Australian Government
Department of Health
Therapeutic Goods Administration

Notice of interim decisions to amend (or not amend) the current Poisons Standard ACMS #34

TGA Health Safety Regulation

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All submissions received will be placed on the TGA's Internet site, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover and clearly marked "IN CONFIDENCE". Reasons for a claim to confidentiality must be included in the space provided on the TGA submission form. For submission made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's Internet site. In addition, a list of parties making submissions will be published. If you do not wish to be identified with your submission you must specifically request this in the space provided on the submission form.

Contents

1. Notice of interim decisions made under Regulation 42ZCZN of the *Therapeutic Goods Regulations 1990*

This web publication constitutes a notice for the purposes of regulation 42ZCZP of the *Therapeutic Goods Regulations 1990* (the **Regulations**). In accordance with regulation 42ZCZP, this notice sets out:

- the interim decisions made by a delegate of the Secretary under regulation 42ZCZN in relation to proposed amendments to the current Poisons Standard which were referred to an expert advisory committee under subdivision 3D.2 of the Regulations in June 2021;
- the proposed date of effect of the proposed amendments (in circumstances where the interim decision proposes an amendment to the current Poisons Standard).

In accordance with regulation 42ZCZP, interested persons (including the applicant requesting the amendment) are invited to make submissions to the Secretary in relation to these interim decisions on or before **1 November 2021**.

We have changed the way to make submissions.

Submissions should now be provided through our consultation hub. Submissions will be considered by the Delegate in making the final decision.

Please note that in accordance with subregulation 42ZCZQ(4) of the Regulations, the Secretary must publish all relevant submissions received, unless the Secretary considers the information to be confidential information.

2. Interim decisions on proposed amendments referred to the Advisory Committee on Medicines Scheduling (ACMS #34, June 2021)

2.1 Interim decision in relation to amygdalin and hydrocyanic acid

Proposal

The applicant proposed 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.

The applicant also proposed a change to the Schedule 4 entry for hydrocyanic acid to allow for unscheduled oral therapeutic use when present as a natural component in Traditional Chinese Medicines (TCM), in adults with a maximum daily dose not exceeding 0.3 mg of hydrocyanic acid.

A previous proposal to amend the scheduling of amygdalin and hydrocyanic acid was also recently considered, including referral to the November 2020 meeting of the ACMS, and a final decision was published on 22 April 2021.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the scheduling for amygdalin and hydrocyanic acid in the current Poisons Standard. A new index entry will be created for apricot kernels, with cross references to both amygdalin and hydrocyanic acid.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to amygdalin and hydrocyanic acid;
- The seven public submissions, all including a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #34);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACMS advice to the delegate

The Committee advised that the current scheduling for amygdalin and hydrocyanic acid remains appropriate, with recommendation to add a new index entry for 'apricot kernels' with cross references in the index entries for both amygdalin and hydrocyanic acid:

Index – New Entry

APRICOT KERNELS
cross reference: AMYGDALIN, HYDROCYANIC ACID

Index – Amend Entry

AMYGDALIN
cross reference: APRICOT KERNELS

Schedule 10

HYDROCYANIC ACID
cross reference: CYANIDES, APRICOT KERNELS

Schedule 7
Schedule 4
Appendix F, Part 3
Appendix G
Appendix J, Part 2

The Committee also recommended an implementation date of **1 February 2022**.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

Risks:

- Risk outweighs benefit as an exemption from scheduling the substance due to concerns about use in children and inappropriate uses, including as a cancer therapy and for COVID-19, which may result in increased severity of illness and even death.
- Exemption from scheduling would mean the public has direct access to these products without consultation with a health professional.

Benefits:

- Limited evidence presented to demonstrate benefits other than increased access.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Therapeutic purpose of use not well defined in the application, though a long history of use in TCM was described. Most of the claimed indications are conditions which require management by a medical practitioner.

