

PARACETAMOL - SCH

PRACTICE GUIDELINE[®]

DOCUMENT SUMMARY/KEY POINTS

- Paracetamol is the drug most frequently administered to small children world-wide. It is a widely used analgesic and antipyretic agent and has a very long safety record when used in optimum dosage. However, it may be under or over-used in certain situations.
- All patients prescribed paracetamol at SCH must undergo a complete and accurate medical and medication history to assess their risk of hepatotoxicity
- Well accepted indications for paracetamol use include analgesia and the prophylaxis and treatment of some immunisation reactions. The appropriateness of its use in the treatment of fever remains controversial.
- The oral route is preferred over rectal use which displays erratic absorption.
- Intravenous use is restricted to authorised prescribers under strict criteria including review every 24 hours.
- Intravenous paracetamol has been associated with dosing errors relating to concurrent use of oral paracetamol, dose calculation errors, non-adherence to labelling directions and tenfold errors due to confusion between 'mg' and 'mL'.

CHANGE SUMMARY

- This document replaces SCH.C.20.08 and provides information on recent changes to safety recommendations for paracetamol IV in children and other recommendations based on up to date references.
- IV paracetamol may be used in term neonates and older
- Link to Paracetamol Overdose-Assessment and Management SCHN added to document
- Oral syringes must be used for the administration of liquid medications

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1 st October 2015	Review Period: 3 years
Team Leader:	QUM & AMS Pharmacist	Area/Dept: Pharmacy

READ ACKNOWLEDGEMENT

- This document should be read & acknowledged by clinical staff involved in medication handling and provision of medicines information education to patients and carers.

TABLE OF CONTENTS

1	Rationale	3
2	Recommendations	3
	Indications	3
	Precautions	3
	<i>Table 1: RISK FACTORS FOR HEPATOTOXICITY</i> ^{2, 3,7-11}	4
2.1	Prescription Requirements.....	4
3	Analgesia	5
	DOSE and ROUTE for Analgesia	5
	<i>Maintenance dose:</i>	5
	<i>Loading dose (e.g. for pre-medication):</i>	6
4	Fever Control ^{1, 6, 7}	6
	DOSE and ROUTE for Fever Control	7
5	IV Paracetamol	7
6	References	7
	Paracetamol Treatment Algorithm	8

1 Rationale

Paracetamol is the drug most frequently administered to small children world-wide. It is a widely used analgesic and antipyretic agent and has a very long safety record when used in optimum dosage. However, it may be under or over-used in certain situations.^{1,2,7} Evidence indicates that in sick children who receive multiple doses of four hourly or high dose paracetamol there may be an increased risk of toxicity. A “risk profile” for potential hepatotoxicity with therapeutic use includes: sustained administration of high doses (greater than 90mg/kg/day) to a sick child who is younger than 2 years for more than 1 day and administration of multiple doses of adult strength formulations.^{2,7,8}

These guidelines are intended to provide recommendations regarding appropriate indications and dosing regimens to ensure safe and efficacious use of paracetamol in hospitalised children.

2 Recommendations

Indications

Well accepted indications for paracetamol use include analgesia and the prophylaxis and treatment of some immunisation reactions.⁵ The appropriateness of its use in the treatment of fever remains controversial.⁷

Precautions

The risk of hepatotoxicity and recommendations for appropriate dosing may differ depending on the specific indication for which paracetamol is being used and any coexisting conditions. Therefore, all paracetamol prescriptions should be preceded by a careful risk assessment and accurate medical and medication history (see [Table 1](#)). If the risk benefit ratio is considered unfavourable, consideration should be given to no treatment or to cautious use of lower doses and shorter duration of therapy with frequent clinical review. If the risk benefit ratio is considered favourable, follow the dosing recommendations outlined below.

Overdose Paracetamol overdose may be initially asymptomatic and can occur due to accidental ingestion, chronic suprathreshold dosing (see table 1), intentional self-harm or administration error. If overdose with liquid or tablet paracetamol is suspected refer to Paracetamol Overdose Assessment and Management Practice Guideline. If IV paracetamol overdose is suspected consult SEATS – South-East Area Toxicology Service as soon as practicable.

