



Australian Government

Department of Health

Therapeutic Goods Administration

OTC medicine monograph: Paracetamol for oral use

Version 1.1, July 2021

TGA Health Safety
Regulation

Copyright

© Commonwealth of Australia 2021

This work is copyright. You may reproduce the whole or part of this work in unaltered form for your own personal use or, if you are part of an organisation, for internal use within your organisation, but only if you or your organisation do not use the reproduction for any commercial purpose and retain this copyright notice and all disclaimer notices as part of that reproduction. Apart from rights to use as permitted by the *Copyright Act 1968* or allowed by this copyright notice, all other rights are reserved and you are not allowed to reproduce the whole or any part of this work in any way (electronic or otherwise) without first being given specific written permission from the Commonwealth to do so. Requests and inquiries concerning reproduction and rights are to be sent to the TGA Copyright Officer, Therapeutic Goods Administration, PO Box 100, Woden ACT 2606 or emailed to tga.copyright@tga.gov.au.

Contents

Introduction	4
Active substance	4
Dosage forms and strengths	4
Indications	5
Therapeutic indications for inclusion in the Australian Register of Therapeutic Goods (ARTG)	5
Label indications	5
Directions for use	5
Adults and children 12 years and over	5
Liquid dose products for children 1 month to 12 years	6
Solid dose products for paediatric use	7
Labels	8
Quality requirements	8
Active premixes	8
Finished product specifications	8
Tablets	9
Soluble tablets	9
Capsules	9
Oral suspensions	9
Oral solutions	10
Powders for oral solution	11
Container/measuring device	11

Introduction

This OTC Medicine Monograph outlines the requirements for Australian market authorisation of oral medicines containing paracetamol as a single active ingredient when applied for as an OTC New Medicine N2 application. Proposed medicines must comply with all aspects of the monograph relevant to their strength and dosage form to qualify for evaluation as an N2 application.

This monograph should be read in conjunction with the document [Requirements for OTC new medicine N2 applications](#).

Active substance

This monograph only applies to medicines containing paracetamol (CAS no. 103-90-2).

Dosage forms and strengths

Acceptable dosage forms and strengths are shown in the table below.

Active substance	Dosage strengths	Dosage forms (excludes modified release dosage forms)
Paracetamol	250 mg	Soluble tablet
	500 mg	Tablet (uncoated, film coated, gelatin coated, soluble, effervescent) Capsule
	500 mg	Oral powder
	600 mg	Oral powder
	1000 mg	Oral powder
	24 mg/mL (120 mg/5 mL)	Oral liquid or suspension
	48 mg/mL (240 mg/5 mL)	Oral liquid or suspension
	100 mg/mL	Oral liquid

Indications

Therapeutic indications for inclusion in the Australian Register of Therapeutic Goods (ARTG)

Temporary relief of pain associated with headache, migraine headache, tension headache, sinus pain, toothache, dental procedures, backache, muscular aches and pains, arthritis, osteoarthritis, rheumatic pain, period pain, fibrositis, neuralgia, sore throat, tennis elbow, and colds and flu. Reduces fever.

For paediatric formulations, in addition to the indications above that are appropriate to the age group, the following indications would be acceptable: relief of pain associated with teething, earache and/or immunisation.

Label indications

All or most of the indications listed above should be included as label indications, as appropriate, depending on the intended age group. Label indications must not be restricted to, or emphasise, a single indication or subset of indications (e.g. cold and flu symptoms only, period pain only or headache only). Terms should be exactly as specified above and qualified by the words “temporary relief of pain associated with...”.

Directions for use

Adults and children 12 years and over

Directions for use must be as shown in the table below.

Dosage form and strength	Single dose	Dose interval	Maximum daily dose
500 mg tablets, capsules, oral powder	1 – 2 tablets, capsules or sachets	every 4-6 hours, as necessary	8 tablets in 24 hours
600 mg oral powder	1 sachet	every 4-6 hours, as necessary	6 sachets in 24 hours
1000 mg oral powder	1 sachet	every 4-6 hours, as necessary	4 sachets in 24 hours

- For soluble and effervescent tablets and oral powders, appropriate instructions for preparation of the dose form must be included.
- Include the statement *Do not give to children under x years* (where ‘x’ years is the youngest age for which dosage instructions are included on the labels).

Liquid dose products for children 1 month to 12 years

Dosages must be as shown in the table below.

Age	Average body weight (kg)	Single dose (mL)	Single dose (mL)	Single dose (mL)
		24 mg/mL oral liquid	48 mg/mL oral liquid	100 mg/mL oral liquid
1 – 3 months	4 – 6	-	-	0.6 – 0.9 mL
3 – 6 months	6 – 8	-	-	0.9 – 1.2 mL
6 – 12 months	8 – 10	-	-	1.2 – 1.5 mL
1 – 2 years	10 – 12	6 – 8 mL	3 – 4 mL	1.5 – 1.8 mL
2 – 3 years	12 – 14	8 – 9 mL	4 mL	-
3 – 4 years	14 – 16	9 – 10 mL	4 – 5 mL	-
4 – 5 years	16 – 18	10 – 11 mL	5 – 6 mL	-
5 – 6 years	18 – 20	11 – 13 mL	6 mL	-
6 – 7 years	20 – 22	13 – 14 mL	6 – 7 mL	-
7 – 8 years	22 – 25	14 – 16 mL	7 – 8 mL	-
8 – 9 years	25 – 28	16 – 18 mL	8 – 9 mL	-
9 – 10 years	28 – 32	18 – 20 mL	9 – 10 mL	-
10 – 11 years	32 – 36	20 – 23 mL	10 – 11 mL	-
11 – 12 years	36 – 41	23 – 26 mL	11 – 13 mL	-

Doses should be given every 4-6 hours as necessary, with no more than four doses in 24 hours.

