

# Acetylcysteine in paracetamol overdose

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## TARGET AUDIENCE and SETTING

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Enrolled nurses within the scope of their practice, Medical Officers, Nurse Practitioners, Pharmacists and Registered Nurses.

This procedure is applicable to all Monash Health clinical staff, patients, clients and their families and carers.

## PURPOSE

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This procedure details how to prescribe and administer acetylcysteine in paracetamol overdose.

## PRECAUTIONS/CONTRAINDICATIONS

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Patients with asthma or a previous anaphylactoid reaction to acetylcysteine may be at increased risk of respiratory adverse effects. Observe carefully while administering infusions.<sup>1-2</sup>

Concomitant medicines (e.g. carbamazepine, rifampicin, isoniazid, phenobarbitone, phenytoin, primidone, valproate) and certain medical conditions (e.g. cystic fibrosis, anorexia nervosa, chronic alcohol abuse) can reduce glutathione stores, reducing the threshold for giving acetylcysteine.<sup>1</sup> Discuss these patients with the on call Toxicologist.

Patients with massive ingestions (greater than or equal to 500 mg/kg) must be discussed with the on-call Toxicologist. Acetylcysteine dosing may vary on a case-by-case basis.

## EQUIPMENT

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- Acetylcysteine 200 mg/mL, 10 mL ampoule. Acetylcysteine is stored below 25°C and must be protected from light.<sup>2-3</sup> It is available in Emergency Departments, Intensive Care Units and intravenous stock cupboards on some wards. Refer to [Medication Location Guide](#) on Pharmacy Department intranet site.
- Sodium chloride 0.9% or glucose 5% infusion bags.
- Smart pump with Guardrails™ dose error reduction software.
- EMR – Medication Administration Record (MAR).

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# Acetylcysteine in paracetamol overdose

## STANDARD REQUIREMENTS

When undertaking any clinical interaction with a patient, staff are expected to;

- Perform routine hand hygiene. Refer to the [Hand Hygiene Procedure](#).
- Introduce themselves to the Patient and Carer/ Family if in attendance
- Check patient identification. Refer to the [Patient Identification Procedure](#).
- Obtain consent as per the [Consent to Medical Treatment Procedure](#).
- Keep the patient/carer informed and involve them in decision making.
- Document interaction in the electronic medical record or health record using black pen; including date, time, signature and designation.

## PROCEDURE

### 1. Acetylcysteine in paracetamol overdose

- 1.1. Determine type of paracetamol overdose:
- Acute overdose presenting less than 8 hours after ingestion
  - Acute overdose presenting 8 hours or more after ingestion
  - Massive acute overdose (more than 500mg/kg or serum paracetamol concentration more than double the nomogram line)
  - Repeated supratherapeutic ingestion
  - Modified release paracetamol ingestion
  - Liquid paracetamol ingestion in paediatric patients less than 6 years of age
- 1.2. Determine if patient has ingested a potentially toxic dose of paracetamol.

**Table 1: Patients at risk of paracetamol toxicity**

<b>Acute single ingestion</b>	Greater than 200 mg/kg or 10 g (whichever is lower) over a period of less than 8 hours. <sup>4, 6</sup>
<b>Repeated supra-therapeutic ingestions</b>	Greater than 200 mg/kg or 10 g (whichever is lower) over a single 24 hour period. <sup>4, 6</sup>
	Greater than 150 mg/kg or 6 g (whichever is lower) per 24 hour period for the preceding 48 hours. <sup>4, 6</sup>
	<p><b>Adult or child greater than 6 years</b>            Greater than 100 mg/kg or 4 g (whichever is lower) per 24 hour period for more than 48 hours in symptomatic patients (e.g. nausea, vomiting, abdominal pain).<sup>4, 6</sup></p> <p><b>Child less than or equal to 6 years</b>            Greater than 100 mg/kg per 24 hour period for more than 48 hours.<sup>6</sup></p>

