MEDSAFE

New Zealand Medicines and Medical Devices Safety Authority

Classification of paracetamol

Information paper for the Medicines Classification Committee

Medsafe
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MANATŪ HAUORA
MINISTRY OF HEALTH

Te Kāwanatanga o Aotearoa
New Zealand Government

Contents

Purpose and scope

Paracetamol is a widely used analgesic and antipyretic. There are many different paracetamol products available in Aotearoa New Zealand, in both single or combination presentations (eg, in combination with caffeine or ibuprofen). Paracetamol is available for self-selection by consumers, with both general sale and pharmacy-only presentations available.

The MCC considers recent changes to medicine scheduling in Australia at every meeting in the interest of Trans-Tasman harmonisation. The Australian Therapeutic Goods Administration (TGA) announced on 3 May 2023 that there would be scheduling changes to paracetamol. These scheduling changes will affect the maximum pack size of immediate release solid dose form paracetamol available in Australia at the general sale, pharmacy-only and restricted (pharmacist only) level. The MCC will consider whether New Zealand should harmonise with Australia on these paracetamol classification changes at the 71st MCC meeting (14 December 2023).

This document aims to provide the MCC with a regulatory background on paracetamol classification, along with data related to paracetamol use and safety in Aotearoa New Zealand.

Part A: Administrative Information

1. Classification of paracetamol

The current classification of paracetamol in Aotearoa New Zealand is described in Table 1.

Table 1: Current classification of paracetamol in Aotearoa New Zealand.

Ingredient	Conditions (if any)	Classification
Paracetamol	**except** when specified elsewhere in this schedule	Prescription
Paracetamol	in modified-release forms containing 665 milligrams or less	Restricted
Paracetamol	in liquid form; in suppositories; in tablets or capsules containing 500 milligrams or less and in packs containing more than 10 grams and not more than 50 grams; in powder form containing not more than 1 gram per sachet and more than 10 grams per pack; except in tablets or capsules containing 500 milligrams or less and in packs containing not more than 10 grams; except in powder form in sachets containing 1 gram or less and in packs of not more than 10 grams	Pharmacy-only
Paracetamol	in tablets or capsules containing 500 milligrams or less and in packs containing not more than 10 grams; in powder form in sachets containing 1 gram or less and not more than 10 grams	General Sale

Source: Medsafe Medicines Classification Database (accessed 20 September 2023).

The maximum pack sizes of immediate release solid dose form paracetamol are as follows:

- 10 grams for general sale medicines (equivalent 20 x 500 mg tablets or capsules)
- 50 grams for pharmacy-only medicines (equivalent 100 x 500 mg tablets or capsules).

In addition, as according to regulation 39A of the Medicines Regulations 1984 there is a limit of three months' supply for prescription medicines. This could consist of up to 720 x 500 mg paracetamol tablets or capsules, 360 grams, if prescribed at the maximum daily dose of 8 x 500 mg paracetamol tablets or capsules. If dispensed for one month's paracetamol prescription at maximum daily dose this would be 240 x 500 mg paracetamol tablets or capsules, 120 grams paracetamol. However, the Pharmaceutical Management Agency (Pharmac) limit funding for prescribed paracetamol (500 mg solid oral dose forms) to 300 tablets per prescription, this limit can be waived by the prescriber under certain circumstances (see Pharmac Community Schedule, accessed on 3 November 2023).

2. Labelling and warning statements

Regulation 22 of the Medicines Regulations 1984 allows for the regulator (Medsafe) to require mandatory warning statements on medicine labels. A list of mandatory warning statements for medicines can be found in the label statements database (LSD).