- Doses must be presented on the labels with ages (in months or years), weights (kg) and volumes (mL). Dosage instructions must also include advice consistent with the following:

If you know that your child's weight is less than the weight corresponding to their age in the table, choose the dose for their weight.

- A medicine label could include only a subset of the age groups – for example, dosing for ages 1-5 years or 6-12 years only.
- Where dosage instructions for children under 6 months of age are included, the dosage instructions should clearly advise that the medicine only be given to this age group following the advice of a doctor.

- Labels must state the maximum daily dose – for liquid preparations that include doses for more than one age group, this should be stated as: *Do not give more than 4 doses in 24 hours.*
- The dosage instructions must include the following statement:
Do not give to children under x years [or months] (where 'x' years / months is the youngest age for which dosage instructions are included on the labels).
- For 100 mg/mL strength liquid products, a measuring device that can accurately deliver the required doses must be included - see [Container/measuring device](#) below.
- A statement to 'Shake the bottle before use' must be included for oral suspensions.
- Instructions on how to use a supplied measuring device may be included if necessary. Requirements for measuring devices are included under [Container/measuring device](#).

Solid dose products for paediatric use

Solid dosage forms, strengths and dosages are acceptable for paediatric use only as specified in the table below.

Dosage form and strength	Age (years)	Average weight (kg)	Single dose (tablets)	Dose interval	Maximum daily dose
250 mg soluble tablets	2 – 3	12 – 14	½ – 1 tablet	every 4-6 hours, as necessary	4 doses in 24 hours
	3 – 7	14 – 22	1 tablet	every 4-6 hours, as necessary	4 doses (4 tablets) in 24 hours
	7 – 10	22 – 32	1 – 2 tablets	every 4-6 hours, as necessary	4 doses in 24 hours
	10 – 12	32 – 41	2 tablets	every 4-6 hours, as necessary	4 doses (8 tablets) in 24 hours
500 mg tablets/capsules	7 – 12	22 – 41	½ – 1 tablet or 1 tablet* or 1 capsule	every 4-6 hours, as necessary	4 tablets/capsules in 24 hours

* 1 tablet single dose may be specified if the tablet is not divisible.

- Half tablet doses are only acceptable if tablets are scored and can appropriately deliver the intended dose (see [Requirements for OTC new medicine N2 applications; Control of finished product](#)).
- 250 mg soluble tablets with directions for use in children 12 years and under must include both ages and weights in the dosing instructions as above.
- For 500 mg tablets/capsules that include dosage for children aged 7-12 years, in addition to adults and children aged 12 years and over, average weight may be omitted from the dosage instructions.

- For soluble tablets, where more than one paediatric age group is specified, the maximum dose should be stated in numbers of tablets for each age group, or as *Do not give more than 4 doses in 24 hours*. For 500 mg tablets/capsules, the maximum paediatric dose should be specified in number of tablets/capsules (i.e. 4 tablets in 24 hours).
- The dosage instructions must include the following statement:
Do not give to children under x years (where 'x' years / months is the youngest age for which dosage instructions are included on the labels).

Labels

Labelling must comply with all relevant Australian requirements, as detailed in the document [Requirements for OTC new medicine N2 applications](#).

Quality requirements

In addition to the quality requirements outlined in the document [Requirements for OTC new medicine N2 applications](#), the following specific requirements apply to paracetamol monograph medicines:

Active premixes

Where paracetamol is sourced by the finished product manufacturer as part of an active premix,¹ the finished product manufacturer must, as a minimum, control the premix for appearance/description, identification (one chromatographic and one non-chromatographic test), assay, related substances, residue on ignition or sulfated ash, and heavy metals. The limits applied should be taken from either the BP or USP monograph for paracetamol/acetaminophen (with all limits to be taken from the same monograph), adjusted where necessary to account for the presence of excipients in the mixture (for example, assay). Additional requirements in relation to active premixes are specified in the document [Requirements for OTC new medicine N2 applications](#).

Finished product specifications

In addition to other requirements specified in the document [Requirements for OTC new medicine N2 applications](#), the finished product specifications must comply, at a minimum, with the relevant set of requirements below.

The requirements below include all relevant BP general monograph/USP General Chapter requirements and TGO 78 requirements. Further reference to these is not required. References to pharmacopoeial monographs below refer to the **current** monograph at time of application.