Note: For obese children, use ideal body weight.<sup>6</sup>

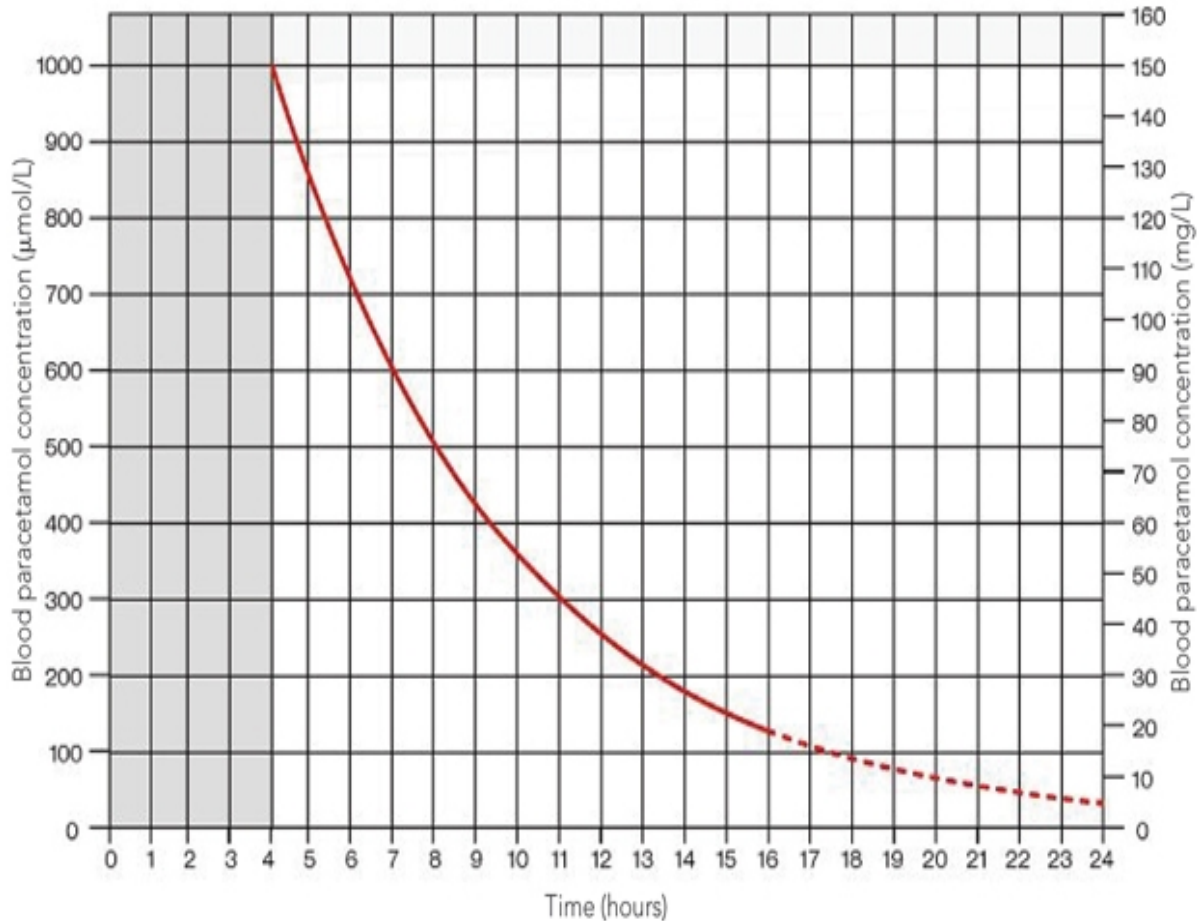
- 1.3. Assess and manage overdose as per appropriate flowchart
- Acute overdose presenting less than 8 hours after ingestion ([Flowchart 1](#))
  - Acute overdose presenting 8 hours or more after ingestion ([Flowchart 2](#))
  - Massive acute overdose (more than 500mg/kg or serum paracetamol concentration more than double the nomogram line ([Flowchart 1](#) and [2](#)))
  - Repeated supratherapeutic ingestion ([Flowchart 3](#))

