ACETYLCYSTEINE – INTRAVENOUS 2019

NEWBORN USE ONLY

Alert	Paracetamol overdose may be asymptomatic initially and early assessment is recommended. Discuss all cases with the Poisons Information Centre (13 11 26 nation-wide) or local toxicology service. Check correct units are read from the nomogram (previously micromol/L and now mg/L). Anaphylactic reactions to acetylcysteine usually occur in the first few hours of infusion.

Indication	**Treatment of ORAL paracetamol overdose:**
	• **Indications for treatment:**
	  • Single acute ingestion ≥200 mg/kg and serum paracetamol concentration (taken 4–16 hours post-ingestion) is above treatment line on the nomogram (see special comments).
	  • Ingestion of liquid paracetamol with a 4-hour serum paracetamol concentration above 150 mg/L (1000 micromol/L).
	  • Ingestion of sustained release paracetamol ≥200 mg/kg or ≥ 10 gram (whichever is less) or, if ingested less than this dose, where either of two serum paracetamol concentrations (taken 4 hours apart) is above the nomogram line.
	  • Repeated supratherapeutic ingestions as per the recommended algorithm:
	  o >200 mg/kg over a single 24-hour period
	  o >300 mg/kg over a 48-hour period for the preceding 48 hours
	  o >60 mg/kg per 24-hour period for more than 48 hours
	  o If above criteria met, measure serum paracetamol and ALT concentrations. If ALT above upper limit of normal or paracetamol concentration >20 mg/L (132 micromol/L), commence acetylcysteine.
	  • Established hepatotoxicity (deranged transaminases or coagulations studies).
	  • When serum paracetamol concentrations will not be available for >8 hours post-acute ingestion
	  • Massive acute ingestion (more than 400mg/kg or paracetamol concentration is greater than twice the nomogram value at that time) needs special attention and urgent consultation
	  • Discuss other presenting scenarios with a Toxicologist.
	
	Treatment of INTRAVENOUS paracetamol overdose:
	• **Consider acetylcysteine treatment for**:
	  • Single IV dose of >60 mg/kg
	  • Serum paracetamol concentration above 50 mg/L (330 micromol/L) at 4 h after exposure
	  • Evidence of acute liver injury

Action	Acetylcysteine prevents glutathione depletion and minimises hepatocyte injury caused by paracetamol overdose.
Drug Type	Antidote.
Trade Name	DBL acetylcysteine injection concentrate, Acetadote Concentrated Injection (Solution for infusion) Acetylcysteine-Link Concentrate for infusion
Presentation	DBL acetylcysteine injection concentrate 20% (200 mg/mL, 10 mL ampoule) Acetadote Concentrated Injection (Solution for infusion) 20 % (200 mg/mL, 30 mL vial) Acetylcysteine-Link Concentrate for infusion 20% (200 mg/mL, 10 mL ampoule).
Dosage/Interval	1st IV infusion – acetylcysteine 200 mg/kg infusion over 4 hours, followed by 2nd IV infusion – acetylcysteine 100 mg/kg infusion over 16 hours.
Maximum daily dose	
Route	**Intravenous**
Preparation/Dilution	**Intravenous preparation for paracetamol toxicity** 1st infusion – dilute acetylcysteine 200 mg/kg in 7 mL/kg 5% glucose (max 500 mL) and administer over 4 hours, followed by 2nd infusion – dilute acetylcysteine 100 mg/kg in 14 mL/kg 5% glucose (max 1000 mL) and administer over 16 hours.
Administration	Intravenous for paracetamol overdose: Administer via syringe driver in 2 steps over different time periods:

<table>
<tr><td></td><td>1st infusion: Over 4 hours.
2nd infusion: Over 16 hours.</td></tr>
<tr><td>Monitoring</td><td>Near the completion of acetylcysteine infusion (i.e., 2 hours before completion of infusion), measure serum ALT and paracetamol concentrations. Infants with acute liver injury:
o Monitoring:
o ALT – every 12 hours
o INR – every 12 hours
o Paracetamol concentration – every 12 hours
o EUC/BGL – daily
o ABG if clinical deterioration
o 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 improving and <2 and the paracetamol concentration is less than 10 mg/L (66 mmol/L).
o Regular clinical review and 12-hourly (or more frequent) blood tests are to be performed until acetylcysteine is ceased.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Precautions</td><td>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 and then restarting the loading dose at a slower infusion rate.</td></tr>
<tr><td>Drug Interactions</td><td>No information is available on the interaction of acetylcysteine with other medicines.</td></tr>
<tr><td>Adverse Reactions</td><td>Gastrointestinal effects such as nausea and vomiting.
The rate of anaphylactic reactions is low with the current 2-bag infusion. Adverse reactions range from mild cutaneous reactions (rashes, flushing/erythema and urticaria) to less common and more severe reactions (angioedema, bronchospasm and hypotension).
May cause hyponatraemia and fluid overload especially in sick and very preterm infants.
What to do when adverse reactions to acetylcysteine occur:
o Cease acetylcysteine immediately
o Steroid
o Antihistamine
o Acetylcysteine may be recommenced after 1 hour at half the rate, if the adverse reactions have abated and clinical improvement occurs.</td></tr>
<tr><td>Compatibility</td><td>
<table>
<tr><td>Acetylcysteine brand</td><td colspan="2">Compatibility</td></tr>
<tr><td></td><td>Sodium chloride 0.9%</td><td>Glucose 5%</td></tr>
<tr><td>Acetadote (Phebra)</td><td>X</td><td>√</td></tr>
<tr><td>Acetylcystenine-DBL (Hospira)</td><td>√</td><td>√</td></tr>
<tr><td>Acetylcysteine-Link (Link)</td><td>√</td><td>√</td></tr>
</table>
Y-site: Cefepime, ceftazidime, , heparin sodium, naloxone hydrochloride, vancomycin hydrochloride</td></tr>
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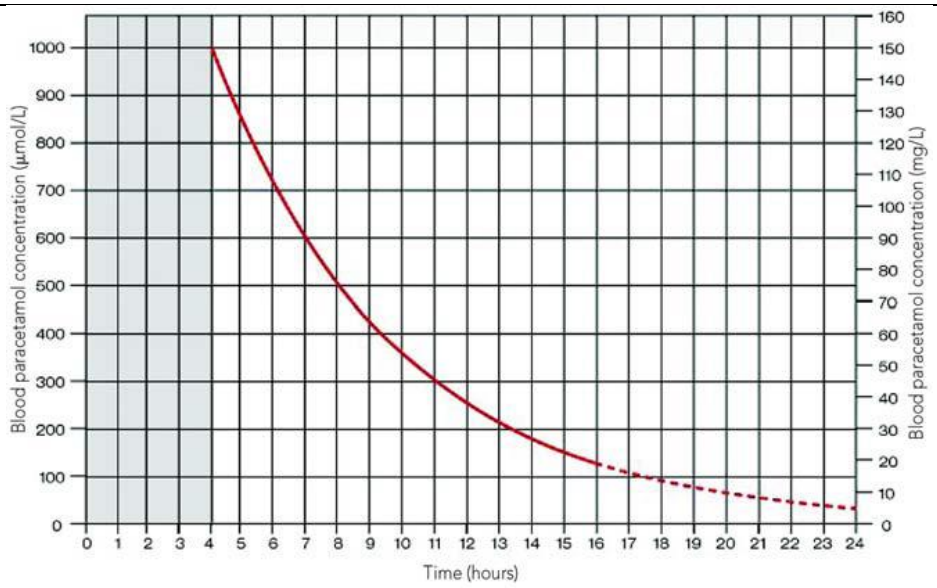
<tr><td>Stability</td><td>To reduce microbiological hazard, use as soon as practicable after dilution. If storage is necessary, hold at 2 to 8°C for not more than 24 hours.</td></tr>
<tr><td>Storage</td><td>Store the unopened vial below 25°C. Protect from light.
Product is for single use in one patient only. Discard any residue.</td></tr>
<tr><td>Special Comments</td><td>Paracetamol treatment nomogram for acute paracetamol ingestion with known time of ingestion [2]</td></tr>
</table>

	 Notes: The paracetamol nomogram is only validated for single acute ingestions in adults. Beware units are different on right and left axes.
Evidence summary	Refer to full version.
References	Refer to full version.

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