All non-prescription medicines containing paracetamol must carry the label statement 'CONTAINS PARACETAMOL', in addition the following warning statements are required for non-prescription paracetamol (excluding liquid formulations, and modified release):

- Keep to the recommended dose.
- Dose: every four to six hours when required, no more than four doses in 24 hours. *This statement should be amended for combination products.*
- If you think you may have given/taken too much paracetamol, or an overdose ring the Poisons Information Centre on 0800 764 766 or go to a hospital straightaway even if you feel well. The damaging effect on the liver can take time for your body to notice.
- Do not give or take with other products containing paracetamol.
- Keep out of reach and sight of children.
- Children and adolescents: Do not give/take this medicine for longer than 48 hours at a time unless advised by a healthcare professional.
- Adults: Do not take this medicine for longer than a few days at a time unless advised by a healthcare professional.

Refer to the LSD for required warning statements for non-prescription liquid and modified-release presentations of paracetamol.

In addition to the required warning statements, there are also specific packaging requirements for paracetamol. Regulation 37(1) of the Medicine Regulations 1984 specifies that paracetamol, and all medicines containing paracetamol, must be enclosed in a safety container (eg, blister pack) for sale.

3. Paracetamol products

There are a number of different paracetamol products available in Aotearoa New Zealand. Table 2 summarises the number of paracetamol products in immediate release solid oral dose forms (at 500 mg strength) consented to in Aotearoa New Zealand by pack size. The most common pack sizes are 20 tablet/capsules packs (containing 10 grams paracetamol) which would be classified as general sale and 100 tablet/capsule packs (containing 50 grams paracetamol) which would be classified as pharmacy-only.

Table 2: Approximate summary of approved solid dose form medicines containing 500 mg paracetamol alone for oral use in Aotearoa New Zealand.

Pack Size (500 mg solid dose forms)	No. of Products Approved
2 tablets/ capsules	1
8 tablets/ capsules	2
10 tablets/ capsules	11
12 tablets/ capsules	11
16 tablets/ capsules	10
20 tablets/ capsules	33
24 tablets/ capsules	3
30 tablets/ capsules	2
32 tablets/ capsules	9
40 tablets/ capsules	1
48 tablets/ capsules	9
50 tablets/ capsules	16
60 tablets/ capsules	2
80 tablets/ capsules	1
96 tablets/ capsules	5
100 tablets/ capsules	19
120 tablets/ capsules	2
150 tablets/ capsules	2
1000 tablets/ capsules	10

Medsafe Medicines Product/ Application Search (accessed 25 October 2023).

Most paracetamol products sold in New Zealand are blister packed tablets. The packing configuration is 2 x 5 blister or 2 x 6 blister strips.

Paracetamol pack sizes of 1000 tablets/ capsules are approved as dispensing packs, they are not available for purchase over-the-counter.

4. Recent considerations of paracetamol classification

Medicine Classification Committee (MCC) consideration

The classification of paracetamol (in various dose forms) has been considered nine times by the MCC since 24 November 2015. A summary of the MCC consideration of paracetamol since 24 November 2015 is summarised in Table 3.

Table 3: Medicine Classification Committee (MCC) meeting discussions and recommendations for paracetamol since 24 November 2015.

MCC Meeting	Date	Comments
54th	24/11/2015	The following article referencing paracetamol overdose in New Zealand was referred to the MCC: Freeman N, Quigley P. Care versus convenience: Examining paracetamol overdose in New Zealand and harm reduction strategies through sale and supply. N Z Med J. 2015 Oct 30;128(1424):28-34. PMID: 27377019. The MCC recommended that Medsafe should review the pack size of paracetamol and report back to the MCC at a future meeting.
57th	1/11/2016	Paracetamol was considered as a Trans-Tasman harmonisation item following scheduling changes in Australia. The MCC recommended that the paracetamol pharmacy-only entry should be amended to a single pack size limit of 100 tablets or capsules, that no other changes should be made to the existing classifications of paracetamol, that Medsafe should write to the Pharmacy Council and the Food and Grocery Council appraising them that general sales packs of paracetamol should not be sold online by grocery retailers. Pack sizes sold by online pharmacies should be restricted to 32 tablets or capsules and similar oversight should be applied as to instore shopping.
58th	16/05/2017	A response letter from Retail New Zealand had been received, which highlighted mixed views from retailers about the effectiveness of limiting the sale of multiple packs and ceasing the sale of paracetamol via online channels. The MCC recommended they write back to Retail NZ explaining committee criteria for medicine reclassification and noting that the sector's approach to the sale of paracetamol will be taken into account when considering the reclassification of future medicines and their availability for general sale.
59th	07/11/2017	A response was received from Retail New Zealand emphasising that in the previous letter they had clearly outlined a mix of views amongst members and that some members were willing to comply with the MCC requests regarding paracetamol.
60th	26/04/2018	Medsafe proposed a reclassification of modified-release paracetamol from pharmacy-only to restricted. The MCC recommended that modified release paracetamol be reclassified from a pharmacy-only to a restricted medicine.
61st	02/11/2018	A valid objection was received to the MCC recommendation that modified release paracetamol be reclassified from a pharmacy-only to a restricted medicine, on the grounds that new safety information has become available. The MCC recommended that modified release

