

Guideline for	SESLHD Adult Inpatients
Authorised Prescribers	Initiation is restricted to hepatologists
Indication for use	Liver support in non-paracetamol induced acute liver failure Note: Acetylcysteine IV in Acute Paracetamol Overdose Prescribing Protocol (SESLHDPR/566)
Clinical condition	<ul style="list-style-type: none"> - Acute liver failure (ALF) irrespective of aetiology (<i>except in cases of paracetamol overdose</i>). ALF can be defined as biochemical evidence of ALF with INR of ≥ 1.5 and any degree of encephalopathy caused by illness of duration < 8 weeks - Severe sepsis - Decompensated cirrhosis - Ischaemia-reperfusion liver injury (e.g., following cardioversion and general anaesthesia) - Major liver resection
Proposed Place in Therapy	First line therapy in the early stages of acute hepatic failure to improve transplant-free survival in non-paracetamol acute liver failure
Adjunctive Therapy	Nil
Contra-indications	Patients with hypersensitivity or a previous anaphylactic reaction to acetylcysteine or any component of the preparation
Precautions	<ul style="list-style-type: none"> • Asthma, history of bronchospasm • History of oesophageal varices and peptic ulceration (treatment induced vomiting may increase risk of haemorrhage) • Bodyweight less than 40 kg or fluid restriction may require adjustment of total fluid volume to minimise risk of hyponatraemia, seizure and death. • Pregnancy (Category B2), breastfeeding and renal impairment: seek advice from consultant hepatologist for risk-benefit analysis
Important Drug Interactions	No information is available on the interaction of acetylcysteine with other medicines.
Dosage	<p>Calculate using actual bodyweight rounded up to the nearest 10 kg (max of 110 kg). Check calculations carefully to avoid dose errors.</p> <p>Loading Dose: Acetylcysteine 150 mg/kg to be added to 250 mL of Glucose 5% and infused over 30 minutes (500 mL/hour)</p> <p>Maintenance Dose: Acetylcysteine 150mg/kg to be added to 1000 mL of Glucose 5% and infused over 24 hours (41.6 mL/hour)</p> <p><i>Note: acetylcysteine is compatible with Glucose 5% and Sodium Chloride 0.9% however glucose 5% is the preferred fluid in liver failure.</i></p> <p>Fluid restricted patients/ patients weighing less than 40kg</p> <p>Loading dose: Acetylcysteine 150 mg/kg to be added to 250 mL of Glucose 5% and infused over 30 minutes (500 mL/hour)</p> <p>Maintenance Dose: Acetylcysteine 150mg/kg to be added to 250 mL of Glucose 5% and infused over 24 hours (10.4 mL/hour).</p>

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Duration of therapy	Continue until recovery of patients' liver injury, up to a maximum of 72 hours then cease.
Prescribing Instructions	Inpatient Prescribing on the eRIC or eMR via eFluids . The infusion order should include dosage, diluent, and infusion rate, e.g., <i>Acetylcysteine x mg in x glucose 5%, infused over x minutes</i>
Administration Instructions	<i>Note: acetylcysteine is compatible with Glucose 5% and Sodium Chloride 0.9% however glucose 5% is the preferred fluid in liver failure.</i> Dilute for infusion: remove the corresponding volume of glucose 5% from bag and then add acetylcysteine. Invert the bag at least 10 times to ensure adequate mixing
Adverse Effects	<div style="border: 2px solid red; padding: 10px; margin-bottom: 10px;"> <p style="text-align: center;">Anaphylactic-like reaction may include airway obstruction (bronchospasm), angioedema, dyspnoea, hypotension, shock, tachycardia, urticaria and injection site reaction (including rash). These reactions occur most commonly either during, or at the end of the period of the loading dose infusion, and may be dose related. Since these anaphylactic-like reactions usually occur following the loading dose, careful monitoring is recommended.</p> <p style="text-align: center; color: red;">Cardiovascular resuscitation equipment MUST be readily available</p> </div> <p>Nausea, vomiting and other gastrointestinal symptoms are common especially with large doses.</p>
Monitoring requirements	Hypersensitivity reactions have occurred following administration of acetylcysteine. Monitor for angioedema, bronchospasm, and rash. After the last maintenance dose check ALT, AST, electrolytes and INR levels.