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- Modified release paracetamol ingestion ([Flowchart 4](#))
- Liquid paracetamol ingestion in patients less than 6 years of age ([Flowchart 5](#))

1.4. Plotting paracetamol serum concentration on the Paracetamol Overdose Treatment Nomogram as required (Chart 1).

**Chart 1: Paracetamol Overdose Treatment Nomogram<sup>5</sup>**



## Acetylcysteine in paracetamol overdose

- 1.5. Calculate acetylcysteine dose, diluent fluid volume and infusion rate using table 2. Prescribe the final acetylcysteine dose in milligrams

**Table 2: Standard 2 bag acetylcysteine intravenous infusions for adults and children<sup>5</sup>**

		Adults	Children greater than 20kg	Children less than or equal to 20kg
<b>Bag 1</b>	Dose	200 mg/kg (Maximum 22,000 mg)	200 mg/kg (Maximum 22,000 mg)	200 mg/kg
	Fluid	Sodium chloride 0.9% (or glucose 5%) 500 mL*	Sodium chloride 0.9% (or glucose 5%) 250 mL*	Sodium chloride 0.9% (or glucose 5%), 7 mL/kg
	Infusion duration	4 hours	4 hours	4 hours
	Infusion rate	125 mL/hr	62.5 mL/hr	(Fluid volume/4) mL/hr
<b>Bag 2</b>	Dose	100 mg/kg <sup>^</sup> (Maximum 11,000 mg)	100 mg/kg <sup>^</sup> (Maximum 11,000 mg)	100 mg/kg
	Fluid	Sodium chloride 0.9%, (or glucose 5%) 1000 mL*	Sodium chloride 0.9% (or glucose 5%) 500 mL*	Sodium chloride 0.9% (or glucose 5%), 14 mL/kg
	Infusion duration	16 hours	16 hours	16 hours
	Infusion rate	62.5 mL/hr	31.25 mL/hr	(Fluid volume/16) mL/hr

\* Do not overfill the infusion bag: Withdraw the equivalent volume from the bag before adding the acetylcysteine dose.

<sup>^</sup>In some situations, a double dose at 200 mg/kg (maximum 22,000 mg) is required for bag 2 (16 hour bag). Refer to flow charts 1 to 4.

- 1.6. Administer acetylcysteine infusion via smart pump with Guardrails™ dose error reduction software and compatible infusion set.

1.6.1. Program smart pump with dose of acetylcysteine in mg, diluent volume in mL and patient weight in kg. See example in *figure 1*.

## Acetylcysteine in paracetamol overdose

1.6.2. Enter volume to be infused (VTBI) in mL and rate in mL/hr. See example in *figure 2*.



Figure 1.



