ACETYLCYSTEINE

Read in conjunction with Disclaimer

HIGH RISK Medication

Formulary: Highly Restricted
Requires Neonatologist or relevant specialist approval before commencing.

Presentation	**Nebulising Solution:** 800 mg/4 mL (20%) (Omegapharm®) **Ampoule**: 2 g/10 mL
Drug Class	• Mucolytic agent • Antidote for paracetamol poisoning – prevents glutathione depletion and minimises hepatocyte injury caused by paracetamol overdose.
Indication	• **Nebulisation:** Reduction of mucous viscosity in bronchopulmonary disease. • **Intravenous:** Paracetamol overdose at risk of developing hepatotoxicity. Contact Poisons Information Centre **13 11 26** for all cases. • **Rectal:** Meconium related ileus of preterm and term infants.
Special Considerations and Precautions	**Contraindication:** Immune-mediated hypersensitivity to acetylcysteine or any components of the formulation.
	Inhalation: • Asthma or bronchospasm – risk of acute bronchospasm. Consider administering bronchodilator 15 minutes prior to nebulised acetylcysteine. • Use with caution in patients with respiratory insufficiency, impaired cough mechanism or gag reflex. • Since increased bronchial secretions may develop after inhalation, percussion, postural drainage, and suctioning should follow. If bronchospasm occurs, administer a bronchodilator; discontinue acetylcysteine if bronchospasm progresses.
	Intravenous: • Hypersensitivity or previous anaphylactic reaction to acetylcysteine or any component of the preparation. Note that non-IgE-mediated anaphylactic reactions are common, usually occur during loading doses and can be managed with discontinuation of the infusion, administration of antihistamines +/- steroids and then restarting the loading dose at half the rate.
	Rectal: • Do not use if intestinal perforation is suspected. • Abnormal liver and/or renal function. • Caution in asthma and bronchospasm.
Monitoring	• Hypersensitivity reactions, bronchial secretions, renal & hepatic function, electrolytes. • IV for Paracetamol Poisoning – see IV 'Monitoring'

Compatibility	**<u>Nebulising Solution</u>** **Compatible Fluids:** Sodium chloride 0.9%, water for injection.
	<u>Intravenous</u> **Compatible fluids DBL®/Link® brands only:** Glucose 5% (preferred), sodium chloride 0.9%. **Compatible fluids Acetadote® brand:** Glucose 5% only.
	Y Site Compatibility: Heparin sodium, meropenem, naloxone hydrochloride, vancomycin hydrochloride.
Incompatibility	**Inhalation:** • Contact with rubber and some metals, particularly, iron, copper and nickel may inactivate acetylcysteine. • Can be used with silicone and plastic. • Acetylcysteine solution for inhalation is incompatible with tetracyclines, erythromycin, amphotericin B and hydrogen peroxide. **This list is not exhaustive, contact pharmacy for advice.**
	Intravenous: Incompatible with cefepime and ceftazidime. **This list is not exhaustive, contact pharmacy for advice.**
Drug Interactions	Glyceryl trinitrate: increased risk of hypotension.
Side effects	**Common:** Nausea, vomiting, cutaneous reaction (such as rash, flushing, pruritis and urticaria) have been reported.
	Intravenous: Anaphylactoid reactions (usually occur in the first few hours of IV infusion), angioedema, bronchospasm, hypotension. Hyponatraemia +/- fluid overload have also been reported in sick or very preterm infants.
	Rectal: Hypernatremia, hepatoxicity, mucosal injury, haemorrhage.
Storage & Stability	**Nebulising Solution:** Store below 25°C. Do not refrigerate or freeze. Protect from light.
	Ampoule: Store below 25°C. Do not refrigerate or freeze. Protect from light.
Comments	• Also known as N-acetylcysteine (NAC) • Under certain conditions, a light purple colour may develop in the inhalation and intravenous solution of acetylcysteine. This does not significantly affect safety or effectiveness.

NEBULISATION

Presentation	**Nebulising Solution:** 800 mg/4 mL (20%)
Dosage	**Mucolytic agent for reduction of mucous viscosity in bronchopulmonary disease.** • **Note:** Patients should receive an aerosolized bronchodilator 10 to 15 minutes prior to acetylcysteine. • 200 to 400 mg (1 to 2 mL of acetylcysteine 800 mg/4 mL) every 2 to 6 hours. • Dose adjustment ○ Renal and/or hepatic impairment: no specific dose adjustment recommended
Preparation	Solution can be diluted with an equal volume of sodium chloride 0.9% prior to nebulisation.
Administration	Nebulisation: administer undiluted or diluted in appropriate volume of sodium chloride 0.9% and nebulised via CPAP, ETT or mask.

INTRAVENOUS

Presentation (for IV use)

Ampoule: 2 g/10 mL

Dosage

Paracetamol overdose

- All cases to be discussed with Poisons Information Centre at **13 11 26**. Refer to Paracetamol Treatment Nomogram in Appendix Figure 1.

	Acetylcysteine dose	Volume of glucose 5% for dilution	Infusion duration
First infusion	200 mg/kg	7 mL/kg	4 hours
Second infusion	100 mg/kg	14 mL/kg	16 hours

- If ongoing acetylcysteine infusion is required, repeat second infusion. Discuss management with clinical toxicologist at the Poisons Information Centre on **13 11 26**.
- If indicated, acetylcysteine should be continued (at the dose and rate of the 2nd infusion) until the patient is clinically improving, ALT levels are decreasing, the INR is less than 2 and the blood paracetamol level (BPL*) is less than 10 mg/L (66 mmol/L).
- Dose adjustment
  - Renal impairment: no specific dose adjustment recommended.