<p>Management of Complications</p>	<p>Hypersensitivity reactions</p> <p>Treatment of Anaphylaxis</p> <ol style="list-style-type: none"> STOP the infusion Call for help as per local clinical emergency response Lie patient flat and raise their feet. If breathing is compromised sit in high fowlers position Administer 100 % oxygen via mask via nonrebreather mask Obtain intravenous access in adults in the event of hypotension and give IV normal saline (20 mL/kg) rapidly and consider large bore IV access Medical Officer to give adrenaline (1:1000) immediately (0.01 mg/kg to a maximum dose of 0.5 mg) IM (repeat at 5-minute intervals if necessary) followed by hydrocortisone (5 mg/kg up to 200 mg) IV if required. Commence CPR in the event of a respiratory or cardiac arrest. <p>For mild reactions, including rash, bronchospasm, and hypotension:</p> <ol style="list-style-type: none"> STOP the infusion Medical Officer review to consider prescribing promethazine. If deemed safe to restart the infusion following medical review, recommence infusion at a slower rate of 60mL/hr or as instructed by the treating Medical Officer <p><i>Once the reaction has resolved, re-initiating acetylcysteine at a reduced rate should be discussed with the hepatologist.</i></p> <div style="border: 2px solid red; padding: 5px; text-align: center;"> <p>The type of infusion related complication and action taken needs to be clearly documented in the patient's health care record and notified through ims+ for investigation.</p> </div>
<p>Basis of Protocol/Guideline:</p>	<ol style="list-style-type: none"> Nabi T, Nabi S et al. 2017 Role of N-acetylcysteine treatment in non-acetaminophen-induced acute liver failure: A prospective study. Saudi J. Volume 23, Issue 3. Pg 170-175. Riordan, S.M.; Williams, R. 2000. Fulminant Hepatic Failure. Hepatology: Clinics in Liver Disease. Volume 4, Issue 1. Pg 25-45. Micromedex. Acetylcysteine: drug interactions, dosing. Stravitz, R.T, Sanya, A.J. 2013. Effects of N-acetylcysteine on cytokines in non-acetaminophen acute liver failure: potential mechanism of improvement in transplant free survival. Liver International. Volume 33. Pg 1324-1331. Wendon JA, Ellis AJ. Circulatory derangements, monitoring and management: heart, kidney, and brain. In Lee WM, Williams R. Acute Liver Failure, Cambridge University Press, Cambridge, United Kingdom 1997: Pg132-143 SHPA 2017. Australian Injectable Drugs Handbook 7th Ed, Acetylcysteine. Acetylcysteine IV in Acute Paracetamol Overdose Prescribing Protocol, SESLHD, November 2018. Lee WM. 2009. Intravenous N-acetylcysteine improves transplant-free survival in early-stage non-acetaminophen acute liver failure. Gastroenterology. Volume 137. Issue 3. Pg 856-864. Hu J, Zhang et al. 2015. Efficacy and safety of acetylcysteine in “non acetaminophen” acute liver failure: A meta-analysis of prospective clinical trials. Volume 39. Pg 594-599. McPheeters CM et al. 2016. N-Acetylcysteine Use in Non- Acetaminophen-Induced Acute Liver Failure. Advanced Emergency Nursing Journal. Volume 28. Issue 3. Pg 183-189. Bass S et al. 2013. Intravenous acetylcysteine for indications other than acetaminophen overdose. Am J Health-Syst Pharm. Volume 70. Pg1496-1501. ASCIA. 2023. Acute Management of Anaphylaxis.
<p>Groups consulted in development of this guideline</p>	<p>Professor Stephen Riordan, Head of Department, Gastroenterology, POWH SESLHD Hepatologists (via Clinical Stream)</p>

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GOVERNANCE	
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