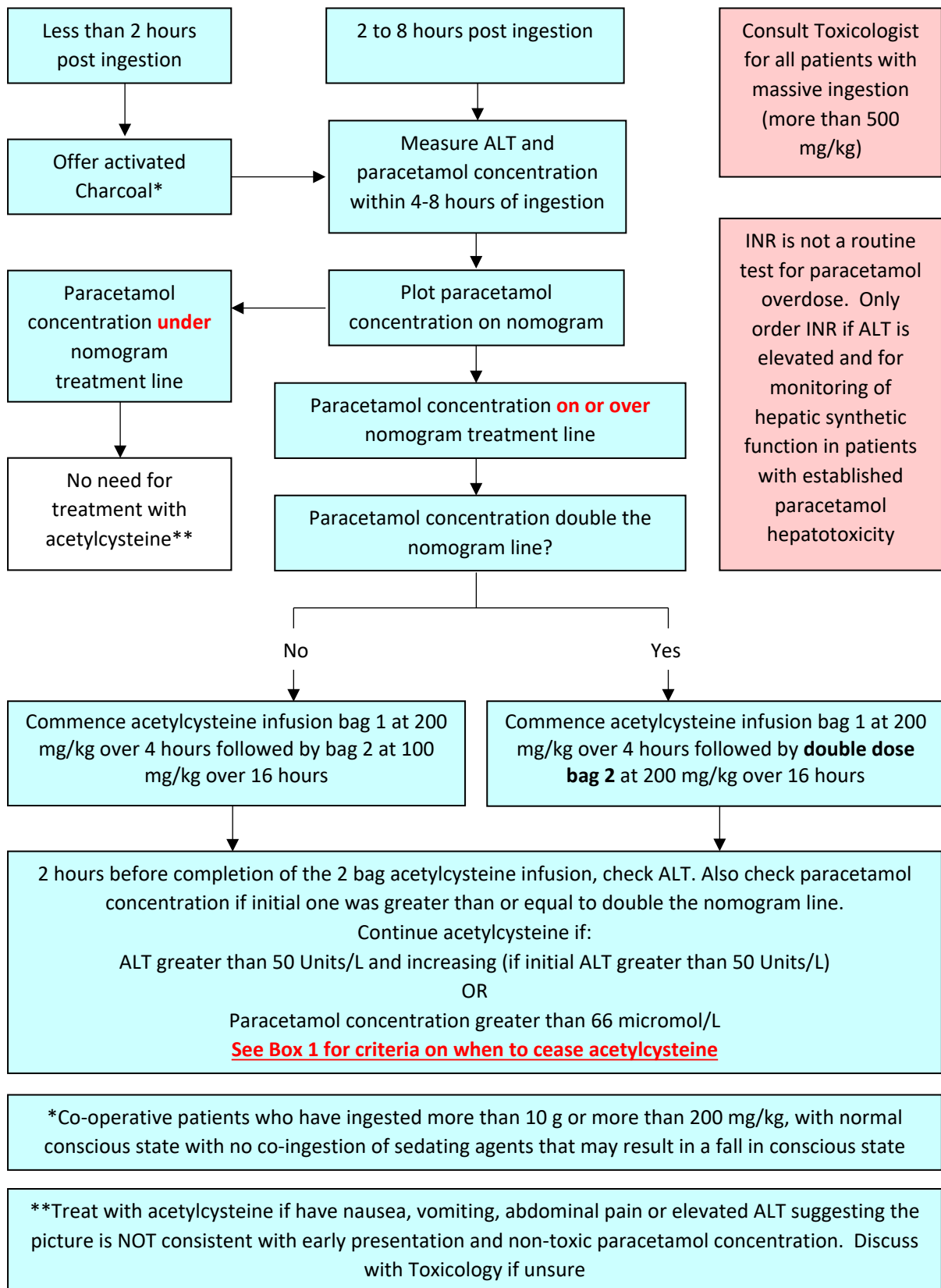
Figure 2.

**Example** of how to program smart pump for Bag 1: 200 mg/kg for 110 kg patient. Figure 1: Dose = 22000, volume = 500 and weight = 110. Figure 2: VTBI = 500 and rate =  $500/4 = 125$  mL/hr.

- 1.7. Monitor vital signs (pulse, blood pressure, respiratory rate) and for signs of anaphylaxis every 15 minutes for the first hour of the acetylcysteine infusion.
- 1.8. Notify medical officer if patient has signs of anaphylaxis.
- 1.9. Manage adverse reactions:
  - 1.9.1. Stop the infusion immediately if a mild reaction (flushing, itching, nausea and vomiting, abdominal pain) occurs in a hemodynamically stable patient. Administer an antihistamine (loratadine or cetirizine). Restart the infusion at a lower rate and increase back to normal rate over 60 minutes.
  - 1.9.2. Stop the infusion immediately if a severe reaction (anaphylaxis: rash, bronchospasm, angioedema, hypotension) occurs. Treat as severe anaphylactic reaction with adrenaline. Seek advice from Clinical Toxicologist on how to restart the infusion. Once reaction is treated, aim is to restart acetylcysteine
- 1.10. Monitor the patient's biochemistry as per appropriate flow chart.
- 1.11. Cease acetylcysteine infusion after completion of the 2 infusion bags. If further bags were required, cease acetylcysteine once criteria are met. ([Box 1](#))

