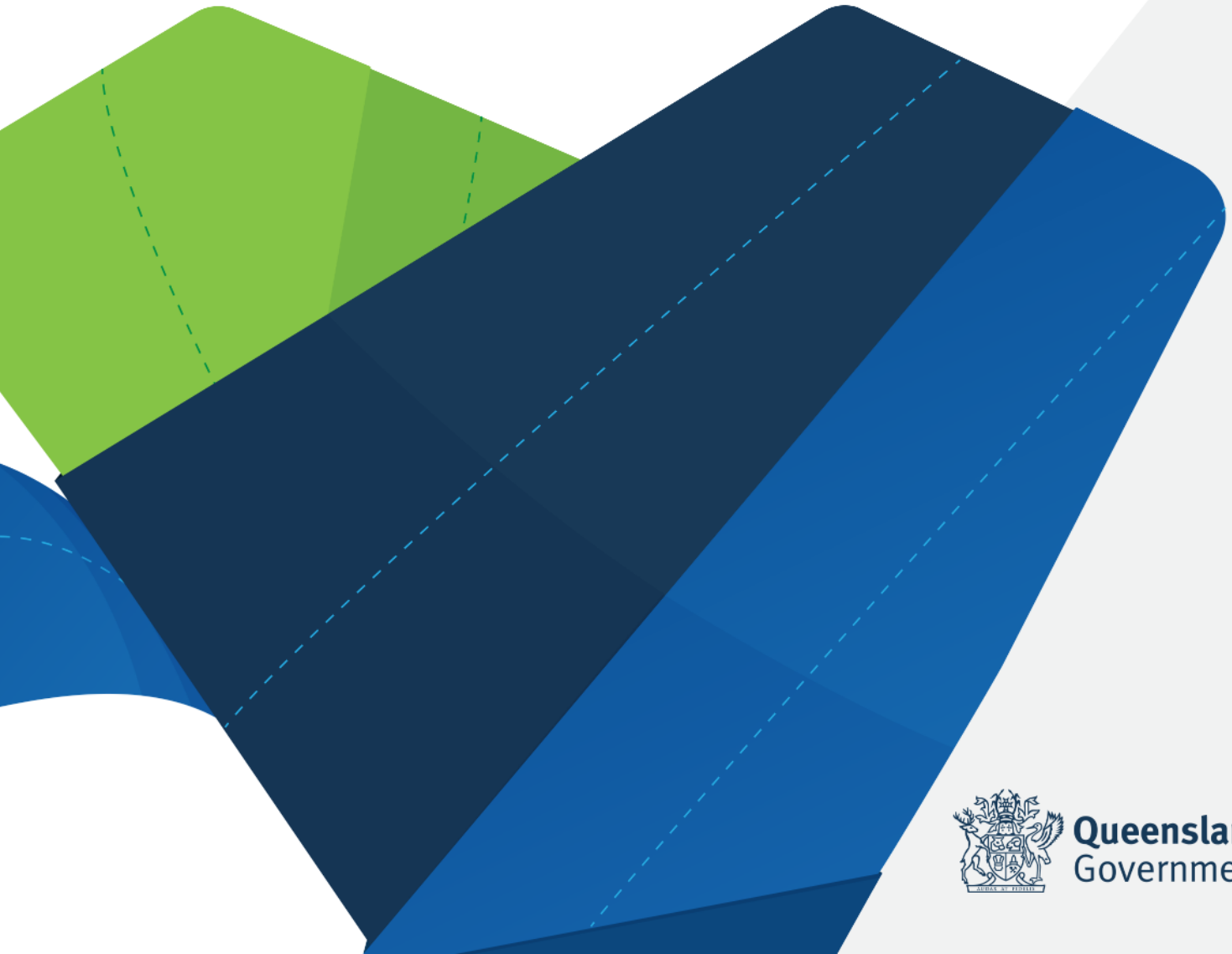
Queensland Health

Guideline for Safe Paracetamol Use

January 2023



Queensland Government

Guideline for Safe Paracetamol Use - January 2023

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Purpose

This guideline provides recommendations regarding best practice for the judicious, effective, and safe use of paracetamol. It is to be used in conjunction with the relevant product information and any local specialist procedures. In the event of paracetamol poisoning refer to local guidelines or procedures for management of toxicity.

