Paediatric Medication Guideline

# Acetylcysteine (Intravenous) for Paracetamol Poisoning

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| Responsible Area | Pharmacist Consultant – Queensland Poisons Information Centre | | | Review date | 24/02/2027 |
| Executive sponsor | Executive Director Medical Services | | | | |
| Accountable Officer | Executive Director Clinical Services | | | | |

## Purpose

The purpose of this guideline is to provide clinical advice around the use of intravenous 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 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

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

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.

Acetylcysteine is available as a 2,000 mg / 10 mL solution for injection[1]

# Prescribing Instructions

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| X | **Contraindications**<br>• None |
| ! | **Precautions**<br>• Fluid restricted patients require adjustment of total volume to minimize risk of hyponatraemia, seizure and death – seek specialist advice.<br>• Risk of anaphylactoid reactions is dose-related and occurs more commonly during the initial infusion. Previous hypersensitivity reactions to Acetylcysteine do not prevent future use. Discussion with Poison Information Centre or toxicologist is recommended.<br>• Nausea, vomiting and other gastrointestinal symptoms are the most common adverse effects experienced with high dose Acetylcysteine infusions. Antiemetic therapy may be required.<br>• Use with caution in children with a history of asthma/bronchospasm. Close monitoring is required.<br>• Use with caution in children with history of oesophageal varices and peptic ulceration as Acetylcysteine induced vomiting can increase risk of haemorrhage. |

## Dose

Care must be taken in dose calculation and administration instructions. Dosage of acetylcysteine is based on actual bodyweight with a ceiling weight of 110 kg.[2] 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, 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 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.**

### 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: Acetylcysteine 200 mg/kg diluted to a total volume of 100 mL with appropriate diluent*****.[3] Infuse over 4 hours, immediately followed by:
- Infusion 2: Acetylcysteine 100 mg/kg diluted to a total volume of 250 mL with appropriate diluent*. [3] Infuse over 16 hours.

- 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: Acetylcysteine 200 mg/kg diluted to a total volume of 250 mL with appropriate diluent*.[3] Infuse over 4 hours, immediately followed by:
- Infusion 2: Acetylcysteine 100 mg/kg diluted to a total volume of 500 mL with appropriate diluent*. [3] Infuse over 16 hours.
- 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: Acetylcysteine 200 mg/kg diluted to a total volume of 500 mL with appropriate diluent*.[2] Infuse over 4 hours, immediately followed by:
- Infusion 2: Acetylcysteine 100 mg/kg diluted to a total volume of 1000 mL with appropriate diluent*.[2] Infuse over 16 hours.
- 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. 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:**

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

# Administration Instructions

## Reconstitution/Dilution

Acetylcysteine is compatible with either sodium chloride 0.9%, glucose 5% or combinations of glucose-sodium chloride not exceeding these concentrations.

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

Once diluted, the solution should be used immediately.

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

## Route and Method of Administration

Acetylcysteine is administered by intravenous infusion using the appropriate profile in dose error reduction software (DERS) (See Appendix 1).

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 acetylcysteine administration:

- Nausea, vomiting (Common reaction with ~30% incidence.[4] 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[4] 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.

**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 acetylcysteine and treat complications. All attempts should be made to recommence and continue the infusion rather than ceasing therapy. Contact the poison centre 13 11 26 for advice.**

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

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 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).[2]**
  - **A very high paracetamol concentration, more than triple the nomogram line.[2]**
- **Intravenous paracetamol errors or overdoses.**
- **Patients with hepatotoxicity (e.g. ALT > 1000 IU/L).**
- **Repeated or chronic overdoses.**

# Additional Information

Refer to the CHQ-GDL-60018 Paracetamol ingestion – Emergency management in children or the Updated guideline for the management of paracetamol poisoning in Australia and New Zealand[2] for additional information regarding the management of supratherapeutic paracetamol ingestion, the paracetamol treatment nomogram and recommendations for optimal use of activated charcoal.