- Amygdalin and hydrocyanic acid (released by the natural degradation of amygdalin by enzymes in the plant preparation) occur naturally in plants used in TCM for health conditions described within the philosophy (theory, pathology, diagnosis, treatment and herbal pharmacology principles) of TCM.

c) the toxicity of a substance

- Amygdalin exhibit considerable toxicity due the production of hydrocyanic acid (HCN) following hydrolysis.
- HCN is highly toxic. While toxicity is dose related, there is also significant inter- individual variability.
- Complete degradation of 1g amygdalin releases 59mg of hydrocyanic acid (5mg amygdalin would be equivalent to 0.3mg HCN). Cyanide is readily absorbed reaching maximum blood levels within minutes and is distributed to all organs. The primary mode of action by which cyanide exerts acute toxicity is the inhibition of oxidative phosphorylation[1].
- In humans, the lethal oral dose of HCN is reported to be 0.5–3.5 mg/kg body weight. A level of 0.5 mg/L (approximately 20 mM) of cyanide in blood is cited in the literature as a toxicity threshold in humans[2].
- A series of poisoning cases are reported from ingestion of preparations containing amygdalin and bitter apricot kernels.
- Concerns about quality control and risk of higher amygdalin levels being present.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- TCM uses various oral dose forms and no specific products were described in the application.

e) ethe potential for abuse of a substance

- Amygdalin has been inappropriately promoted and used as an alternative cancer treatment.
- Claims for use in treating or preventing cancer are unproven.
- Exemption from scheduling means there is no requirement for any input from a health professional.

f) any other matters that the Secretary considers necessary to protect public health

- Due to the potential toxicity of amygdalin, it is important to prevent label claims of amygdalin and the promotion of other herbal medicines as a source of amygdalin.
- Labelling and packaging controls apply only for products on the Australian Register of Therapeutic Goods (ARTG). If unscheduled, there would be no controls on exempted products, including on packaging and labelling, available through sate and territory medicines and poisons legislation.

[1] EFSA - European Food Safety Authority Journal, March 2016: Acute health risks related to the presence of cyanogenic glycosides in raw apricot kernels and products derived from raw apricot kernel; doi: 10.2903/j.efsa.2016.4424 https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4424

[2] EFSA -European Food Safety Authority Journal, March 2016: Acute health risks related to the presence of cyanogenic glycosides in raw apricot kernels and products derived from raw apricot kernel; doi: 10.2903/j.efsa.2016.4424 https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4424

- Risk to public health due to inherent issues with labelling and determining content of TCM, particularly when imported into Australia.
- Limiting amygdalin to being a natural component of TCM for oral use by adults does not provide sufficient regulatory safety.
- Exemptions under the therapeutic goods legislation allow for health practitioners who prepare a medicine for an individual patient following a consultation with that patient, or to fill a prescription for that patient. This exemption would apply to direct supply of a compounded medicine to patients of a compounded medicine by a registered Chinese medicine practitioner, who holds registration in the Chinese herbal medicine practitioner or Chinese herbal dispenser category.
- No healthcare professional, including TCM practitioners, would be required to be consulted if this proposal was accepted.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the scheduling for amygdalin and hydrocyanic acid in the current Poisons Standard. The detailed reasons for my decision follow.

I agree with the Committee's findings that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are: (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

In my view, the relevant parts of the Scheduling Policy Framework (SPF 2018) are the scheduling factors for Schedule 10:

- Amygdalin poses such a high public health risk that its sale, supply and use require very strict control, with access generally being prohibited.
- The risks of amygdalin substantially outweigh the benefits to the extent that no other schedule would provide appropriate public access to any proposed or known products.

The applicant proposed to exempt amygdalin from scheduling when it is a natural component in TCM, where the maximum daily dose does not exceed 5 mg of amygdalin. It was also proposed that hydrocyanic acid is exempted from scheduling at a maximum daily dose of 0.3 mg. In considering these amendments, I note that a similar proposal was discussed at the November 2020 meeting of the Advisory Committee on Medicines Scheduling (ACMS #32), and that the final decision was to retain the current scheduling of these substances. In my view, the concerns raised in the previous Committee advice, along with the interim and final decisions, remain pertinent.

I note that 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. It is converted into hydrocyanic acid (cyanide) in the gut, which halts cellular respiration. At high enough doses, this can cause nausea, fever, headaches, insomnia, thirst, lethargy, nervousness, joint and muscle pains, falling blood pressure and (in some cases) death[3]. The toxicity is also highly variable between individuals and is influenced by factors such as other ingested plants/nutrients, vitamin B12 levels and individual gut flora. Given the large variation

[3] https://emergency.cdc.gov/agent/cyanide/basics/facts.asp

in toxicity, I emphasise that it is necessary to exercise a high degree of caution in considering the public access to these substances – even at low concentrations.

