

# Paediatric Medication Guideline

## N-Acetylcysteine (Intravenous) for Paracetamol Poisoning

<b>Document ID</b>	CHQ-PMG-01230	<b>Version no.</b>	2.0	<b>Approval date</b>	28/06/2019
<b>Executive sponsor</b>	Executive Director Medical Services			<b>Effective date</b>	28/06/2019
<b>Author/custodian</b>	Pharmacist Advanced – Safety & Quality			<b>Review date</b>	28/06/2021
<b>Supercedes</b>	1.0				
<b>Applicable to</b>	All Children's Health Queensland clinical staff				
<b>Authorisation</b>	Executive Director Clinical Services (QCH)				

### Purpose

The purpose of this guideline is to provide clinical advice around the use of intravenous N-Acetylcysteine in paediatric patients at the Queensland Children's Hospital (QCH).

### Scope

This guideline is intended to assist all clinical staff to prescribe and administer intravenous N-Acetylcysteine appropriately to patients at QCH. It is not intended to be a substitute for specific professional or clinical advice, or to replace consultation with senior staff, which should always be sought if clinically relevant.

This material is published by Queensland Health with the intention of providing a guideline for use at QCH. Anyone wishing to use this guideline outside QCH should refer to their local Medicines Committee before using.

### Description and Indications for Use

N-Acetylcysteine is an effective antidote to paracetamol overdose by increasing the synthesis and availability of glutathione and also directly binding to NAPQI (N-acetyl-p-benzoquinone imine).

N-Acetylcysteine reduces mortality even if commenced in patients presenting with established paracetamol-induced fulminant hepatic failure. The mechanisms of action in this period may be different.

N-Acetylcysteine (Acetadote<sup>®</sup>, DBL<sup>®</sup>, Link<sup>®</sup>) is available as a 2,000 mg / 10 mL solution for injection<sup>1</sup>.

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## Prescribing Instructions

<b>X</b>	<b>Contraindications</b> <ul style="list-style-type: none"> <li>• None</li> </ul>
<b>!</b>	<b>Precautions</b> <ul style="list-style-type: none"> <li>• Fluid restricted patients require adjustment of total volume to minimize risk of hyponatraemia, seizure and death – seek specialist advice.</li> <li>• Risk of anaphylactoid reactions is dose-related and occurs more commonly during the initial infusion (though less frequently than with previous 3-bag infusion regimens). Previous hypersensitivity reactions to N-Acetylcysteine do not prevent future use. Discussion with toxicologist is recommended.</li> <li>• Nausea, vomiting and other gastrointestinal symptoms are the most common adverse effects experienced with high dose N-Acetylcysteine infusions. Antiemetic therapy may be required.</li> <li>• Use with caution in children with a history of asthma/bronchospasm. Close monitoring is required.</li> <li>• Use with caution in children with history of oesophageal varices and peptic ulceration as N-Acetylcysteine induced vomiting can increase risk of haemorrhage.</li> </ul>

## Dose

Care must be taken in dose calculation and administration instructions. Dosage of N-Acetylcysteine is based on actual bodyweight with a ceiling weight of 110 kg.<sup>2</sup> Doses are written in **milligrams**.

The regimen involves a two-bag infusion and both infusions should be charted by treating medical officer at time of initiation to avoid delays in treatment.

**ALERT**

For safety and prescription clarity, N-Acetylcysteine should be prescribed using the 'Acetylcysteine IV' order sequence in ieMR, or in Metavision (PICU only).

During downtime procedures, prescribe using the Paediatric Intravascular and Subcutaneous Fluid Order Form or N-Acetylcysteine Fluid Order form if available.

Final solution volume and rate of infusion must be clearly prescribed.

Chart both infusions at time of initiation to avoid delays in treatment.

**ALERT**

Previous guidelines used a three bag infusion<sup>3</sup>, which is no longer best practice. If a three-bag infusion is prescribed, please refer for toxicological advice.

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**N-Acetylcysteine dosing:**

**For infants and children weighing less than or equal to 20 kg (total fluid volumes have been standardised to reduce calculation errors):**

- Infusion 1: N-Acetylcysteine 200 mg/kg diluted to a total volume of 100 mL with appropriate diluent\*.<sup>4</sup> Infuse over 4 hours, immediately followed by:
- Infusion 2: N-Acetylcysteine 100 mg/kg diluted to a total volume of 250 mL with appropriate diluent\*.<sup>4</sup> Infuse over 16 hours.
- [N-Acetylcysteine Fluid Order less than 20kg](#) pre-printed infusion chart showing this dosing are available for sites that do not prescribe on ieMR.