¹ For more information on proprietary ingredient mixtures that contain an active ingredient see Streamlining proprietary ingredient categories.

Tablets

The tests and limits in the BP monograph **Paracetamol Tablets** with the addition of:

- tablet appearance
- uniformity of dosage units (BP)
- microbiological quality, in compliance with TGO 77.

Soluble tablets

The tests and limits in the BP monograph **Soluble Paracetamol Tablets** with the addition of:

- tablet appearance
- uniformity of dosage units (BP)
- dissolution (900 mL phosphate buffer pH 5.8, paddle at 50 rpm, NLT 70% after 45 minutes)
- microbiological quality, in compliance with TGO 77.

Capsules

The tests and limits in the BP monograph **Paracetamol Capsules** with the addition of:

- capsule appearance
- uniformity of dosage units (BP)
- microbiological quality as required by USP, BP and Ph Eur and in compliance with TGO 77.

Oral suspensions

The tests and limits in the BP monograph **Paracetamol Oral Suspension** with the addition of:

- suspension appearance
- dissolution (900 mL phosphate buffer pH 5.8, paddle at 50 rpm, NLT 70% after 45 minutes)
- content of 4'-chloroacetanilide² (NMT 10 ppm wrt paracetamol)
- content of unspecified impurities² (any individual NMT 0.1% wrt paracetamol, total NMT 0.5% wrt paracetamol)
- content of any preservatives included in the formulation
- microbiological quality, in compliance with TGO 77.

or

The tests and limits in the BP monograph **Paediatric Paracetamol Oral Suspension** with the addition of:

- suspension appearance
- dissolution (900 mL phosphate buffer pH 5.8, paddle at 50 rpm, NLT 70% after 45 minutes);
- content of any preservatives included in the formulation

² Use assay methods specified for Paediatric Paracetamol Oral Suspension BP, or alternative equivalent or superior methods. Methods must be appropriately validated as described in [Requirements for OTC new medicine N2 applications](#).

- microbiological quality, in compliance with TGO 77.

or

The tests and limits in the USP monograph **Acetaminophen Oral Suspension** with the addition of:

- suspension appearance
- dissolution (900 mL phosphate buffer pH 5.8, paddle at 50 rpm, NLT 70% after 45 minutes)
- content of 4'-chloroacetanilide² (NMT 10 ppm wrt paracetamol)
- content of unspecified impurities² (any individual NMT 0.1% wrt paracetamol, total NMT 0.5% wrt paracetamol)
- content of any preservatives included in the formulation
- microbiological quality, in compliance with TGO 77.

Oral solutions

The tests and limits in the BP monograph **Paediatric Paracetamol Oral Solution** with the addition of:

- solution appearance
- content of 4'-chloroacetanilide² (NMT 10 ppm wrt paracetamol)
- content of unspecified impurities² (any individual NMT 0.1% wrt paracetamol, total NMT 0.5% wrt paracetamol)
- content of any preservatives included in the formulation
- microbiological quality, in compliance with TGO 77.

or

The tests and limits in the USP monograph **Acetaminophen Oral Solution** with the addition of:

- solution appearance
- content of 4-aminophenol³ (NMT 0.5% wrt paracetamol)
- content of 4'-chloroacetanilide² (NMT 10 ppm wrt paracetamol)
- content of unspecified impurities² (any individual NMT 0.1% wrt paracetamol, total NMT 0.5% wrt paracetamol)
- content of any preservatives included in the formulation
- microbiological quality, in compliance with TGO 77.

³ Use assay method specified for Acetaminophen Oral Suspension USP or Paediatric Paracetamol Oral Suspension BP, or an alternative equivalent or superior method. The method must be appropriately validated as described in [Requirements for OTC new medicine N2 applications](#).

Powders for oral solution

The following tests/limits:

- powder appearance
- solution appearance
- identification (as for Paracetamol Tablets BP)
- suitable test and limit for pH of solution
- dissolution (using conditions and limits for Paracetamol Tablets BP)
- uniformity of dosage units (BP)
- assay⁴ (90.0-110.0% LC)
- impurities (as for Paracetamol Tablets BP)
- microbiological quality, in compliance with TGO 77.

Container/measuring device

- Paracetamol products must be sold in containers that comply with Therapeutic Goods Order No 80, Child Resistant Packaging Requirements for Medicines.
- If a measuring device is to be supplied with the medicine, calibrations must be exclusively in metric units and must allow all the doses shown on the labels to be measured accurately. Details of the calibrations on the measuring device must be provided with the submission (a sample may also be requested). Further considerations and requirements regarding measuring devices are detailed in [ARGOM Appendix 2 – Guidelines on quality aspects of OTC applications, Section 8: Finished product container](#).

⁴ Use assay methods specified for Paracetamol Tablets BP or Acetaminophen Tablets USP, or alternative equivalent or superior methods. Methods must be appropriately validated as described in [Requirements for OTC new medicine N2 applications](#).

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	OTC Medicines Evaluation/OMA	06/09/2013
V1.1	Addition of footnote to information about active premixes	COMB	June 2021

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6203 1605
<https://www.tga.gov.au>

Reference/Publication #D21-2714960