I agree with the Committee's advice that amygdalin preparations are not appropriate for exclusion from the Schedule 10 entry at any dosage. Exemption from scheduling would enable the public to purchase and use these products without any interaction with a health professional, including TCM practitioners, and without any regulation through the Poisons Standard. As such, there would be no labelling or packaging requirements through state and territory medicines and poisons legislation. It also would be difficult to prevent use at higher dosages that cause severe toxicity. These risks are exacerbated when considering the potential for poisoning in children, who can experience severe cyanide toxicity at particularly low dosages. I am of the view that the proposed scheduling does not provide sufficient regulatory control to mitigate against known risks of the substance.

I further note that medicinal preparations exempted from scheduling must able to be supplied with 'reasonable safety'. However, amygdalin does not fit the definition of reasonable safety, as provided in the Scheduling Handbook, at any dosage:

- Indications for medicines that contain amygdalin and hydrocyanic acid include cough and wheezing, profuse sputum, masses, lung abscess and intestinal abscess[4]; the consumer is not able to identify and self-manage these conditions without health professional input.
- Amygdalin and hydrocyanic acid can cause severe toxicity, even at low dosages; the risks to human health are significant and cannot be managed by packaging and labelling.
- There is evidence that these substances are inappropriately used in the treatment of cancer and possibly in other serious health conditions, including in the context of TCM; the risk of inappropriate use is not negligible.
- There is no compelling evidence of a public health benefit from wider availability to consumers.

On the basis of evidence provided in the application, I am not satisfied that amygdalin meets the standard for 'reasonable safety'.

In making my decision, I have taken into account the seven public submissions received during the pre-meeting consultation, noting that one was supportive of the proposed changes, two were partially supportive and four were opposed. Supportive responses referenced the need for a concentration limit that is aligned with food regulations and is easily detectable at analytical facilities. However, I note the Committee's advice that even a 5mg dose presents a significant risk to children, and that the preparations used in TCM are not checked for amygdalin content in practice. I find that the points raised in the submissions from the Australian Medical Association (AMA), NSW Poisons Information Centre (NSW PIC) and Pharmacy Guild of Australia (the Guild) were particularly pertinent:

- The AMA noted that the applicant's comparison between cyanide levels in food and TCM products is not appropriate; TCM products should go through the same process as other medicines to become registered on the Australian Register of Therapeutic Goods, including assessment for safety, quality, and efficacy. The AMA also reiterated their previous concerns regarding the risks of cyanide poisoning and the potential for misuse as an alternative to cancer therapy.
- The NSW PIC reported 4 calls regarding ingestion of amygdalin-containing preparations since September 2020. It was noted that TCM products can be relatively safe at low doses of

[4] Pharmacopeia of the People's Republic of China. 2015 edition. Chinese Pharmacopoeia Commission. People's Medical Publishing house.

amygdalin; however, serious concern was expressed regarding deliberate self-poisoning, chronic overuse and quality control of these products.

- The Guild opposed the amendments due to a lack of scientific evidence to support the purported indications for use, the potential for patients to delay appropriate treatment, and the risk of cyanide poisoning.

On balance, I find that amygdalin and hydrocyanic acid have an unfavourable risk/benefit profile to the extent that they should not exempted from scheduling and allowed for general retail sale at any concentration (outside of the current hydrocyanic acid cut-off in Appendix G). I consider that they meet the Schedule 10 factors and as such, I have made an interim decision to retain the current scheduling of these substances. To clarify the scheduling of TCM ingredients containing these substances, I have also decided to add a cross reference to apricot kernels in the index entries for amygdalin and hydrocyanic acid.

2.2 Interim decision in relation to bufexamac

Proposal

A Delegate of the Secretary of the Commonwealth Department of Health (the Delegate) proposed to amend the Schedule 4 entry for bufexamac to remove the existing exceptions for suppositories and dermal use.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision to amend the scheduling for bufexamac in the current Poisons Standard as follows:

Schedule 4 – Amend Entry

BUFEXAMAC ~~except:~~

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

~~b) in suppositories.~~

Index

BUFEXAMAC

Schedule 4

Materials considered

In making this interim decision, the Delegate considered the following material:

- The two public submissions, both including a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #34);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of

use of a substance; (c) the toxicity of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;

- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018);
- The Scheduling handbook: Guidance for amending the Poisons Standard; and
- A recent TGA safety alert regarding first aid creams containing bufexamac.