**For children weighing more than 20 kg and less than 50 kg:**

- Infusion 1: N-Acetylcysteine 200 mg/kg diluted to a total volume of 250 mL with appropriate diluent\*.<sup>4</sup> Infuse over 4 hours, immediately followed by:
- Infusion 2: N-Acetylcysteine 100 mg/kg diluted to a total volume of 500 mL with appropriate diluent\*.<sup>4</sup> Infuse over 16 hours.
- [N-Acetylcysteine Fluid Order 20 kg – 50 kg](#) pre-printed infusion chart showing this dosing are available for sites that do not prescribe on ieMR.

**For children and adolescents weighing more than or equal to 50 kg (max 110 kg):**

- Infusion 1: N-Acetylcysteine 200 mg/kg diluted to a total volume of 500 mL with appropriate diluent\*.<sup>5</sup> Infuse over 4 hours, immediately followed by:
- Infusion 2: N-Acetylcysteine 100 mg/kg diluted to a total volume of 1000 mL with appropriate diluent\*.<sup>5</sup> Infuse over 16 hours.
- [N-Acetylcysteine Fluid Order greater than 50 kg](#) pre-printed infusion chart showing this dosing are available for sites that do not prescribe on ieMR.

**\*Note: An appropriate diluent is glucose 5%, sodium chloride 0.9% or combinations of glucose-sodium chloride not exceeding these concentrations.<sup>5</sup> Where possible, use of a diluent that is available as a premade bag in the desired final volume is preferred.**

**ALERT**

In case of large/massive paracetamol overdose with a serum paracetamol concentration more than double the nomogram line, Infusion 2 should be replaced with:

N-Acetylcysteine 200 mg/kg diluted to an appropriate volume of appropriate diluent. Infuse over 16 hours.

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### Administration Instructions

#### Reconstitution/Dilution

Dilute N-Acetylcysteine before infusion. N-Acetylcysteine is compatible with either sodium chloride 0.9%, glucose 5% or combinations of glucose-sodium chloride not exceeding those concentrations.<sup>5</sup>

Before adding the N-Acetylcysteine to the infusion bag, an equal volume should first be withdrawn from the bag. Ensure that N-Acetylcysteine is thoroughly mixed after dilution.

Once diluted, the solution should be used immediately. However, the diluted solution is stable for up to 24 hours when refrigerated between 2°C and 8°C.

Patients who are fluid restricted may need the fluid volume reduced. Contact the prescriber and pharmacy if required.

#### Route and Method of Administration

N-Acetylcysteine is administered by intravenous infusion using the appropriate profile in dose error reduction software (DERS).

N-Acetylcysteine is generally not compatible with other medications and should not be diluted or infused with other drugs. Contact pharmacy for advice if required.

### Clinical Considerations

#### Adverse Reactions

Clinical effects associated with N-Acetylcysteine administration:

- Nausea, vomiting (Common reaction with ~30% incidence.<sup>6</sup> May require antiemetic treatment).
- Shortness of breath, wheeze.
- Rash, flushing, itchiness.
- Hypotension.

If adverse effects occur, notify medical officer. Most of the above reactions are related to the release of histamine<sup>6</sup> and can be managed by stopping the infusion briefly, treating any effects, and recommencing at the same rate. An antiemetic and antihistamine may be given if required.

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#### ALERT



In case of severe anaphylactoid reaction including widespread or generalised rash, urticaria, flushing, or (rarely) hypotension and/or bronchospasm, pause infusion immediately and notify medical officer. Do not disconnect.

If severe anaphylactoid reaction occurs, stop N-Acetylcysteine for one hour and treat complications. All attempts should be made to recommence and continue the infusion rather than ceasing therapy. Contact toxicologist for advice.

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Previous adverse events (including anaphylactoid reactions) do not preclude the future use of N-Acetylcysteine.

### Monitoring

Patients can be moved to the Acute/Short Stay Unit in the Emergency Department (ED) once the first infusion has been commenced. Administration of N-Acetylcysteine is not restricted to the ED providing adequate monitoring can be performed.

#### Specific observations:

- Heart rate.
- Blood pressure.
- Oxygen saturation.
- Temperature.
- Respiration rate.

Obtain at baseline, before infusion is commenced, every 30 minutes for the first two hours, and then every hour until the end of the first infusion. Continue observations every four hours during the second infusion.<sup>5</sup>

Telemetry monitoring is not routinely required but could be considered in cases of polypharmacy overdose with drugs that would require cardiac monitoring.

Be aware of the risk of hyponatremia and hypoglycaemia in the choice of diluting fluid.