# Supporting documents

### Authorising Legislation, Policy and Standard/s

- Queensland Health List of Approved Medicines

### Procedures, Guidelines and Protocols

- Updated guideline for the management of paracetamol poisoning in Australia and New Zealand[2]
- 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: Acetylcysteine intravenous infusion for paracetamol poisoning – Prescription and Administration

**Forms and Templates**

- Acetylcysteine Fluid Order form (less than 20 kg)
- Acetylcysteine Fluid Order form (20 – 50 kg)
- Acetylcysteine Fluid Order form (greater than 50 kg)

# Consultation

Key stakeholders who reviewed this version include Pharmacist Senior – Queensland Poisons Information Centre and Pharmacist Senior – Safety Quality

Key stakeholders who reviewed the previous version:

- 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
- Pharmacist Consultant – Electronic Medication Management

# Definition of terms

| Term | Definition |
|---|---|
| ALT | Alanine transaminase |
| INR | International normalised ratio |

# References and suggested reading


1. Product information: *Acetylcysteine 200 mg/mL injection.* (2012). Link Medical Products Pty Ltd, NSW Australia. Available from: http://www.tga.gov.au.
2. Chiew AL, Reith D, Pomerleau A, Wong A, Isoardi KZ, Soderstrom J, et al. Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. Med J Aust 2020; 212:175-183
3. Marzullo L. An update of N-acetylcysteine treatment for acute acetaminophen toxicity in children. Curr. Opin. Pediatr. 2005;17 (2): 239-45.
4. Metro South Health. (2018). *Prescribing guideline: Adult – N-Acetylcysteine (NAC) Infusion Procedure of Paracetamol Poisoning.* Queensland, Australia.

# Revision and approval history

| Version No. | Modified by | Amendments authorised by | Approved by |
|---|---|---|---|
| 1.0<br>01/02/17 | Pharmacist Team Leader – Critical Care | Medicines Advisory Committee | General Manager Operations |
| 2.0<br>28/06/19 | Pharmacist Advanced – Safety & Quality | Medicines Advisory Committee | Executive Director Clinical Service (QCH) |
| 3.0<br>24/02/23 | Pharmacist Senior – Queensland Poisons Information Centre | Director of Pharmacy | Executive Director Medical Service |

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|---|---|
| **Keywords** | Paracetamol, Acetylcysteine, 01230, paracetamol poisoning, overdose |
| **Accreditation references** | NSQHS Standards (1-8): 4 – Medication Safety<br>ISO 9001:2015 Quality Management Systems: (4-10) |

# Appendix 1 Usage guidelines for Braun Pumps



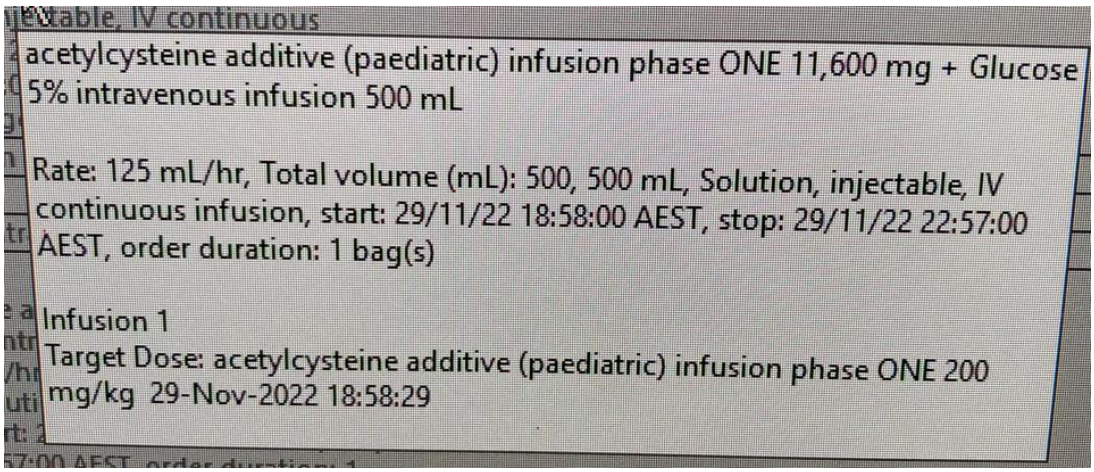
## Appendix 1.1 Usage guideline for Braun L Pump

50kg – 110kg Max. (Do not exceed 110kg for weight)

**FIRST INFUSION: Acetylcysteine 200mg/kg in 500ml fluid and infused over 4 hours**

1. Turn on pump
2. Use Drug Library → YES
3. Scroll to Change ward → OK
4. Select General Ward OR Paediatric ICU → OK
5. Select All Drugs → OK
6. Scroll down to *acetylcysteine Step 1* → OK


7. Go to the ieMR order for the patient in MAR and find acetylcysteine Phase ONE (have the order box up in front of you).