		paracetamol be reclassified from a pharmacy-only to a restricted medicine.
65th	27/10/2020	A recommendation was received from the coroner that classification changes should be made to the quantities of paracetamol that should be available for purchase. The MCC noted that the recommendation received relates to restrictions on numbers of packs in grams per retail transaction, therefore was not a formal submission within the mandate of the Committee for decision. However, the MCC acknowledged that the issues surrounding paracetamol are serious and require extensive consultation. The MCC recommended that there be no change to paracetamol classification.
66th	11/05/2021	Paracetamol (liquid formulations) and modified release paracetamol were referred to the MCC as Trans-Tasman harmonisation items following classification changes in Australia. The MCC recommended that they defer recommendations for paracetamol (liquid formulations) to a later meeting. The MCC recommended that the classification of modified release paracetamol should remain unchanged.
70th	25/05/2023	Paracetamol (liquid formulations) was considered as a Trans-Tasman harmonisation item following deferral from the 66th MCC meeting. Paracetamol (liquid formulations) was considered for a maximum pack size limit for presentations available pharmacy-only. The MCC recommended that the consideration of the classification of paracetamol (liquid formulations) be deferred to a future meeting.

Medicines Classification Committee Minutes URL: https://www.medsafe.govt.nz/profs/class/minutes.asp. (accessed 31 October 2023).

Health Select Committee consideration of paracetamol classification

A petition to 'place a purchase limit on pharmaceuticals such as paracetamol in supermarkets' was presented to the House of Representatives on 8 June 2022. The petitioner requested: that the House of Representatives pass legislation which places a purchase limit on pharmaceuticals such as paracetamol.

The Health Select Committee (the Committee) published their report in response to the aforementioned petition on 8 June 2023. The report examined the petitioner's request along with the availability and safe use of paracetamol in Aotearoa New Zealand. The petitioner noted concerns of paracetamol misuse and overdose (both intentional and accidental).

The Committee noted that Australia had announced on 3 May 2023 that the classification of paracetamol was to change to further restrict pack sizes available over-the-counter, with an implementation date for February 2025. The Committee noted that Medsafe planned to refer Australia's change in paracetamol classification to the MCC as a Trans-Tasman harmonisation item for review. The Committee stated that they intend to monitor the results of this review with interest.

5. Classification of paracetamol in other countries

The classification of paracetamol differs internationally. The classification of paracetamol in Australia, Canada, United Kingdom (UK) and United States is outlined in Table 4.

Country	Paracetamol Pack Size Classification	Notes
Australia	Unscheduled: in packs with less than 16 tablets or capsules Pharmacy-only: in packs with less than 50 tablets or capsules Pharmacist only: in pack sizes up to 100 tablets or capsules.	Announced classification on 3 May 2023. This classification will come into effect 1 February 2025.
Canada	Unscheduled	No formal pack size limit found.
United Kingdom	Unscheduled: in packs with less than 16 tablets or capsules. Pharmacist only: in packs with less than 48 tablets and more than 16 tablets. Prescription: in packs with 100 tablets.	
United States	Unscheduled	No formal pack size limit found.