Summary of ACMS advice to the delegate

The Committee advised that the Schedule 4 entry for bufexamac be amended as follows:

Schedule 4 – Amend Entry

BUFEXAMAC ~~**except:**~~

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

~~b) in suppositories.~~

Index

BUFEXAMAC

Schedule 4

The Committee also recommended an implementation date of **1 February 2022.**

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the toxicity of a substance

Risks:

- Risk of allergic dermatitis, in some cases very severe, requiring hospitalisation.
- Efficacy is questionable.

b) the purposes for which a substance is to be used and the extent of use of a substance

- There are currently no registered medicines in Australia that use bufexamac as an active ingredient. The TGA has previously determined that there is insufficient evidence that bufexamac is an effective medicine in anti-inflammatory preparations.

c) the toxicity of a substance

- Severe allergic contact dermatitis in susceptible persons.
- There have been reports of hospitalisation due to serious skin reactions believed to be caused by bufexamac. All products containing bufexamac were cancelled from the ARTG in September 2020.

d) the dosage, formulation, labelling, packaging and presentation of a substance

Nil

e) the potential for abuse of a substance

Nil

f) any other matters that the Secretary considers necessary to protect public health

- No current products are registered for bufexamac.
- Given the nature of the risks, it is warranted that consultation with a medical practitioner is conducted prior to supply.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision to amend the Schedule 4 entry for bufexamac to remove the existing exceptions for suppositories and dermal use. The detailed reasons for my decisions follow.

I agree with the Committee's findings that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are: (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

I note that bufexamac is a non-steroidal anti-inflammatory drug (NSAID) previously used in first aid creams and suppositories in Australia. In September 2020, the TGA cancelled all bufexamac products in the ARTG after concluding that the safety and effectiveness profile of the substance was unacceptable[5]. It was determined that use of the substance is associated with a risk of serious skin reactions, and that there is little evidence demonstrating its effectiveness. I concur that the widespread use of bufexamac is not supported by the safety nor efficacy data.

I am of the view that the risk profile for bufexamac is not consistent with the exceptions listed in its Schedule 4 entry. The Scheduling Handbook provides that medicinal preparations exempted from scheduling must be able to be supplied, with reasonable safety, without any access to advice from a health professional. Given the risk of adverse reactions highlighted in the TGA review, and the absence of evidence that there is any public health benefit from wider availability, bufexamac does not fit these criteria. I have therefore determined that all preparations containing bufexamac require control through scheduling.

In considering appropriate controls for bufexamac, I note that the substance meets the Schedule 4 Scheduling Factors set out in the Scheduling Policy Framework (SPF 2018); in particular, the seriousness and severity of adverse effects are such that intervention by a medical practitioner is required. As such, I agree with the Committee's advice that bufexamac is appropriate for inclusion in Schedule 4 of the Poisons Standard.

In making my decision, I have taken into account the two public submissions received during the pre-meeting consultation, from the Australasian Medical Association and the Australasian College of Dermatologists. I note that both submissions were supportive of the proposal, citing the recent TGA review on bufexamac and the cancellation of all products containing the substance. It was also noted that preparations containing bufexamac can cause severe allergic

[5] https://www.tga.gov.au/alert/bufexamac

reactions that require treatment similar to that of burn victims and can sometimes result in long lasting sensitivities.

On balance, I find that the risk/benefit profile of bufexamac requires access only on the advice of medical practitioner and I have therefore decided to remove all exceptions from the current Schedule 4 entry.

Proposed implementation date

1 February 2022

2.3 Interim decision in relation to ibuprofen

Proposal

The applicant proposed to amend the Schedule 2 entry for ibuprofen to include a modified release (MR) 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.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, a Delegate of the Secretary has, in relation to the proposed amendment, made an interim decision not to amend the scheduling for ibuprofen in the current Poisons Standard.

Materials considered

In making this interim decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to ibuprofen;
- The six public submissions, all including a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the Meeting of the Advisory Committee on Medicines Scheduling (ACMS #34);
- Subsection 52E(1) of the *Therapeutic Goods Act 1989,* in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- The Scheduling handbook: Guidance for amending the Poisons Standard.

Summary of ACMS advice to the delegate

The Committee advised that the current scheduling for ibuprofen remains appropriate.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included: (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

Risks:

- Increased risk to the elderly, those with cardiovascular disease, renal disease and asthma and a rare incidence of hypersensitivity reactions and liver damage.
- Increased risk of gastrointestinal bleeding in persons who have a past history of gastric bleeding, stomach ulcers or prolonged use of ibuprofen.
- It should not be taken by those who have an allergy to aspirin or NSAIDs.

