Drugs: An A–Z Guide

ACETAZOLAMIDE

Acetazolamide is a carbonic anhydrase inhibitor normally used to reduce intra-ocular pressure in glaucoma. Metabolic alkalosis may be partially corrected by the use of acetazolamide. The most common cause of metabolic alkalosis on the ICU is usually the result of furosemide administration.

Uses
Metabolic alkalosis (unlicensed)

Contraindications
Hypokalaemia
Hyponatraemia
Hyperchloraemic acidosis
Severe liver failure
Renal failure
Sulphonamide hypersensitivity

Administration
- IV: 250–500 mg, given over 3–5 min every 8 hours

  Reconstitute with 5 ml WFI
  Monitor: FBC, U&E and acid/base balance

How not to use acetazolamide
IM injection – painful
Not for prolonged use

Adverse effects
Metabolic acidosis
Electrolyte disturbances (hypokalaemia and hyponatraemia)
Blood disorders
Abnormal LFT

Cautions
Avoid extravasation at injection site (risk of necrosis)
Avoid prolonged use (risk of adverse effects)
Concurrent use with phenytoin (↑ serum level of phenytoin)

Organ failure
Renal: avoid if possible (metabolic acidosis)

CC (ml/min)	Dose (mg)	Interval (h)
20–50	250	Up to 6
10–20	250	Up to 12
<10	250	24

Hepatic: avoid (abnormal LFT)

ACETYLCYSTEINE (Parvolex)

Acetylcysteine is an effective antidote to paracetamol if administered within 8 hours after an overdose. Although the protective effect diminishes progressively as the overdose–treatment interval increases, acetylcysteine can still be of benefit up to 24 hours after the overdose. In paracetamol overdose the hepatotoxicity is due to formation of a toxic metabolite. Hepatic reduced glutathione inactivates the toxic metabolite by conjugation, but glutathione stores are depleted with hepatotoxic doses of paracetamol. Acetylcysteine, being a sulphydryl (SH) group donor, protects the liver probably by restoring depleted hepatic reduced glutathione or by acting as an alternative substrate for the toxic metabolite.

Acetylcysteine may have significant cytoprotective effects. The cellular damage associated with sepsis, trauma, burns, pancreatitis, hepatic failure and tissue reperfusion following acute MI may be mediated by the formation and release of large quantities of free radicals that overwhelm and deplete endogenous antioxidants (e.g. glutathione). Acetylcysteine is a scavenger of oxygen free radicals. In addition, acetylcysteine is a glutathione precursor capable of replenishing depleted intracellular glutathione and, in theory, augmenting antioxidant defences (p. 288).

Acetylcysteine can be used to reduce the nephrotoxic effects of intravenous contrast media. Possible mechanisms include scavenging a variety of oxygen-derived free radicals and the improvement of endothelium-dependent vasodilation.

Nebulised acetylcysteine can be used as a mucolytic agent. It reduces sputum viscosity by disrupting the disulphide bonds in the mucus glycoproteins and enhances mucociliary clearance, thus facilitating easier expectoration.

Uses
Paracetamol overdose
Antioxidant (unlicensed)
Prevent IV contrast-induced nephropathy (unlicensed)
Reduce sputum viscosity and facilitate easier expectoration (unlicensed)
As a sulphydryl group donor to prevent the development of nitrate tolerance (unlicensed)