8. Type in the Amount = dose of acetylcysteine in mg (11600mg) → OK


9. Enter the Volume to be infused (500mL) → OK


10. Enter the Weight from ieMR ( 58kg) →OK


11. Volume to be Infused (VTBI) = 500mL.

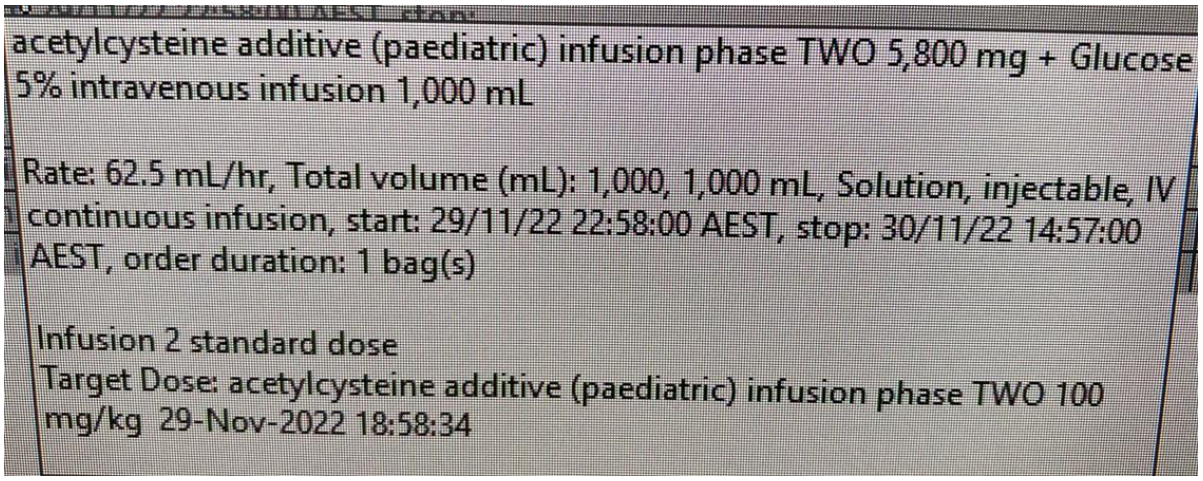
    This results in 125mL/h infusion rate (check on screen)