Table. 4. Classification of immediate release solid dose form paracetamol pack sizes in selected OECD countries (Buckley et al 2022).

Paracetamol scheduling in Europe

The UK reduced the maximum pack size of paracetamol available at outlets other than registered pharmacies (equivalent New Zealand general sales) from 25 to 16 tablets or capsules in 1998 (Hawkins et al 2007). This change was in response to the larger number of paracetamol poisoning in the UK. There are number of studies that have investigated the effectiveness of this classification change on paracetamol poisonings, with varied results (Hawkins et al 2007).

In France, Germany and Italy there are no paracetamol packs available for general sale. Instead, they can only be purchased from a pharmacy and in smaller pack sizes than those available in New Zealand (France 8 g (16 tablets), Germany 10 g (20 tablets), Italy 15 g (30 tablets)) (Buckley et al 2022).

Paracetamol scheduling changes in Australia

On the 3 May 2023, the TGA announced final scheduling changes for paracetamol (Therapeutic Goods Administration 2023). These changes resulted in new maximum pack sizes for immediate release paracetamol of:

- 16 tablets/capsules for unscheduled products (*previously 20 tablet/ capsule limit)*,
- 50 tablets/capsules for pharmacy-only (schedule 2) products *(previously 50 tablet/ capsule limit)*,

- 100 tablets/ capsules for pharmacist only (schedule 3) products.

Paracetamol classification changes in Australia will also mean that blister or strip packaging is mandated for all tablet/capsules products containing paracetamol which are unscheduled or pharmacy-only.

Australia's scheduling changes also placed greater restrictions on the pack sizes of paracetamol containing wrapped powders or sachets of granules. The new pack size limits are:

- 10 wrapped powders or sachets (each containing 1000 mg) for unscheduled products,
- 25 wrapped powders or sachets (each containing 1000 mg) for pharmacy-only (schedule 2) products (*previously was 50 sachets)*,
- 50 wrapped powders or sachets (each containing 1000 mg) for pharmacist only (schedule 3) products.

Implementation of paracetamol scheduling changes in Australia will take place on 1 February 2025. The scheduling changes in Australia were made taking into consideration the benefits of paracetamol as an effective and widely used analgesic and the risks of morbidity and mortality associated from intentional misuse, and a need for effective self-poisoning harm minimisation.

6. Classification of paracetamol options

The MCC is to consider whether a recommendation for a reduction in paracetamol immediate release solid dose form pack size limits available at general sales, pharmacy-only and restricted level to align with Australia is appropriate in the Aotearoa New Zealand context.

Option one:

Should the MCC recommend alignment with Australia, the classification would be changed to (or something similar):

For paracetamol (500 mg) tablets/ capsules:

- *General sale: maximum pack size limit changes from 10 grams to 8 grams.*
- *Pharmacy-only: maximum pack size limit changes from 50 grams to 25 grams.*
- *Pharmacist only: new maximum pack size limit of 50 grams.*

For paracetamol (1000 mg) sachets in powder form:

- *General sale: maximum pack size limit remains at 10 grams.*
- *Pharmacy-only: new maximum pack size limit of 25 grams.*
- *Pharmacist only: new maximum pack size limit of 50 grams.*

Option two:

Recommend that the classification of immediate release solid dose form paracetamol in Aotearoa New Zealand remains unchanged.

Limitations

The Medicines Act 1981 and Medicines Regulations 1984 do not allow for restrictions to be placed on the number of packs of paracetamol that can be sold in supermarket. There may be opportunity under the Therapeutic Products Act 2023 (which will supersede the Medicines Act 1981 and Dietary Supplements Regulations 1985 when it comes into effect) to establish provision for the regulator to place restrictions on the number of packs of paracetamol that can be sold over-the-counter.