Table 1: RISK FACTORS FOR HEPATOTOXICITY^{2, 3,7-11}

- 1.** Impaired liver function which may be associated with any of the following and compounded by previous paracetamol administration prior to admission.
 - Prolonged fasting or dehydration (e.g. poor oral intake for greater than 24hrs)
 - Chronic under-nutrition
 - Intercurrent febrile illness
 - Underlying hepatic injury or metabolic problems
 - Younger age (under 2 years)
 - Obesity
 - Genetic predisposition (e.g. family history of hepatotoxic reaction)
- 2.** Co-administration of drugs which induce hepatic microsomal enzymes (Cytochrome P450 inducers)
 - Anticonvulsant e.g. barbiturates, carbamazepine, primidone
 - Anti-tuberculosis agents e.g. isoniazid, rifampicin
 - Alcohol
- 3.** Co-administration of other products containing paracetamol (e.g. liquid cough/cold remedies).
 - These products are not generally recommended in young children. However, if they are used, the paracetamol component must be included in calculations for the maximum total daily dose.
- 4.** Administration and dosing errors
 - Lack of awareness or understanding regarding the multiple different dose strengths of paediatric different formulations of paracetamol: e.g. infant drops (100mg/mL) vs liquid paracetamol (120mg/5mL or 240mg/5mL).¹²
 - Potential overdosing of an overweight child according to actual body weight OR underweight child according to age group on product
 - Exceeding the total allowable dose by dosing every 4 hours

Every effort should be made to educate parents and other caregivers on the appropriate use of paracetamol. "Adult strength" formulations (including "slow release" preparations) should not be administered to young children.

2.1 Prescription Requirements

All paracetamol prescriptions should specify:

Indication for use (e.g. pain; symptomatic high fever [e.g. > 38.5°C]; immunisation)

Dose (in mg/kg) appropriate for specific indication, risk factor status, route of administration, age and weight of child.

If a patient is oedematous or obese, the **ideal weight** for age and height should be used. See C.20.22 Drug Dosing for Overweight and Obese Patients-SCH

Frequency of dosing

Route of administration (single route only: no IV/PO)

Maximum daily dose (specified in mg/kg) or maximum number of doses per day

Maximum duration of therapy

3 Analgesia

- Children experiencing pain should receive appropriate analgesia. Optimum management involves individualised doses given at regular intervals. Ad hoc or “prn” doses should only be used if pain is truly of an intermittent nature.
- Suggested maximum doses are those above which analgesia is unlikely to be further improved and risk of toxicity increases.
- If pain AND fever are present concurrently, then lower doses (as for fever control) are recommended (and this should be specified in a single order).
- Other pharmacological methods (e.g. concurrent administration of NSAIDs or opiates) or non-pharmacological methods can be used in addition to the regular use of paracetamol in providing adequate pain relief.
- Single ingredient products are preferred at SCH. Where combination products are necessary patients should be dosed according to the paracetamol component of the product with consideration of the maximum dose of the other ingredients.
- The use of multiple paracetamol containing products at any one time should be limited where possible. When used the total daily dose should not exceed the recommendations below with clear prescribing to ensure the risk of overdosing is minimised.

DOSE and ROUTE for Analgesia

Maintenance dose:

- **ORAL:** 15 mg/kg/dose 4 to 6 hourly (up to 1g) maximum 60[#] to 90mg/kg/day (do not exceed 4g in 24 hours)
- Patients receiving 90mg/kg must be reviewed at 48hrs
 - # The lower maximum oral dosage of 60 mg/kg/day is recommended in:
 1. Younger infants (e.g. less than about 6 months of age)
 2. Those with other risk factors for hepatotoxicity (see [Table 1](#))
 3. Discharged home; reasons for any exceptions should be specifically indicated on the discharge script (e.g. management of post-operative pain, chronic pain and palliative care may require the higher maximum daily dose for defined periods of time)

Rectal administration should be avoided if oral administration is at all possible

- **RECTAL:** 15- 20mg/kg/dose (up to 1g) 6 hourly maximum 60-90mg/kg/day (do not exceed 4g in 24 hours).
- **Patients receiving 90mg/kg must be reviewed at 48 hours**
 - Rectal absorption can be erratic and delayed; oral administration is preferred where possible. If the rectal route is necessary (e.g. peri-operatively), this route should only be used until oral dosing is possible.
 - Suppositories should not be cut¹². The calculated dose should be rounded to the nearest suppository strength. If smaller doses need to be given, liquid paracetamol (100mg/mL paracetamol drops) can be administered rectally. However, the rectal absorption of liquid paracetamol can be more erratic and suppositories are preferred. (**Note:** Liquid paracetamol is not licensed for rectal administration)

- The rectal route should not be used in the immunocompromised child or those with a coagulopathy.

