SESLHDMG/111

Medicine Guideline for the Safe Use of

PARACETAMOL

Health
South Eastern Sydney
Local Health District

Paracetamol IS A HIGH-RISK MEDICINE **USE WITH CAUTION AND ENSURE THE DIRECTIONS WITHIN THIS PROTOCOL ARE FOLLOWED CAREFULLY**	
Areas where Protocol/Guideline applicable	SESLHD Facilities
Authorised Prescribers:	Medical Officers, Nurse Practitioners, Nurses/Midwives (under approved SESLHD Nurse/Midwife medicine protocols)
Important Safety Considerations	Adverse events associated with paracetamol toxicity have been associated with: • The concurrent use of multiple paracetamol-containing products and confusion between different strengths, formulations, and route of administration • Incorrect dosing including using Actual Body Weight instead of Ideal Body Weight (IBW) in obese paediatric patients and prescribing standard dosing regimens in patients with identified risk factors for toxicity • Inadequate review of treatment • Accidental overdose through ongoing administration of regular and PRN paracetamol Electronic Medication Management systems provide safeguard (e.g., prescribing and administration alerts) to assist with safe prescribing and administration of paracetamol where eMM is implemented. Hybrid (electronic and paper) medication management systems require caution to avoid duplication of doses or dose administration within 4 to 6-hour dosing interval. Information about paracetamol administration must be included in handover. Prior to prescribing or administering paracetamol clinicians MUST: 1. ascertain if paracetamol has been recently ingested, 2. check that no other formulations of paracetamol are concurrently prescribed or administered, 3. ensure the time interval between doses are appropriate and that the administration of the dose will not exceed the safe maximum daily dose of paracetamol (from all sources including combinations containing paracetamol). In circumstances where the dose is calculated based on patient weight (e.g., paediatrics) ensure it does NOT exceed the maximum recommended paracetamol dose (i.e., do not exceed 1 g per dose). This protocol sets out measures to reduce the likelihood of adverse events with use of paracetamol in SESLHD facilities.

Indication for use	Consider non-pharmacological intervention prior to paracetamol use. Paracetamol is an effective analgesic and antipyretic agent and may be used as first line therapy for: • mild to moderate pain • the symptoms of fever, when temperature is above 37.5°C The SESLHD Medicines Formulary outlines the paracetamol preparations available for inpatient initiation or continuation and the associated prescribing restrictions.
Clinical condition	Before prescribing paracetamol a full medical history and medication history (to include over the counter products and complementary medicines) should be obtained to determine the potential for paracetamol toxicity and/or any possible adverse drug reaction and to identify paracetamol intake from all sources. According to emerging evidence paracetamol use during pregnancy may influence premature closure of the foetal ductus arteriosus; it is recommended that use in pregnancy is limited to the minimum dose and duration clinically necessary.
Proposed Place in Therapy	**Oral route** Oral paracetamol is recommended for first line use wherever possible. **Rectal route** Rectal paracetamol is effective and indicated when oral dosing is not possible. Absorption of paracetamol given rectally is erratic and the time taken to achieve maximum concentration is unpredictable. Oral dosing should be resumed as soon as possible. **Intravenous route** Intravenous (IV) paracetamol is reserved for short-term management of mild to moderate pain or fever when oral/NG or rectal administration is not feasible, limited to patients who are nil by mouth or under specialist supervision in anaesthesia, intensive care, or pain management. Use must be reviewed every 24 hours, with a prompt transition to oral, enteral, or rectal administration, or cessation, as soon as clinically appropriate.
Adjunctive Therapy	Paracetamol is first-line analgesic in adults and children for acute nociceptive pain because of its favourable adverse effect profile. It can be used alone, or as a component of multimodal analgesia. Multimodal analgesia combines analgesic agents with different mechanisms of action which can result in synergistic effects while reducing individual drug dosages. Most commonly, paracetamol is combined with a non-steroidal anti-inflammatory drug (NSAID) or an opioid regimen.

Contra-indications	• Patients with a previous history of hypersensitivity to paracetamol or to any of the product's excipients. • **IV Paracetamol:** Severe liver disease • **Rectal Paracetamol:** Avoid use in neutropenic patients
Precautions	Hypovolemia: Use the IV formulation with caution in patients with severe hypovolemia (e.g., due to dehydration or blood loss). . Clinical judgement should be used to adjust dose/frequency of paracetamol for patients with any of the following potential risk factors that may increase the risk of acute liver injury: • systemic sepsis/febrile illness (particularly in children) • prolonged fasting, vomiting or dehydration • chronic malnutrition • hepatic impairment • renal impairment • sustained administration of high doses • chronic, excessive alcohol use • tobacco use • frail elderly patients • underweight patients • oedematous patients and those above a healthy weight • prolonged use of IV preparations • chronic use of interacting medicines
Important Drug Interactions	**Warfarin:** The anticoagulant effect of warfarin may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect. Warfarin dosage may require reduction if paracetamol and warfarin are taken concurrently for a prolonged period of time. **Other hepatotoxic medications:** The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes such as carbamazepine, phenytoin, rifampicin, and isoniazid. **Probenecid:** Probenecid may increase the serum concentration of paracetamol by inhibiting their hepatic glucuronidation. **Cholestyramine:** Cholestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