12. Scroll through the setting to confirm the order is correct then click START


**SECOND INFUSION: Acetylcysteine dose is in 1000ml fluid and infused over 16 hours**

1. Follow steps 1-5 above
2. Scroll down to acetylcysteine Step 2 → OK

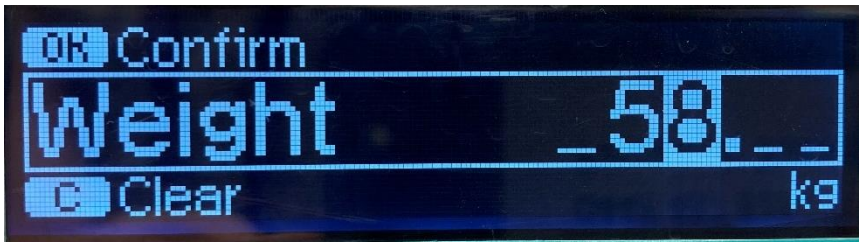

3. Go to the ieMR order for the patient in MAR and find acetylcysteine Phase TWO (have the order up in front of you).




4. Type in the Amount = dose of acetylcysteine in mg (5800mg) → OK


5. Enter the Volume to be infused (1000mL) → OK

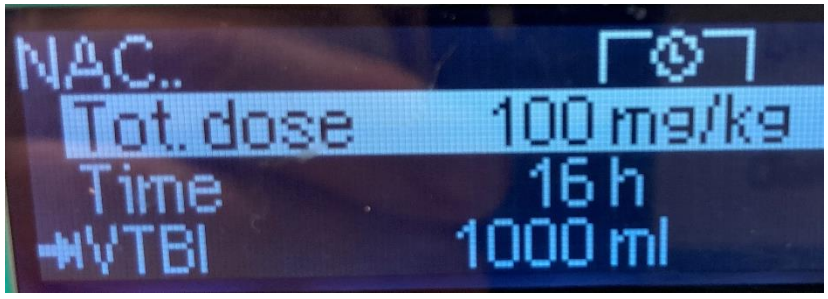

6. Enter the Weight from ieMR ( 58kg) → OK




7. Enter the VTBI (volume to be infused) = 1000mL → OK

   This results in rate of 62.5mL/h


8. Scroll through the setting to confirm the order is correct then click **START**

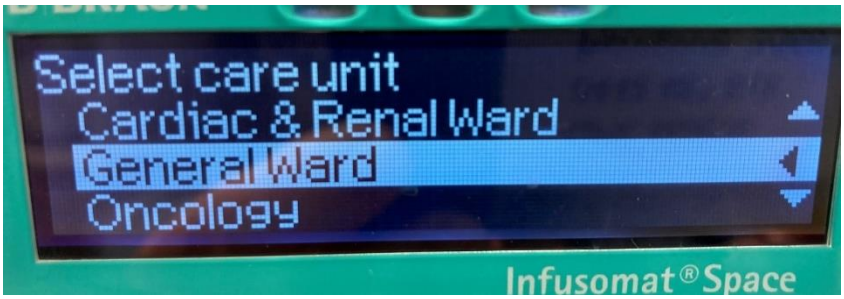



# Appendix 1.2 Usage guideline for Braun M Pump

50kg – 110kg Max. (Do not exceed 110kg for weight)

**FIRST INFUSION: Acetylcysteine 200mg/kg in 500ml fluid and infused over 4 hours**

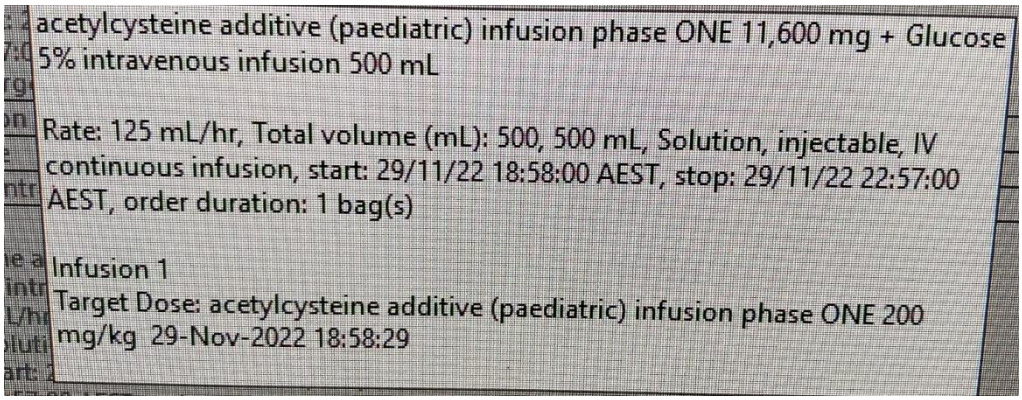
1. Turn on pump
2. Use Drug Library → YES
3. Scroll to change care unit → OK
4. Select General Ward OR Paediatric ICU → OK




5. Select All Drugs → OK


*6.* Scroll down to *acetylcysteine Step 1* → OK


7. Go to the ieMR order for the patient in MAR and find acetylcysteine Phase ONE (have the order in front of you)




8. Type in the Amount =dose of acetylcysteine in mg (eg 11600mg) → OK


9. Enter the Volume to be infused (eg 500mL) → OK


10. Enter the Weight from ieMR ( 58kg) → OK

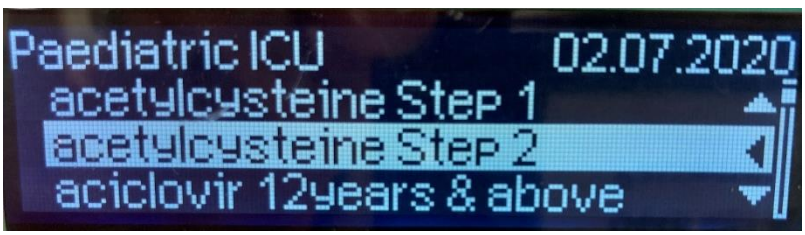
11. Enter the <u>Total dose</u> in mg/kg (200mg /kg) see order in ieMR Note: VTBI (Volume to Be Infused) is 500mL