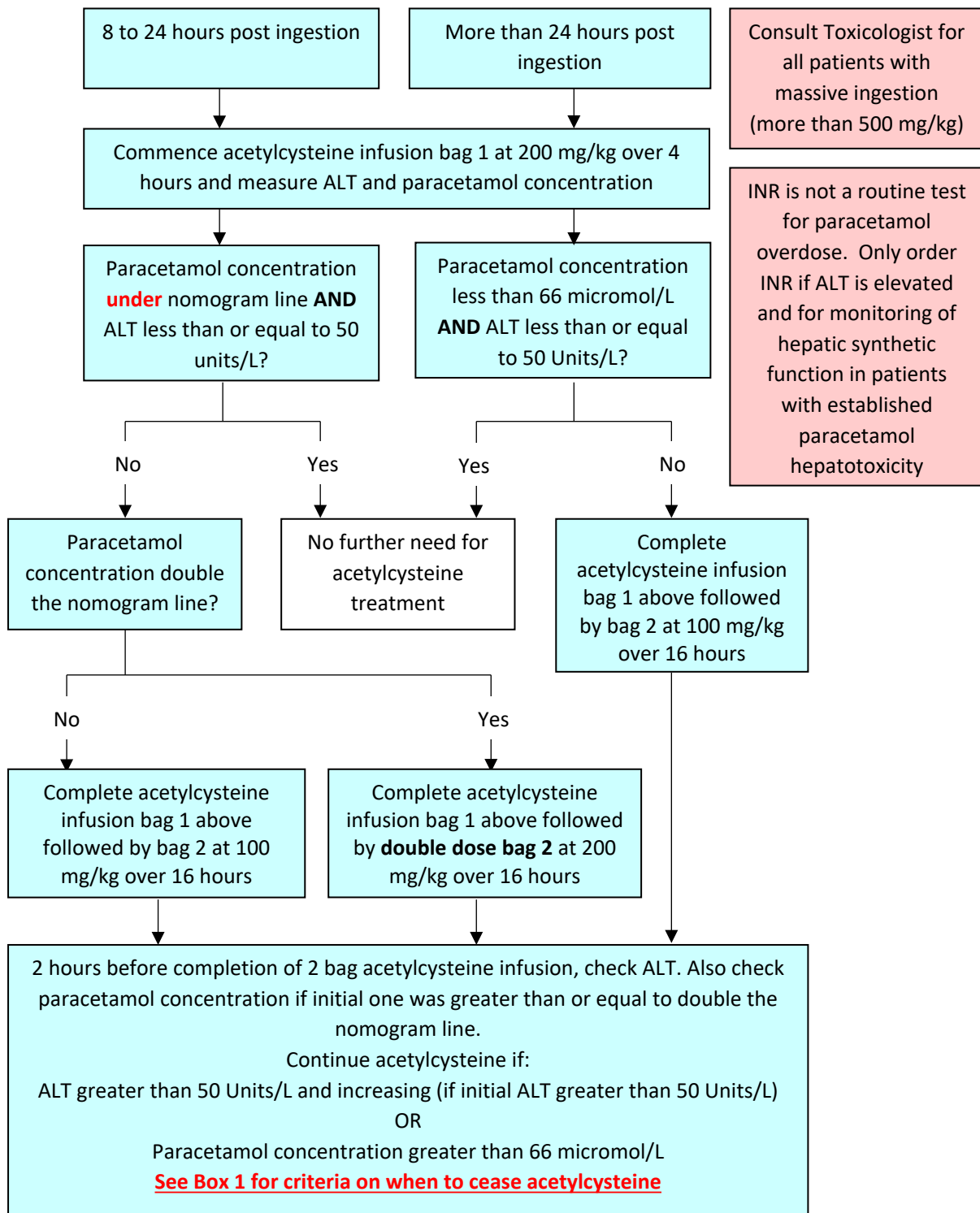
## Acetylcysteine in paracetamol overdose

Flowchart 1: Acute overdose presenting less than 8 hours after ingestion<sup>5</sup>