Scope

This guideline provides information for all employees, contractors and consultants within the Department of Health divisions, commercialised business units and Hospital and Health Services.

Background

Paracetamol (also known as acetaminophen) is a common and widely used non-opioid analgesic. It is also an effective and commonly used antipyretic medication. Paracetamol has a favourable safety profile when used in therapeutic doses, particularly when compared to alternative analgesics such as non-steroidal anti-inflammatory drugs (NSAIDs) or opioids. This safety profile sees it commonly used as the first-line analgesic for mild to moderate pain, particularly of soft tissue and musculoskeletal origin.

However, it is important to balance the need for effective pain management with any potential safety implications. In acute overdose (intentional or unintentional), paracetamol can lead to severe and sometimes fatal hepatotoxicity. Liver damage does not result from paracetamol itself, but from its toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI). There have been case reports where patients receiving therapeutic paracetamol doses have had liver toxicity; this is extremely rare and has generally occurred in patients who are acutely unwell with additional proposed risk factors for toxicity (such as old age, low body weight, concomitant medicines that induce liver enzymes, hepatitis or chronic alcohol consumption) (DTB, 2018).

Prescribing

Non-pharmacological intervention is considered first line option prior to paracetamol use. If paracetamol is to be used, consider whether a dose adjustment is required. Although there is limited evidence for clinical factors that increase risk of paracetamol toxicity, **clinical judgement should be used to adjust dose/frequency of paracetamol for acutely unwell patients with any of the following potential risk factors** (see Table 1).

Table 1: Clinical factors that may increase risk of paracetamol toxicity in acutely unwell patients

Clinical consideration	Comments
Severe hepatic impairment (i.e. Child Pugh C)	• Extremely rare. • In stable chronic liver disease, there is no accumulation of paracetamol or toxic metabolites. (Caparrotta, Antoine, & Dear, 2018)
Systemic sepsis or febrile illness	
Extremes of bodyweight	• Dose according to ideal bodyweight (refer to dosing calculator). However, if chronically underweight it may be more appropriate to use actual bodyweight. • There is no evidence to support an increase to the maximum daily dose. (van Rongen, et al., 2016) (Zempsky, Bhagat, & Siddiqui, 2020) • Dose adjustment for lower bodyweight range (i.e. less than 50 kg) is recommended in this guideline. However, an appropriate dose has not been investigated using liver injury or hepatotoxicity as a primary end point. (Caparrotta, Antoine, & Dear, 2018)
Age	• Neonates are at greater risk of hepatotoxicity. • Paracetamol is the preferred non-opioid analgesic for older people. (Schug, et al., 2020) • Lack of good quality clinical evidence to suggest older people have a clinically significant difference in risk of paracetamol toxicity. (Caparrotta, Antoine, & Dear, 2018) • Consider dose adjustment (lower starting dose and/or reduced frequency) for frail elderly patients. (DTB, 2018)
Chronic use of interacting medicines	• Check for drug interactions. This list is not exhaustive however carbamazepine, phenytoin, and isoniazid are examples of medicines that may increase the risk of hepatotoxicity due to induction of liver enzymes. (DTB, 2018)

Continued overleaf

Clinical consideration	Comments
Recent prior paracetamol intake	• Review paracetamol intake within the previous 6 to 8 hours. • Include over-the counter cough and cold preparations, administration by parent/carer. • Consider patient/carer confusion between multiple strengths of liquid formulations. • Note potential use of inappropriate formulation according to patient age. Examples include an adult rather than paediatric formulation, paediatric formulation designed for an older age group (e.g. sibling).
Chronic under-nutrition	• The effect of malnutrition and starvation is difficult to assess as patients may have concurrent acute or chronic illness which may increase risk of paracetamol toxicity. (Caparrotta, Antoine, & Dear, 2018) • Prolonged fasting or vomiting. • Malnutrition impacting on synthetic liver function.
Chronic, excessive alcohol consumption	• Note there is no high-quality clinical evidence from prospective trials to indicate chronic alcohol consumption alone increases the risk of paracetamol toxicity. (Caparrotta, Antoine, & Dear, 2018)
Glutathione depletion	• Conditions such as cystic fibrosis, HIV infection, and eating disorders can cause depletion of glutathione which is involved in metabolism of paracetamol. However, a literature review suggested no convincing evidence that these diseases increase the risk of paracetamol toxicity. (Caparrotta, Antoine, & Dear, 2018)