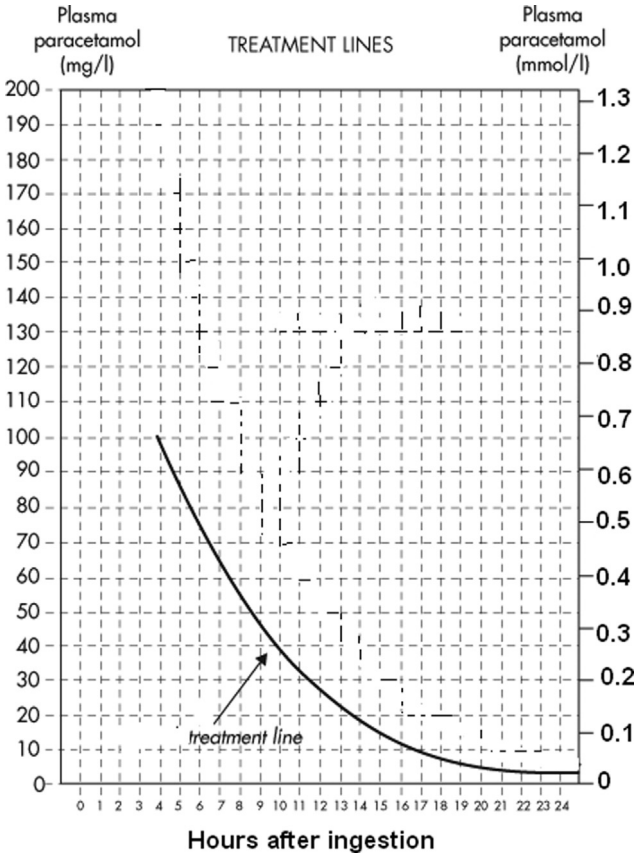
Administration
Paracetamol overdose

- IV infusion: 150 mg/kg in 200 ml glucose 5% over 60 min, followed by 50 mg/kg in 500 ml glucose 5% over 4 h, then 100 mg/kg in 1 litre glucose 5% over the next 16 h

Weight (kg)	Initial	Second	Third
	150 mg/kg in 200 ml glucose 5% over 60 min	50 mg/kg in 500 ml glucose 5% over 4 h	100 mg/kg in 1 litre glucose 5% over 16 h
	Parvolex (ml)	Parvolex (ml)	Parvolex (ml)
50	37.5	12.5	25
60	45.0	15.0	30
70	52.5	17.5	35
80	60.0	20.0	40
90	67.5	22.5	45
x	0.75x	0.25x	0.5x

For children >20 kg: same doses and regimen but in half the quantity of IV fluid

Treatment nomogram



Patients whose plasma concentrations fall on or above the treatment line should receive acetylcysteine. The prognostic value after 15 hours is uncertain, although a plasma-paracetamol concentration on or above the treatment line is likely to carry a serious risk of liver damage. Use acetylcysteine for paracetamol overdose irrespective of the plasma paracetamol level if the overdose is staggered or there is doubt over the time of paracetamol ingestion, or paracetamol overdose with a timed plasma paracetamol concentration on or above a single treatment line joining points of 100 mg/L at 4 hours and 15 mg/L at 15 hours regardless of risk factors of hepatotoxicity.

Antioxidant

- IV infusion: 75–100 mg/kg in 1 litre glucose 5%, give over 24 h (rate 40 ml/h)

Prevent IV contrast-induced nephropathy (not required for oral/enterally administered contrast)

- IV bolus 1200 mg pre-contrast, then after 12 hours 1200 mg PO/NG (or IV if nil-by-mouth) 12 hourly for 48 hours (there is also evidence for 600 mg as an alternate dose)

Dilution: make up to 20 ml with glucose 5%

To be given in conjunction with IV sodium bicarbonate 1.26% at 3 ml/kg/hr over 1 hour prior to IV contrast. Continue at reduced rate of 1 mg/kg/hr for 6 hours following contrast

Reduce sputum viscosity

- Nebulised: 4 ml (800 mg) undiluted Parvolex (20%) driven by air, 8 hourly

Administer before chest physiotherapy

How not to use acetylcysteine
Do not drive nebuliser with oxygen (oxygen inactivates acetylcysteine)

Adverse effects
Anaphylactoid reactions (nausea, vomiting, flushing, itching, rashes, bronchospasm, hypotension)
Fluid overload

Cautions
There are no contraindications to treatment of paracetamol overdose with acetylcysteine
Asthmatics (risk of bronchospasm)
Pulmonary oedema (worsens)
Each 10 ml ampoule contains Na^+ 12.8 mmol (↑ total body sodium)

ACICLOVIR (Zovirax)

Interferes with herpes virus DNA polymerase, inhibiting viral DNA replication. Aciclovir is renally excreted and has a prolonged half-life in renal impairment.