Preparation

First infusion:

- Dilute 200 mg/kg of acetylcysteine in 7 mL/kg glucose 5% and administer over 4 hours, followed by;

Second infusion:

- Dilute 100 mg/kg of acetylcysteine in 14 mL/kg glucose 5% and administer over 16 hours.

Note: Glucose 5% is the preferred diluent; if unsuitable sodium chloride 0.9% can be used if clinically necessary.

Administration

- Invert prepared acetylcysteine infusion at least 10 times to ensure adequate mixing.
- Administer via syringe driver.
- Refer to Dosage section for dilution volume and infusion duration.
- If IV access is not possible, acetylcysteine may be administered orally; contact Poisons Information Centre **13 11 26** for advice.

INTRAVENOUS

Monitoring

IV (paracetamol overdose):

- Regular clinical review and blood tests are to be performed until Acetylcysteine is ceased. See below:

Time (hours) from paracetamol ingestion to Acetylcysteine treatment	Baseline Investigations	Investigations at the completion of Acetylcysteine
Less than 24 hours	ALT and BPL*	ALT
Greater than 24 hours	ALT, BPL*, INR	ALT and INR

*Check correct units are read from the nomogram (available in micromol/L and now mg/L)

- For patients with abnormal ALT (greater than 50 units/L), check baseline UEC, LFT, INR, PGL, Phosphate, VBG (looking at pH and lactate) and repeat every 12 hours.
- Repeat LFT and BPL* 2 hours prior to completion of second infusion to determine if ongoing treatment is required.
- Continuous cardiac monitoring for the first infusion bag. Discontinue cardiac monitoring after this period unless hypersensitivity reaction occurred or if clinically indicated.
- Monitor vitals every 30 minutes for first 2 hours of treatment then hourly if clinically stable.
- Observe for hypersensitivity and anaphylactoid reactions. See below for management.

Management of acetylcysteine adverse reactions with IV infusions:

- Mild/moderate hypersensitivity reactions (e.g. rash, bronchospasm, hypotension) – slow or stop infusion and treat reactions.
- Severe anaphylactoid reactions – stop infusion and treat reactions.
- Infusion may be recommenced after 1 hour or when symptoms resolve. The first infusion may be restarted at half the rate, the second infusion may be restarted at the same rate.

RECTAL

Presentation	**Ampoule**: 2 g/10 mL
Dosage	**Rectal Enema for Meconium-related ileus** 40 to 200mg/dose (1 to 5 mL/dose) every 6 to 8 hours.
Preparation	**Ampoule**: 2 g/10 mL = 2000 mg/10 mL • Dilute 1 mL (200 mg) with 4 mL of glucose 5% or sodium chloride 0.9% to make a final volume of 5mL. *Concentration now equal to **40 mg/mL (4%)***
Administration	Measure required dose of 4% solution and administer slowly into the rectum.
Monitoring	Monitor vitals, electrolytes and liver function test (particularly with repeated administration).

Appendix Figure 1:

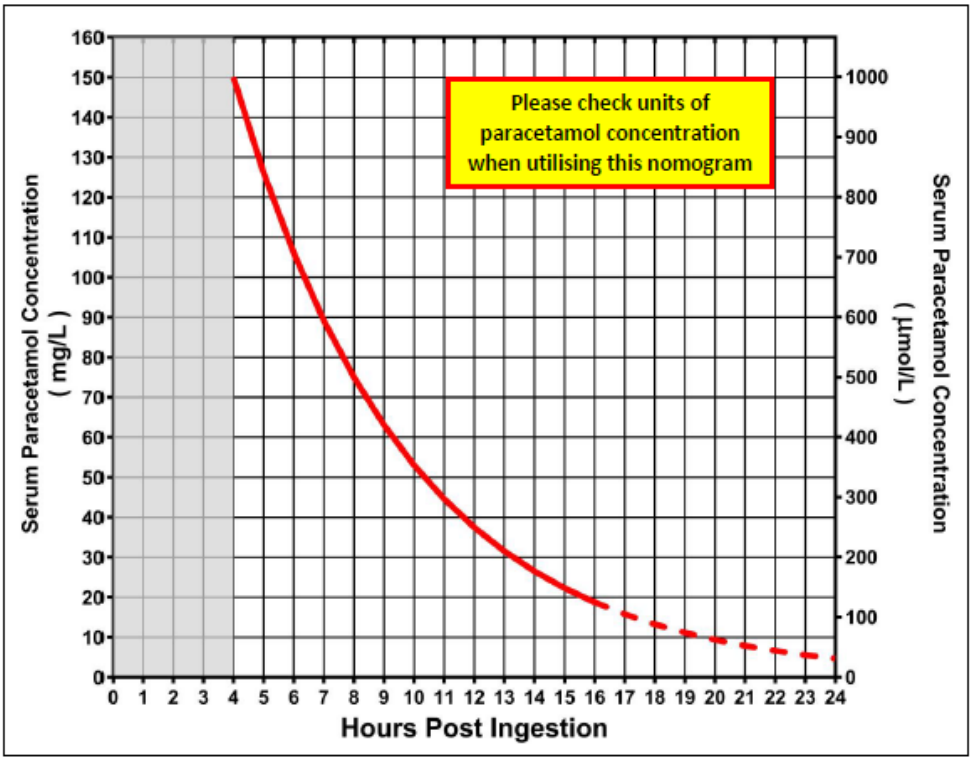

Figure 1: Paracetamol Treatment Nomogram (Rumack-Matthew Nomogram)

Note: µmol/L = micromol/L = nmol/mL

Related Policies, Procedures, and Guidelines

HDWA Mandatory Policies:

MP 0131/20: WA High Risk Medication Policy

Clinical Practice Guidelines:

PCH ED Paracetamol Poisoning Guideline

WNHS Pharmaceutical and Medicines Management Guidelines:

High Risk Medicines

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