Benefits:

- Relief of pain and fever.
- Ibuprofen is well tolerated with an excellent safety profile at these dosages.
- Only a single tablet is required to be taken at reduced frequency.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Short term treatment for the relief of mild to moderate pain and fever associated with colds and flu, headaches, back pain, muscular aches and pain, dental related pain, arthritis, primary dysmenorrhoea, and other inflammatory conditions.

c) the toxicity of a substance

- Minimal toxicity at recommended dosage.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- 600mg MR formulation adding to the existing 200mg and 400mg IR formulations in Schedule 2.
- In addition to concerns about accidental overuse normal dosing, may lead to increased exposure to ibuprofen when IR dose may have been sufficient.

e) the potential for abuse of a substance

- Low.

f) any other matters that the Secretary considers necessary to protect public health

- Potential for patient confusion in a complex product landscape comprised of multiple products with differing administration instructions with regards to number of tablets to be taken and frequency of administration.

Reasons for the interim decision (including findings on material questions of fact)

I have made an interim decision not to amend the scheduling for ibuprofen in the current Poisons Standard. The detailed reasons for my decision follow.

I agree with the Committee's findings that the relevant provisions of section 52E of the *Therapeutic Goods Act 1989* are: (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

In making my decision, I have determined that the modified release ibuprofen 600mg formulation does not fit the Schedule 2 scheduling factors set out in the Scheduling Policy Framework (SPF 2018):

- The quality use of the medicine cannot be achieved by labelling, packaging, or provision of other information; advice from a pharmacist is required.
- Risks of dosing errors cannot be managed by a consumer through appropriate packaging and labelling.
- The use of the medicine is substantially safe for short term use. However, modified release formulations may facilitate longer term use of the substance, for the treatment of ailments that would require pharmacist or, more commonly, medical practitioner oversight.

I note that ibuprofen is a common nonsteroidal anti-inflammatory drug (NSAID) with a well-established safety profile in humans. While use is generally safe, it has the potential to cause significant adverse effects – including an increased risk of gastrointestinal bleeding, heart attack, stroke and kidney damage. These risks are relatively low when the substance is taken as indicated, as acknowledged through the inclusion of several ibuprofen preparations in Schedule 2 (and general sale). However, the current proposal relates to a modified release form, with different indications and patterns of use. As such, while the chemical safety profile is generally favourable, the dosing, uses and consumer awareness of these products require careful consideration.

I note that down-scheduling modified release preparations would result in a complex range of ibuprofen products in Schedule 2. These include 200 mg and 400 mg immediate release preparations, along with a 600 mg modified release preparation. Each has a unique set of administration instructions, which without pharmacist advice may heighten the risk of dosing errors. I also note that Australian consumers are predominantly familiar with immediate release tablets. In the case of modified release preparations, a consumer could inadvertently administer the maximum daily dose of ibuprofen in a single dose if not appropriately advised by a pharmacist. In the current environment, I consider that consultation with a pharmacist is required to prevent overdose.

I further note that the conditions treated by modified release products require pharmacist consultation irrespective of the potential for inadvertent overdose. These preparations are indicated for 'persistent pain' – which is inconsistent with minor, short term and self-diagnosable ailments that are treated by Schedule 2 medicines. I also note that any benefits of modified release preparations, including a reduction in 'dosing burden' and the smoothing out of peaks and troughs of action, relate to extended treatment courses that favour the long-term treatment of chronic conditions. I am of the view that labelling cannot adequately address these issues, and that the current scheduling of ibuprofen remains appropriate.

In making my decision, I have taken into account all six public submissions received during the pre-meeting consultation, including those from the Australasian Medical Association (AMA) and the Pharmacy Guild of Australia (the Guild):

- The AMA noted both public awareness and clinical experience relating to modified release preparations are too low – leading to an increased risk of dosing errors and irreversible side effects. The submission also noted that immediate release preparations with a moderate dose can already achieve good analgesic outcomes.
- The Guild further raised that there are significant drug interactions between NSAIDs and other medicines, as well as contraindications for use, which could be affected by a higher than recommended dose of ibuprofen. It was noted that pharmacist intervention is essential to identifying and managing the adverse effects, drug interactions and contraindications of modified release ibuprofen.

I concur with the concerns raised in these public submissions and the advice of the Committee. I am of the view that the risks of administrative errors, and difficulties in managing overdoses, outweigh the benefits of supply as a Schedule 2 substance. I have therefore made the interim decision to retain the current scheduling of modified release ibuprofen. Pharmacist intervention and appropriate referral to a medical practitioner is central to reducing potential harm to consumers and ensuring quality use of the medicine.