12. Scroll through the setting to confirm the order is correct. Confirm the rate is 125mL/hour. Then click **START**

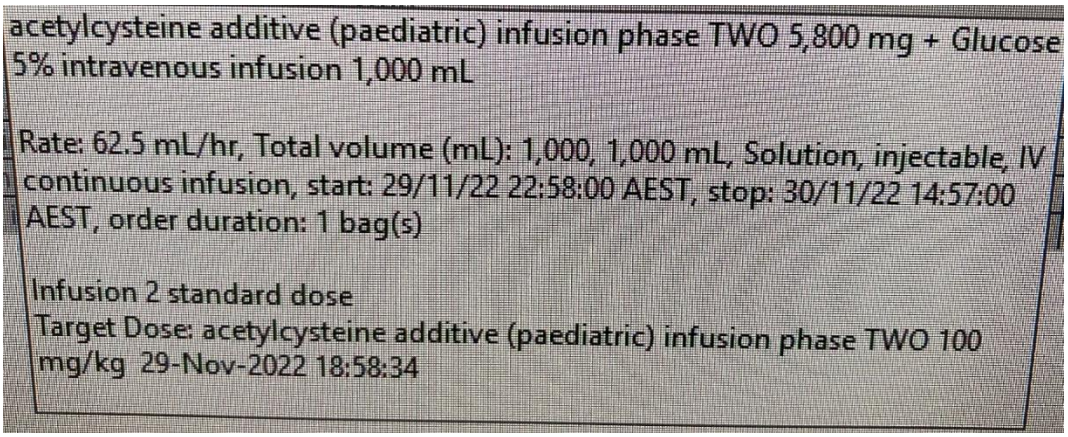


**<u>SECOND INFUSION: acetylcysteine dose 100mg/kg in 1000ml fluid and infused over 16 hours</u>**.

1. Follow steps 1-5 above
2. Scroll down to acetylcysteine Step 2 → OK



3. Go to the ieMR order for the patient in MAR and find acetylcysteine phase TWO




4. Type in the Amount = the dose of acetylcysteine in mg (5800mg) → OK


5. Enter the Volume to be infused (eg 1000mL) → OK


6. Enter the Weight from ieMR (eg 58kg) → OK

7. Enter the Total Dose in mg/kg (100mg /kg). Confirm the VTBI (Volume to Be Infused) = 1000mL


8. Scroll through the setting to confirm the order is correct. The infusion rate should read 62.5mL /hour. Then click START.



## Appendix 1.3 Usage guideline for Braun N Pump

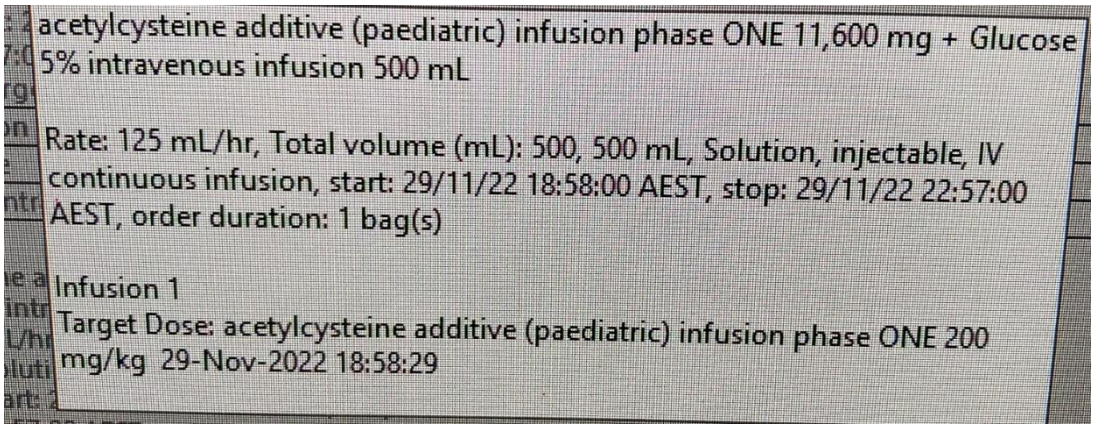
50kg – 110kg Max. (Do not exceed 110kg for weight)