### Therapeutic Drug Monitoring

Additional monitoring including serum paracetamol concentration, ALT, blood sugar level, INR, urea, electrolytes, serum creatinine and blood gas analysis may be required.

Additional N-Acetylcysteine infusions may be required based on ALT and serum paracetamol concentration.

#### ALERT



It is strongly recommended to seek further advice from Poisons Information Centre in the following situations where the risk of hepatotoxicity may be greater and optimum advice is potentially changing:

- Very large overdoses:
  - Immediate release or modified release paracetamol (e.g. Panadol Osteo®, Osteomol®) overdoses of greater than 50 g or 1 g/kg (whichever is lower).
  - A very high paracetamol concentration, more than double the nomogram line.
- Intravenous paracetamol errors or overdoses.
- Patients with hepatotoxicity (e.g. ALT > 1000 IU/L).
- Repeated or chronic overdoses.

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### Additional Information

Refer to the [CHQ-GDL-60018 Paracetamol ingestion – Emergency management in children](#) or the [Guidelines for the management of paracetamol poisoning in Australia and New Zealand<sup>2</sup>](#) for additional information regarding the management of supratherapeutic paracetamol ingestion, the paracetamol treatment nomogram and recommendations for optimal use of activated charcoal.

### Related documents

#### Policy and standard(s)

- [Queensland Health List of Approved Medicines](#)

#### Procedures, Guidelines, Protocols

- [Guideline for the management of paracetamol poisoning in Australia and New Zealand<sup>2</sup>](#)
- [CHQ-GDL-60018 Paracetamol ingestion – Emergency management in children](#)
- [CHQ-PROC-01001 Medication – Prescribing](#)
- [CHQ-PROC-01039 Medication – Administration](#)
- [CHQ-PROC-01017 Adverse Drug Reaction – Documentation and Reporting](#)
- [CHQ ieMR Quick Reference Guide: N-Acetylcysteine \(NAC\) intravenous infusion for paracetamol poisoning – Prescription and Administration](#)

#### Forms and templates

- N-Acetylcysteine pre-printed infusion charts for non ieMR sites:
  - [N-Acetylcysteine Fluid Order form \(less than 20 kg\)](#)
  - [N-Acetylcysteine Fluid Order form \(20 – 50 kg\)](#)
  - [N-Acetylcysteine Fluid Order form \(greater than 50 kg\)](#)

### Consultation

Key stakeholders who reviewed this version:

- Pharmacist Critical Care (Emergency)
- Pharmacist Team Leader – Critical Care
- Senior Medical Officer, Department of Emergency Medicine
- Medical Director, Queensland Poisons Information Centre
- Manager, Queensland Poisons Information Centre
- Pharmacist Advanced – Safety and Quality

## Paediatric Medication Guideline – N-Acetylcysteine (intravenous) for Paracetamol Poisoning

- Pharmacist Consultant – Electronic Medication Management

### Definition of terms

Term	Definition
ALT	Alanine transaminase
INR	International normalised ratio
NAC	N-Acetylcysteine

### References and suggested reading

1. Product information: *N-Acetylcysteine 200 mg/mL injection*. (2012). Link Medical Products Pty Ltd, NSW Australia. Available from: <http://www.tga.gov.au>.
2. Chiew AL, Fountain JS, Graudins A, et al. *Summary statement. New guidelines for the management of paracetamol poisoning in Australia and New Zealand*. Med J Aust 2015; 203: 215-218.
3. Daly FF, Fountain JS, Murray L et-al. *Guidelines for the management of paracetamol poisoning in Australia and New Zealand-explanation and elaboration. A consensus statement from clinical toxicologists consulting to the Australasian poisons information centres*. Med. J. Aust. 2008;188 (5): 296-301.
4. Marzullo L. An update of N-acetylcysteine treatment for acute acetaminophen toxicity in children. Curr. Opin. Pediatr. 2005;17 (2): 239-45.
5. The Royal Children's Hospital, Melbourne. (2018). *Paracetamol Poisoning*. Victoria, Australia.
6. Metro South Health. (2018). *Prescribing guideline: Adult – N-Acetylcysteine (NAC) Infusion Procedure of Paracetamol Poisoning*. Queensland, Australia.

### Guideline revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by
1.0 (01/02/2017)	Pharmacist Team Leader – Critical Care	Medicines Advisory Committee	General Manager Operations
2.0 (28/06/2019)	Pharmacist Advanced – Safety & Quality	Medicines Advisory Committee	Executive Director Clinical Service (QCH)

<b>Keywords</b>	Paracetamol, NAC, N-Acetylcysteine, 01230
<b>Accreditation references</b>	NSQHS Standards (1-8): Standard 4. Medication Safety