Part B: Parameters for consideration

7. Paracetamol safety

Mechanism of toxicity

Paracetamol toxicity is driven by the formation of the toxic N-acetyl-P-benzo-quinone (NAPQI) alkylating metabolite. The human liver has endogenous glutathione stores which can conjugate NAPQI and produce a non-toxic metabolite, mercapturic acid, which can then be eliminated through urinary excretion. However, if a paracetamol overdose occurs the glutathione stores can become exhausted and thereby unable to detoxify the NAPQI metabolite. If NAPQI is not detoxified, it can bind to hepatocytes (cells in the liver) which can result in hepatic toxicity (Ghaffar and Tadvi 2014).

Therapeutic index

Paracetamol is a widely-used medicine. The toxicity profile of paracetamol is well established. In adults the toxic dose of paracetamol is considered to be ≥10 grams or ≥200 mg/kg/24 hours, in a 10 kg child this would only equate to ≥2 grams of paracetamol (Therapeutic Goods Administration 2020; Chiew et al 2020). The maximum daily dose of paracetamol is 4 grams per day (Noumed Pharmaceuticals Limited 2021).

Signs and symptoms of paracetamol toxicity

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Following paracetamol overdose patients may initially be asymptomatic or only develop nausea, vomiting and abdominal pain. Signs of liver injury usually occur after 24 to 48 hours after the overdose and peak after 4-6 days. Individuals should call the Poisons Information Centre on 0800 764 766 or go to the hospital straightaway if they think they have given/ taken too much paracetamol, or an overdose even if they feel well because of the risk of delayed, serious liver damage (Noumed Pharmaceuticals Limited 2021; Meriative Micromedex 2023).

8. Paracetamol in community

Paracetamol poisoning has long been a topic of discussion for the MCC, with paracetamol being an agenda item at an MCC meeting nine times since 24 November 2015.

Paracetamol was found to be the most commonly misused or overdosed medication in Wellington Hospital Emergency Department between 2007-2012, accounting for 23% (*N= 747 people)* of medication poisoning episodes (Freeman and Quigley 2015).

Paracetamol is a readily accessible medicine in New Zealand for common indications of pain and fever. Individuals are able to access paracetamol over-the-counter, or by prescription which as of 1 July 2023 does not require a co-payment (previously was $5) and can be for up to 720 x 500 mg paracetamol tablets or capsules for those who clinically require long-term therapy. A risk of paracetamol overdose is that individuals may unknowingly or knowingly combine different paracetamol products. For example, individuals may take solid, oral dose paracetamol at the maximum daily dose along with other paracetamol combination products or presentations.

A New Zealand 2020 study of 201 households found that 19% of homes had between 10 grams to 30 grams of paracetamol present and 53% had 30 grams (*equivalent to 60 tablets)* or more present (Kumpula et al 2020). The study also found that the majority of paracetamol in the combined total sample and in the individual households was prescribed paracetamol (Kumpula et al 2020).

Summary of data from contacts to the New Zealand National Poisons Centre regarding exposures to paracetamol and where medical assessment was advised in 2017 to 2022

Paracetamol poisoning is the most common cause of severe acute liver injury in Western countries and the most common reason for calls to Poisons Information Centres in Australia and New Zealand (Chiew et al 2020).

Medsafe contacted the New Zealand National Poisons Centre (NPC) for any up-to-date information they may have on paracetamol overdose in Aotearoa New Zealand. The NPC provided a report on 28 February 2023 for the MCC which can be accessed here.

The time-period of 1 January 2017 to 31 December 2022 were investigated and reported, key findings in this report are as follows (National Poisons Centre 2023):

- 3,267 human exposure records with acute paracetamol table/ capsule ingestions exposures with NPC advising medical assessment were identified,
- Proportion of cases with a reported ingested total of 30 grams or more of paracetamol increased from 2017 to 2020, cases remain relatively consistent from 2020 to 2022.
- A significant proportion of paracetamol exposures occurred in young people aged 15 to 24 years.

There are a number of significant limitations to the data summarised above, which are highlighted in the full report.

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