Source: Adapted from (Schug, et al., 2020), (DTB, 2018), (Micromedex, 2022), (Caparrotta, Antoine, & Dear, 2018), (van Rongen, et al., 2016), (Zempsky, Bhagat, & Siddiqui, 2020)

Notes:

1. Paracetamol may be associated with a higher risk of end-stage kidney disease in patients with newly diagnosed chronic kidney disease; the risk is higher with increased paracetamol dose exposure. (Kuo, Tsai, Liu, Lee, & Yang, 2010)
2. According to emerging evidence paracetamol use during pregnancy may influence premature closure of the fetal ductus arteriosus; it is recommended that use in pregnancy is limited to the minimum dose and duration clinically necessary. (Schug, et al., 2020)

Although there is limited evidence supporting dose reduction for patients with risk factors that may increase the risk of paracetamol toxicity (Caparrotta, Antoine, & Dear, 2018), incidents have occurred in these patients and a conservative approach may be warranted. In particular, consider a reduction in dose and frequency for frail elderly patients or patients with low bodyweight (i.e. less than 50 kg).

Safe dosing of paracetamol requires consideration of the patient's age and body weight and duration of therapy. Refer to the following tables for recommended doses. Additionally, for

paediatric patients aged 1 month to 11 years refer to the Children's Health Queensland Hospital and Health Service guidelines (Paediatric Acute Pain Management (health.qld.gov.au), if applicable. For neonates and infants less than 1 month seek specialist advice and refer to the Queensland Clinical Guidelines Neonatal medicine: Paracetamol (health.qld.gov.au) monograph.

Table 2: Paracetamol Dosing for Infants and Children aged up to 11 years

Age	Dose	Frequency	Maximum Paracetamol Dose in 24 hours
Neonate and Term infant up to 1 month	Refer to the Queensland Clinical Guidelines Neonatal medicine: Paracetamol (health.qld.gov.au) monograph		
Infant from 1 month to 11 years	15mg/kg/dose **Maximum 1g/dose**	Every 6 hours	4 doses (i.e. 60mg/kg) **(Maximum 4g/24 hours)**
			Dose adjustment advice: If risk factors for toxicity (as per Table 1) or if less than 5kg bodyweight, reduce frequency to every 8 hours, therefore maximum dose in 24 hours: 3 doses (i.e. 45mg/kg)

Notes:

1. Product Information for paracetamol solution for intravenous infusion advises lower IV doses for children 10kg or less (7.5mg/kg every 6 hours). However, the upper limit of these doses has been used safely at the Children's Hospital Queensland and is supported by the New South Wales Therapeutic Advisory Group.
2. Avoid controlled release preparations in paediatrics.

Table 3: Paracetamol Dosing for Adults and Children aged 12 years and older

Bodyweight	Dose	Frequency	Maximum Paracetamol Dose in 24 hours
50kg or greater	500mg to 1g	Every 6 hours	4 doses **(Maximum 4g/24 hours)**
			Dose adjustment advice: If risk factors for toxicity (as per Table 1) maximum: 3g/24 hours If severe hepatic impairment: 2g/24 hours
Less than 50kg	15mg/kg/dose **Maximum 750mg/dose**	Every 6 hours	4 doses **(Maximum 3g/24 hours)**
			Dose adjustment advice: If severe hepatic impairment, maximum: 3 doses/24 hours

Notes:

1. If giving a controlled release preparation, dose as 2 tablets (1,330mg) every 8 hours. Maximum 3 doses in 24 hours (i.e. 3,990mg/24 hours). Dose adjustment may still be required—see above for advice.
2. Avoid controlled release preparations in paediatrics.

When prescribing any liquid medication (including intravenous paracetamol solution for infusion), the dose in milligrams must always be specified.