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Dosage

Adults and children 12 years and above

Formulation		*Dose and frequency*	*Max dose in 24 hours*
Oral / Rectal	Weight		
	> 50kg	1 g every four to six hours	**Maximum of 4 doses in 24 hours**
	≤ 50 kg and > 33 kg	15 mg/kg/dose every four to six hours	**60 mg/kg/day (not exceeding 3g)**
	≤ 33 kg and > 10 kg	15 mg/kg/dose every four to six hours	**60 mg/kg/day (not exceeding 2g)**
Oral controlled release (665 mg)		2 tablets every 6–8 hours swallowed whole.	**Maximum 6 tablets (3990 mg) daily**
IV	Weight		
	> 50kg	1 g every four to six hours	**Maximum of 4 doses in 24 hours**
	≤ 50 kg and > 33 kg	15 mg/kg/dose every four to six hours	**60 mg/kg/day (not exceeding 3g)**
	≤ 33 kg and > 10 kg	15 mg/kg/dose every four to six hours	**60 mg/kg/day (not exceeding 2g)**

1. Reduce dose and dosing frequency in frail elderly patients or under-weight patients < 50 kg and those with risk factors for toxicity (see Precautions)
2. Avoid controlled release preparations in paediatrics.

Children 3 months to 11 years *

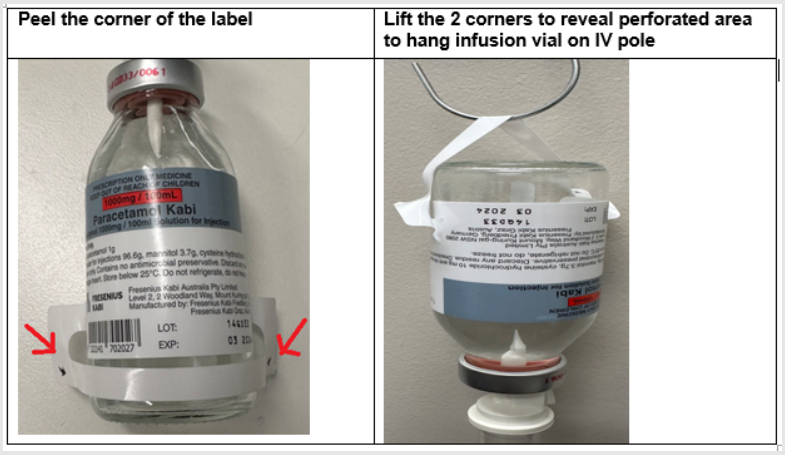
Route	*Dose and frequency*	*Max dose in 24 hours*
Oral	15 mg/kg/dose# every four to six hours **(do not exceed 1 g per dose)** In acute injury or surgery an initial loading dose of 20mg/kg# may be considered.	Maximum of 90 mg/kg in 24 hours for a maximum of 48 hours Subsequent days: maximum of 60 mg/kg in 24 hours After 8 days: specialist review recommended **Do not exceed 4 grams total in 24 hours**
Rectal	Loading dose 30-40mg/kg# then 20mg/kg# every 6 to 8 hours. Round dose down to nearest suppository strength	
IV	15mg/kg# every 6 hours **(do not exceed 1 g per dose)**	Maximum of 60 mg/kg in 24 hours

for obese children lean body weight should be used for dosing. Ideal weight can be estimated from growth charts.

Neonates and infants less than 3 months treatment with paracetamol requires specialist management.

Duration of therapy	Paracetamol requires regular medical review to ensure treatment continues to be appropriate **Oral and rectal paracetamol for acute pain or symptomatic high fever:** Review no later than 24 hours after commencement and at least every 48 hours thereafter. **IV paracetamol:** Review every 24 hours and replace with enteral paracetamol at the earliest opportunity. If dosing for longer than 48 hours, monitoring of liver function tests, including International Normalised Ratio (INR) should be carried out. **Patients receiving paracetamol for chronic pain:** Review no later than 48 hours after commencement, then as required. Care should be taken when prescribing paracetamol for extended periods of time in children, frail elderly and/or patients with risk factors for toxicity.