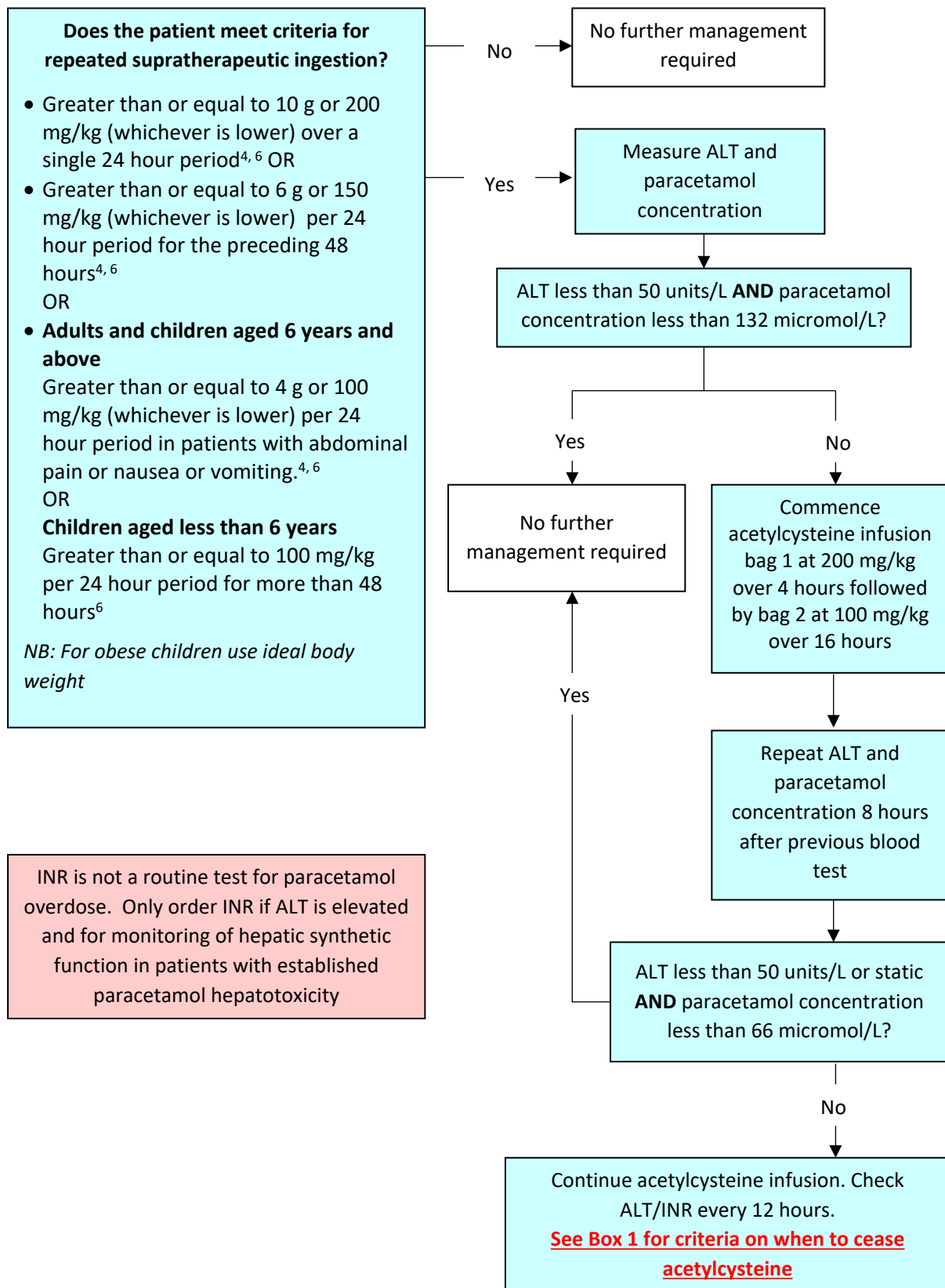
## Acetylcysteine in paracetamol overdose

Flowchart 2: Acute overdose presenting 8 hours or more after ingestion<sup>5</sup>