Loading dose (e.g. for pre-medication):

- A loading dose may be helpful as a single dose as long as the maximum daily dose (60-90mg/kg/day) is not exceeded.
- Loading doses must be clearly documented on the medication chart and communicated at handover.
 - **ORAL**¹³: 20-30mg/kg(up to 1g)
 - **RECTAL**¹³:
 - 1 to 3 months: 30mg/kg
 - 3 months and older: 30-40mg/kg (up to 1g)
- No loading dose should be administered if a child has been receiving paracetamol or codeine/paracetamol combination preparations in the preceding 24 hours.
- If a loading dose is administered, post-operative paracetamol should be prescribed as 15mg/kg/dose 4 to 6 hourly (regular or PRN) with maximum of 4 such doses within the first 24 hours from the time that the loading dose was administered (i.e. total maximum dose not exceeding 60 - 90mg/kg within first 24 hours).
- Subsequent daily maintenance paracetamol dosing should follow the standard recommendation.

4 Fever Control^{1, 6, 7}

The use of paracetamol in treating fever associated with acute infections is controversial.

In considering use of paracetamol for fever control, the following should be borne in mind:

- Fever as such is not harmful. Infants and children tolerate low-grade fever (e.g. $\leq 38.5^{\circ}\text{C}$)
- Antipyretic treatment has not been shown to prevent febrile convulsions and there may be no advantage to giving paracetamol in this situation. Evidence regarding the possible symptomatic benefits of antipyretic treatment (in terms of mood, comfort, feeding, activity and alertness) is weak.
- Fever generation may be a protective mechanism. Aggressive pharmacological efforts to reduce fever may be counterproductive to the body's efforts to mount an immunological response to viral agents. Antipyretic treatment may therefore prolong the course of illness.
- The risk of liver toxicity with therapeutic use of paracetamol appears to be higher in children with intercurrent febrile illness.

DOSE and ROUTE for Fever Control

- **ORAL or RECTAL:** 15mg/kg/dose 6 hourly (up to 1g) maximum 60mg/kg/day review at 48hrs. *(No more than 4 grams should be administered in any 24 hr period)*
- Lower dosage and duration of treatment is recommended for younger infants and those with any recognised risk factors (see [Table 1](#)).
- Rectal administration should be avoided if oral administration is at all possible. Also see above for general recommendations regarding rectal administration for analgesia.
- **Alternating dosing of paracetamol with ibuprofen is not recommended.** Neither the clinical efficacy nor the safety of this regimen has been demonstrated. It can potentially be associated with higher risk of dosing error and hence toxicity.⁷

5 IV Paracetamol

See [Intravenous Paracetamol – SCH](#)

6 References

1. Heubi JE, Bien JP. Acetaminophen use in children: More is not better. *J Paediatr* 1997;130:175-7
2. Kozer E, Greenberg R. Repeated supratherapeutic doses of paracetamol in children—a literature review and suggested clinical approach. *Acta Paediatrica* 2006; 95: 1165-1171
3. Medicines and Healthcare products Regulatory Agency, UK Public Assessment Report: Liquid paracetamol for children, November 2011
4. Fontana R. Acute liver failure including acetaminophen overdose, *Med. Clin. North Am.* 2008 July; 92(4) 761-794
5. Australian Immunisation Handbook (9th edition) 2008
6. Knoebel EE, Narang AS, Ey JL. Fever: To treat or not to treat. *Clin Pediatr* 2002;41:9-16 edition) 2000
7. American Academy of Pediatrics: Clinical Report –Fever and antipyretic use in children *Pediatrics* 2011;127(3):581-587
8. Saviano F et al. Fulminant hepatitis after 10 days of acetaminophen treatment at recommended dosage in an infant. *Pediatrics*; 2011, February; 127(2) 489-492
9. Leonis MA, Alonso KI et al. Chronic acetaminophen exposure in pediatric acute liver failure. *Pediatrics*, 2013 March; 131(3) 740-746
10. Ferner R, Dear J et al. Management of paracetamol poisoning, *British Medical Journal*, 2011; 342, 2218
11. Chun L, Tong M. Acetaminophen hepatotoxicity and acute liver failure. *Journal of Clinical Gastroenterology*; 2009, 43(4) 342-349
12. MIMSONline. St Leonards, NSW: UBM Medica; Accessed 29/04/2013
13. Paediatric Formulary Committee. BNF for Children [online]. London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. [Accessed via <http://www.ciap.health.nsw.gov.au/home.html> Last Updated June 2015 Accessed on 16/06/2015]

Copyright notice and disclaimer:

The use of this document outside Sydney Children's Hospitals Network (SCHN), or its reproduction in whole or in part, is subject to acknowledgement that it is the property of SCHN. SCHN has done everything practicable to make this document accurate, up-to-date and in accordance with accepted legislation and standards at the date of publication. SCHN is not responsible for consequences arising from the use of this document outside SCHN. A current version of this document is only available electronically from the Hospitals. If this document is printed, it is only valid to the date of printing.

Paracetamol Treatment Algorithm