Prescribing Instructions	Before prescribing paracetamol (including under a nurse/midwife-initiated protocol), a full medical history, including medication history, should be obtained from the patient or their carer to identify factors with the potential to increase the risk of paracetamol toxicity. Prior to prescribing, clinicians are to ascertain if paracetamol has been recently ingested, check that no other formulations of paracetamol are concurrently prescribed or administered, ensure the time interval between doses are appropriate and that the administration of the dose will not exceed the safe maximum daily dose of paracetamol (from all sources including combinations containing paracetamol). The following information is to be documented on all paracetamol orders: • Accurate weight (for children, frail elderly patients and adults with low body weight) • Orders must be expressed in milligrams (mg) or grams (g) per dose • For children, frail elderly patients and/or adults less than 50 kg: calculate dose in mg/kg • Frequency • Route • Indication • For IV orders: Maximum duration of therapy (or stop date/time) • For PRN orders: Maximum dose in 24 hours **To reduce potential for dosing errors:** • Paracetamol (and/or paracetamol containing products) should not be prescribed both regularly and 'PRN'. Order in one section of the medication chart ONLY. Ordering in both the regular and as required 'PRN' sections of the chart may potentially lead to overdose. • Paracetamol orders should specify a single route of administration, (i.e., oral OR rectal OR intravenous) particularly relevant for paper-based charts. • Do not prescribe multiple formulations concurrently. • Different paracetamol-containing products should not be prescribed concurrently. • Orders should be written using the active ingredient drug name. Where a brand name is used on the order (e.g., combination products) the active ingredient term 'paracetamol' or 'contains paracetamol' should be documented adjacent to the brand name. • Orders must be expressed in milligrams (mg) or grams (g) per dose

Administration Instructions	When being used to treat fever, patients should have their temperature recorded prior to the first administration of paracetamol to gain accurate baseline of temperature. Prior to administering paracetamol (including nurse/midwife-initiated paracetamol), clinicians are to ascertain: 1. if paracetamol has been recently ingested (by checking with the patient and the medication chart) to ensure sufficient time has lapsed between doses 2. check that no other formulations of paracetamol are concurrently prescribed or administered, and 3. that the administration of the dose will not exceed the safe maximum daily dose of paracetamol (from all sources including combination paracetamol / codeine combinations). **4. if de-escalating to an alternative route is possible (for IV paracetamol ONLY).** A second person check is required for administration of: • intravenous paracetamol • all doses administered to paediatric patients (irrespective of the route of administration) • opioids in accordance with NSW health Policy Directive *Medication Handling* (PD2022_032) requirements. **<u>Paracetamol IV Infusion</u>**: Administer over 15 minutes. To hang the paracetamol 1 g in 100 mL infusion vial on IV pole, carefully peel the corner of the label on vial in the direction of the arrow (see picture below). Then lift the 2 corners of the vial to reveal perforated area to hang the infusion vial on IV pole (see picture below) **Peel the corner of the label** / **Lift the 2 corners to reveal perforated area to hang infusion vial on IV pole**  IV paracetamol is 10 mg/mL. Do NOT confuse the dose for IV paracetamol in mg and mL as this can lead to 10-fold dosing error. To mitigate the risk of “ten-fold” errors, IV paracetamol doses for paediatric patients should be drawn up in the appropriate syringe size (avoid hanging a part vial) – see below.

	13 – 30 kg use 50 mL syringe | < 13 kg use 20 mL syringe
Monitoring requirements	For patients receiving IV paracetamol, if treatment is to continue beyond 48 hours, monitoring of liver function tests (LFTs), including International Normalised Ratio (INR), should be carried out.
Management of Complications	It is important for clinicians to promptly identify patients at risk of developing acute liver injury with paracetamol poisoning. The prognosis for recovery is good with early recognition and treatment. Treatment of paracetamol toxicity should be guided by Prescribing Protocol SESLHDPR/566 - Acetylcysteine IV in Acute Paracetamol Overdose
Storage requirements	Oral liquid Formulations – where possible/appropriate only one strength of oral liquid paracetamol products should be kept as ward stock. Preparations compounded with codeine are to be handled as accountable drugs (S4D).
Patient Education	Patients and/ or their parents or carers being discharged on paracetamol should be provided with specific information and education regarding paracetamol administration. They should also be counselled that many over-the-counter products recommended for cold, cough, headache etc. may also contain paracetamol and should not be taken concurrently. Refer to SESLHD Paracetamol Fact Sheet. Professional Health Care Interpreters should be utilised for patient education for patients and/ or carers who are not fluent in English or who are Deaf.
Additional Resources	Safety Alert - UPDATED: Critical disruption to supply – Intravenous (IV) paracetamol solution for injection/infusion – 01 March 2024
Basis of Protocol/Guideline:	1. NSW Health PD2020_045 - High-Risk Medicines Management 2. Australian Medicines Handbook – Paracetamol, last updated January 2020 3. The Children's Hospital at Westmead Pain Management Guideline, March 2021 4. NSW TAG Inc. PARACETAMOL USE. A Position Statement of the NSW Therapeutic Advisory Group Inc. December 2008 5. Pain and analgesia [published 2020 December]. In: Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; accessed 25/08/2023. https://www.tg.org.au
Groups consulted in development of this guideline	Medication Safety Pharmacists Network

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AUTHORISATION	
Author (Name)	Katie Hargreaves
Position	Quality Use of Medicines Pharmacist
Department	SESLHD Pharmacy
Position Responsible (for ongoing maintenance of Protocol)	Quality Use of Medicines Pharmacist
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