**FIRST INFUSION: acetylcysteine 200mg/kg in 500ml fluid and infused over 4 hours**

1. Turn on pump
2. Use Drug Library → YES
3. Scroll to Change care unit → OK
4. Select General Ward OR Paediatric ICU → OK
5. Select All Drugs → OK


6. Scroll down to *acetylcysteine Step 1* → OK


7. Go to the ieMR order for the patient in MAR and find acetylcysteine Phase ONE




8. Type in the Amount =dose of acetylcysteine in mg (eg 11600mg) → OK

9. Enter the Volume to be infused (eg 500mL) → OK


10. Enter the Weight from ieMR (58kg) → OK

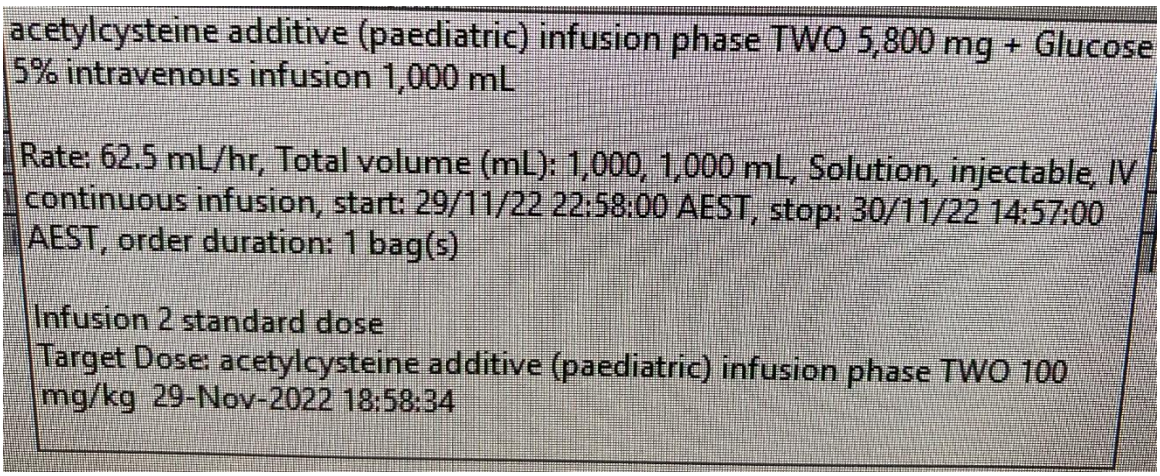

11. Enter the Total dose in mg/kg (200mg/kg) ** Note: VTBI (Volume to Be Infused) is 500mL


12. Scroll through the setting to confirm the order is correct. The rate should read 125mL/hour. Then click **START**.


**SECOND INFUSION: acetylcysteine dose 100mg/kg is in 1000ml fluid and infused over 16 hours.**

1. Follow steps 1-5 above
2. Scroll down to *acetylcysteine Step 2* → OK

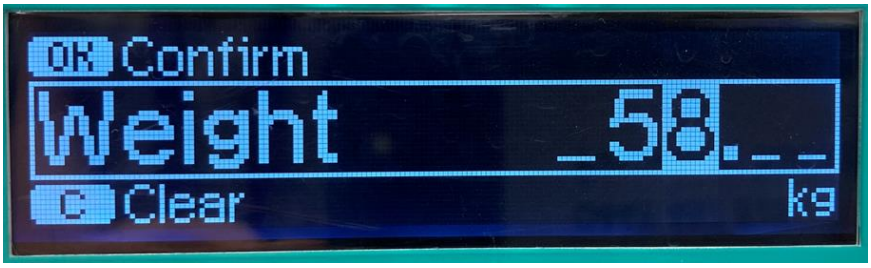

3. Go to the ieMR order for the patient in MAR and find Acetylcysteine Phase TWO




4. Type in the Amount = the dose of acetylcysteine in mg (5800mg) → OK

5. Enter the Volume to be infused (eg 1000mL) → OK


6. Enter the Weight from ieMR (eg 58kg) → OK




7. Enter the Total Dose in mg/kg (100mg /kg). Confirm the VTBI (Volume to Be Infused) = 1000mL


8. Scroll through the setting to confirm the order is correct. The rate should read 62.5mL/hour. Then click START