Uses
Herpes simplex virus infections:

- HSV encephalitis
- HSV genital, labial, peri-anal and rectal infections

Varicella zoster virus infections:

- Beneficial in the immunocompromised patients when given IV within 72 hours: prevents complications of pneumonitis, hepatitis or thrombocytopenia
- In patients with normal immunity, may be considered if the ophthalmic branch of the trigeminal nerve is involved

Contraindications
Not suitable for CMV or EBV infections

Administration

- IV: 5–10 mg/kg 8 hourly (i.e. 5 mg/kg for herpes simplex, herpes zoster; 10 mg/kg for herpes zoster in immunocompromised, herpes simplex encephalitis

Available in 250 mg/10 ml and 500 mg/20 ml ready-diluted or in 250 mg and 500 mg vials for reconstitution
Reconstitute 250 mg vial with 10 ml WFI or sodium chloride 0.9% (25 mg/ml)
Reconstitute 500 mg vial with 20 ml WFI or sodium chloride 0.9% (25 mg/ml)
Take the reconstituted solution (25 mg/ml) and make up to 50 ml (for 250 mg vial) or 100 ml (for 500 mg vial) with sodium chloride 0.9% or glucose 5%, and give over 1 hour

Ensure patient is well hydrated before treatment is administered

If fluid-restricted, can give centrally via syringe pump undiluted (unlicensed)

In renal impairment:

CC (ml/min)	Dose (mg/kg)	Interval (h)
25–50	5–10	12
10–25	5–10	24
<10	2.5–5	24

How not to use aciclovir
Rapid IV infusion (precipitation of drug in renal tubules leading to renal impairment)

Adverse effects
Phlebitis
Reversible renal failure
Elevated liver function tests
CNS toxicity (tremors, confusion and fits)

Cautions
Concurrent use of methotrexate
Renal impairment (reduce dose)
Dehydration/hypovolaemia (renal impairment due to precipitation in renal tubules)

Renal replacement therapy
CVVH dose dependent on clearance rate as described in Short Notes Renal Replacement Therapy (p. 300–303) and CC table given previously. Not significantly cleared by PD or HD, dose as if CC <10 ml/min, i.e. 2.5–5 mg/kg IV every 24 hours. The dose is dependent upon the indication.

ADENOSINE (Adenocor)

This endogenous nucleoside is safe and effective in ending >90% of re-entrant paroxysmal SVT. However, this is not the most common type of SVT in the critically ill patient. After an IV bolus effects are immediate (10–30 seconds), dose-related and transient (half-life <10 seconds; entirely eliminated from plasma in <1 minute, being degraded by vascular endothelium and erythrocytes). Its elimination is not affected by renal/hepatic disease. Adenosine works faster and is superior to verapamil. It may be used in cardiac failure, in hypotension and with β-blockers, in all of which verapamil is contraindicated.

Uses
It has both therapeutic and diagnostic uses:

- Alternative to DC cardioversion in terminating paroxysmal SVT, including those associated with WPW syndrome
- Determining the origin of broad complex tachycardia; SVT responds, VT does not (predictive accuracy 92%; partly because VT may occasionally respond). Though adenosine does no harm in VT, verapamil may produce hypotension or cardiac arrest

Contraindications
Second- or third-degree heart block (unless pacemaker fitted)
Sick sinus syndrome (unless pacemaker fitted)
Asthmatic – may cause bronchospasm
Patients on dipyridamole (drastically prolongs the half-life and enhances the effects of adenosine – may lead to dangerously prolonged high-degree AV block)

Administration

- Rapid IV bolus: 3 mg over 1–2 seconds into a large vein, followed by rapid flushing with sodium chloride 0.9%

  If no effect within 2 min, give 6 mg
  If no effect within 2 min, give 12 mg
  If no effect, abandon adenosine
  Need continuous ECG monitoring
  More effective given via a central vein or into right atrium

How not to use adenosine
Without continuous ECG monitor

Adverse effects
Flushing (18%), dyspnoea (12%) and chest discomfort are the commonest side-effects but are well tolerated and invariably last <1 min. If given to an asthmatic and bronchospasm occurs, this may last up to 30 min (use aminophylline to reverse).