Examples:

1. For an 85-year-old adult weighing 45 kilograms, who requires a liquid paracetamol formulation, determine the appropriate strength by considering available stock and what is most appropriate. If the 240mg/5mL strength is available, the dose would be calculated as follows:

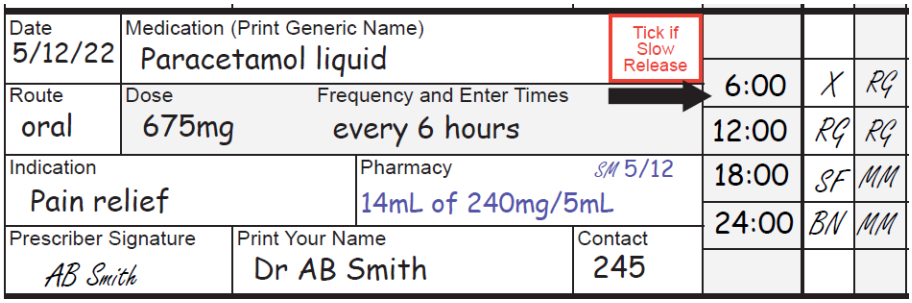
   15mg/kg/dose x 45kg = 675mg

   240mg ÷ 5mL = 48mg/mL

   675mg ÷ 48mg/mL = 14mL

   Enteral paracetamol dose = 675mg (14mL x 240mg/5mL) every 6 hours (see Figure 1)

Figure 1: Example paracetamol oral prescription for adult weighing 45kg



Date	Medication (Print Generic Name)	Tick if Slow Release			
5/12/22	Paracetamol liquid				
Route	Dose	Frequency and Enter Times	6:00	X	RG
oral	675mg	every 6 hours	12:00	RG	RG
Indication	Pharmacy SM 5/12		18:00	SF	MM
Pain relief	14mL of 240mg/5mL		24:00	BN	MM
Prescriber Signature	Print Your Name	Contact			
AB Smith	Dr AB Smith	245			

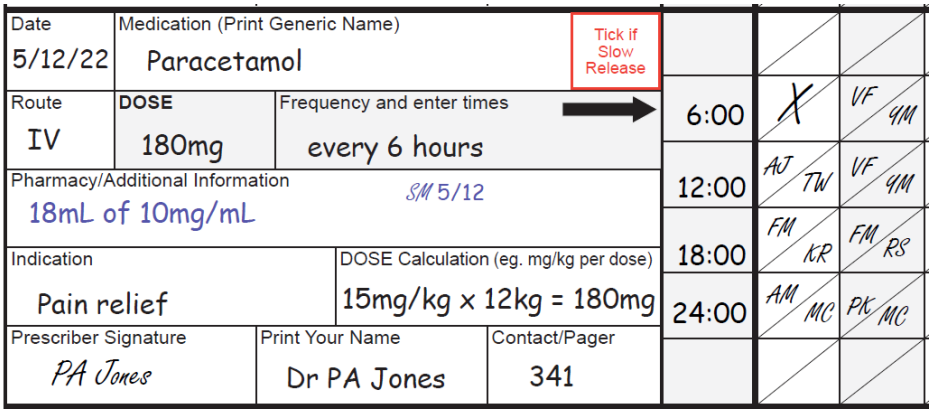
2. For a two-year-old child weighing 12 kilograms, who is unable to take paracetamol by the oral or nasogastric route and for whom rectal paracetamol is not suitable, intravenous paracetamol would be given. The concentration of intravenous paracetamol is 10mg/mL. Therefore, the dose would be calculated as follows:

    15mg/kg/dose x 12kg = 180mg

    180mg ÷ 10mg/mL = 18mL intravenous paracetamol

    IV paracetamol dose = 180mg (18mL) IV every 6 hours

Figure 2: Example paracetamol intravenous prescription for 2-year-old weighing 12kg



Date	Medication (Print Generic Name)	Tick if Slow Release			
5/12/22	Paracetamol				
Route	DOSE	Frequency and enter times	6:00	X	VF / YM
IV	180mg	every 6 hours	12:00	AJ / TW	VF / YM
Pharmacy/Additional Information	SM 5/12		18:00	FM / KR	FM / RS
18mL of 10mg/mL			24:00	AM / MC	PK / MC
Indication	DOSE Calculation (eg. mg/kg per dose)				
Pain relief	15mg/kg x 12kg = 180mg				
Prescriber Signature	Print Your Name	Contact/Pager			
PA Jones	Dr PA Jones	341			

Administration

Right patient

Confirm the patient's name, address, and date of birth against the medication order in the medication chart or electronic medication management system. Also check the unique record number on the patient's identification band to ensure it matches the medication order. Confirm with the patient whether there are any adverse drug reactions to paracetamol.

