibuprofen, aspirin or other anti-

		inflammatory medicines or with medicines that you are taking regularly, unless advised to do so by a doctor or pharmacist. • If an overdose is taken or suspected, ring the Poisons Information Centre (Australia 13 11 26, New Zealand 0800 764 766) or go to hospital straight away even if you feel well because of the risk of delayed, serious liver damage.
Ibuprofen (6 of 6)	In preparations for dermal use	• Do not use [this product/*insert name of product*] if you are allergic to ibuprofen or other anti-inflammatory medicines. • If you get an allergic reaction, stop taking and see your doctor immediately. • Unless a doctor or pharmacist has told you to, do not use [this product/*insert name of product*] with other medicines that you are taking regularly.

- Since January 2010, there have been 748 reports of adverse events for products containing ibuprofen as an active ingredient on the Database of Adverse Event Notifications (DAEN)[31], with 491 reports where ibuprofen was the single suspected medicine.
- As of March 2021, there were no products containing ibuprofen listed on the Public Chemical Registration Information System Search (PubCRIS)[32]

International regulations

- Ibuprofen is included in the WHO Model List of Essential Medicines 2019[33]
- The Health Products Regulatory Authority of Ireland[34] regulates ibuprofen as an over-the-counter and prescription-only medicine.
- The United States Food and Drug Administration Approved Drug Products database (Drugs@FDA) [35] approve use of ibuprofen as an over-the-counter and prescription medicine.
- Ibuprofen is approved for use as an over-the-counter and prescription medicine according to the Canadian (Health Canada) Drug Product Database[36]

[31] Database of Adverse Event Notifications – medicines https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[32] Database of Adverse Event Notifications – medicines https://portal.apvma.gov.au/pubcris
[33] WHO model list of essential medicines – 21st list, 2019 www.who.int/publications/i/item/WHOMVPEMPIAU2019.06
[34] Health Products Regulatory Authority (HPRA) https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=&field=
[35] FDA Approved Drug Products Database https://www.accessdata.fda.gov/scripts/cder/daf/
[36] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp

- According to the New Zealand Medicines and Medical Devices Safety Authority (MedSafe)[37] ibuprofen is available as follows:

Ingredient	Conditions	Classification
Ibuprofen	**except** when specified elsewhere in this schedule	Prescription
Ibuprofen	for oral use in tablets or capsules containing up to 400 milligrams per dose form and in packs containing not more than 50 dose units and that have received the consent of the Minister or the Director-General to their distribution as restricted medicines and that are sold in the manufacturer's original pack labelled for use by adults and children over 12 years of age	Restricted[38]
Ibuprofen	for oral use in liquid form with a recommended daily dose of not more than 1.2 grams for the relief of pain and reduction of fever or inflammation when sold in the manufacturer's original pack containing not more than 8 grams; for oral use in solid dose form containing not more than 200 milligrams per dose form and with a recommended daily dose of not more than 1.2 grams when sold in the manufacturer's original pack containing not more than 100 dose units; **except** in divided solid dosage forms for oral use containing 200 milligrams or less per dose form with a recommended daily dose of not more than 1.2 grams and when sold in the manufacturer's original pack containing not more than 25 dose units	Pharmacy Only
Ibuprofen	for external use; in divided solid dosage forms for oral use containing 200 milligrams or less per dose form with a recommended daily dose of not more than 1.2 grams and when sold in the manufacturer's original pack containing not more than 25 dose units per pack	General Sale

2 How to respond

Submissions must be provided by the closing date of **27 May 2021** through our consultation hub. Any submission about any of the proposals to amend the Poisons Standard will be considered at the next meeting of the Advisory Committee on Medicines Scheduling (ACMS), meeting of the Advisory Committee on Chemicals Scheduling (ACCS), or a joint meeting of these two committees.

[37] New Zealand Medicines and Medical Devices Safety Authority (MedSafe) https://www.medsafe.govt.nz/profs/class/classintro.asp

[38] Restricted medicines in NZ are also referred to as Pharmacist Only medicines. See https://www.medsafe.govt.nz/Consumers/PharmOnly.asp for details

3 What will happen

All public submissions will be published on the TGA website at Public submissions on scheduling matters, unless marked confidential or indicated otherwise in the submission coversheet (see Privacy information).

Following consideration of public submissions received before the closing date and advice from the expert advisory committee/s, decisions on the proposed amendments will be published as interim decisions on the TGA website: Scheduling delegate's interim decisions & invitations for further comment in **September 2021**.

4 Enquiries

Any questions relating to submissions should be directed by email to medicines.scheduling@health.gov.au