Right drug

Check for duplicate paracetamol orders both within and across the regular and PRN sections of all medication charts or electronic medication management systems. Duplicate paracetamol orders should be ceased. If there are duplicate orders, contact the prescriber for clarification of the patient's analgesic requirements.

Check for combination products that contain paracetamol. Examples include:

- 'cold and flu' preparations
- paracetamol powder preparations (e.g. Lemsip)
- paracetamol with codeine
- paracetamol with tramadol
- paracetamol with ibuprofen
- paracetamol with metoclopramide
- paracetamol with caffeine.

Query unfamiliar products with a pharmacist or a product reference (e.g. MIMS) to ascertain whether or not the product contains paracetamol.

Right dose

Check the strength of any liquid formulations prescribed and double check the dose is correct according to patient weight. Confirm the order does not exceed the maximum daily dose after accounting for clinical risk factors and associated dose adjustment.

Right route

Ensure paracetamol is administered by the route ordered and ensure the route is appropriate for the patient.

Right time

Check the timing of previous paracetamol doses (including the stat dosing section on the front of the NIMC, or if the patient had taken paracetamol prior to hospital presentation) to ensure that the dose intended to be administered is within the prescribed dosing interval.

Right to refuse

Patients have the right to refuse to take a medicine. Ensure the patient/carer has been counselled on the associated benefits and risks so that they can make well informed decisions about whether to take the medicine. Discuss with medical staff the ongoing requirement for paracetamol if the patient is refusing.

Clinicians have the right to refuse to administer a medicine when, for whatever reason, they feel uncomfortable with the order. Examples include clinical risk factors for toxicity, apparent excess, or duplicate orders. Refusal by a clinician must be discussed with senior nursing staff and medical staff. Details of decisions must be documented in the progress notes.

Documentation

When paracetamol is given to the patient, document administration immediately afterwards in the medication chart, or the medication section of the electronic medication management system. If a regular order for paracetamol is not administered for any reason, annotate the administration section of the medication order as appropriate and document details in the progress notes.

Monitoring

Intravenous paracetamol orders should be reviewed within 48 hours. If ongoing paracetamol treatment is required, consider converting to oral administration as appropriate. If treatment continues beyond 72 hours with intravenous administration, liver function and INR monitoring should commence from this point.

Regular enteral (oral/rectal) paracetamol orders should be reviewed after 96 hours. Liver function and INR should be checked after 5 to 7 days with oral or rectal administration, especially if the patient has clinical factors that may increase the risk of paracetamol toxicity (see Table 1).

Practice points

- Take a full history and assess for potential risk factors for toxicity prior to initiation of paracetamol treatment. Identify if, and when, any products containing paracetamol have been ingested including both prescribed and over-the-counter products.
- Recognise and treat any suspected cases of paracetamol hepatotoxicity without delay according to local protocols. Advice on suspected poisoning with paracetamol is available from the Poisons Information Centre on 131126.
- Consider limiting the number of paracetamol-containing preparations available in the facility.
- Medicine orders should be written using the active ingredient ‘paracetamol’. For intravenous paracetamol the order should specify ‘IV paracetamol’ as the active ingredient to emphasise route of administration and intended formulation, minimising the risk of inadvertent administration of an oral formulation being given via the IV route.
- Avoid using the rectal route of administration in patients with neutropenia.

Guideline custodian

Medication Services Queensland

Email: medicationsafety@health.qld.gov.au

Version control

Version	Amendments	Author/s	Approved
Version 1_0	Original guidance	Justin Lee	May 2014
Version 2_0	Reviewed against current evidence and practice	Sarah Mathers	Feb 2023
Version 2_1	Amendment to Table 1 extremes of bodyweight; Amendment to Table 3 to clarify maximal dosing for less than 50kg; Amendment to Figures 1 and 2	Sarah Mathers	March 2023
Version 2_2	Link to document amended; Table 2 information clarified	Sarah Mathers	April 2023

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