## Acetylcysteine in paracetamol overdose

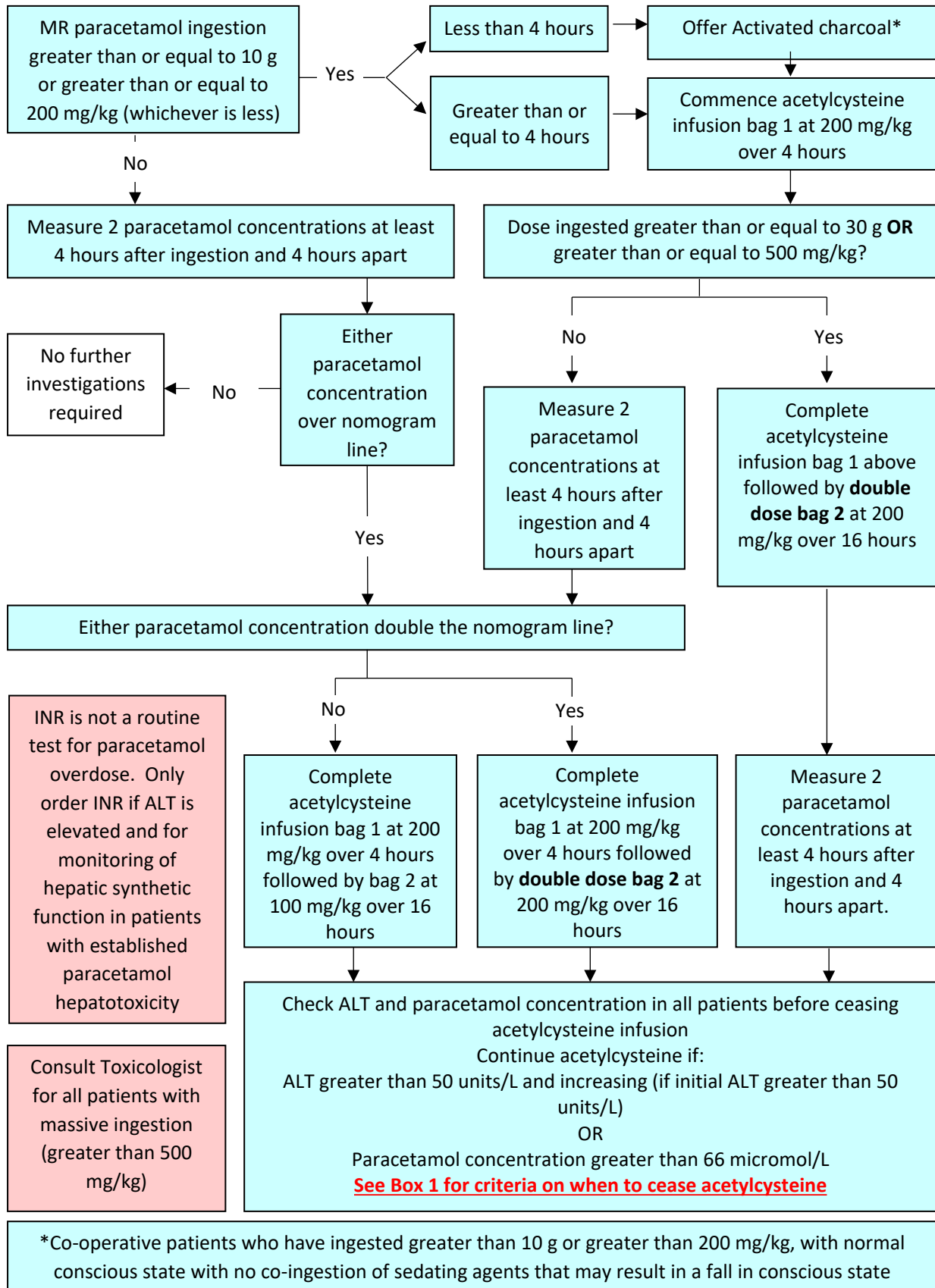
Flowchart 3: Repeated suprathreshold ingestion<sup>5</sup>





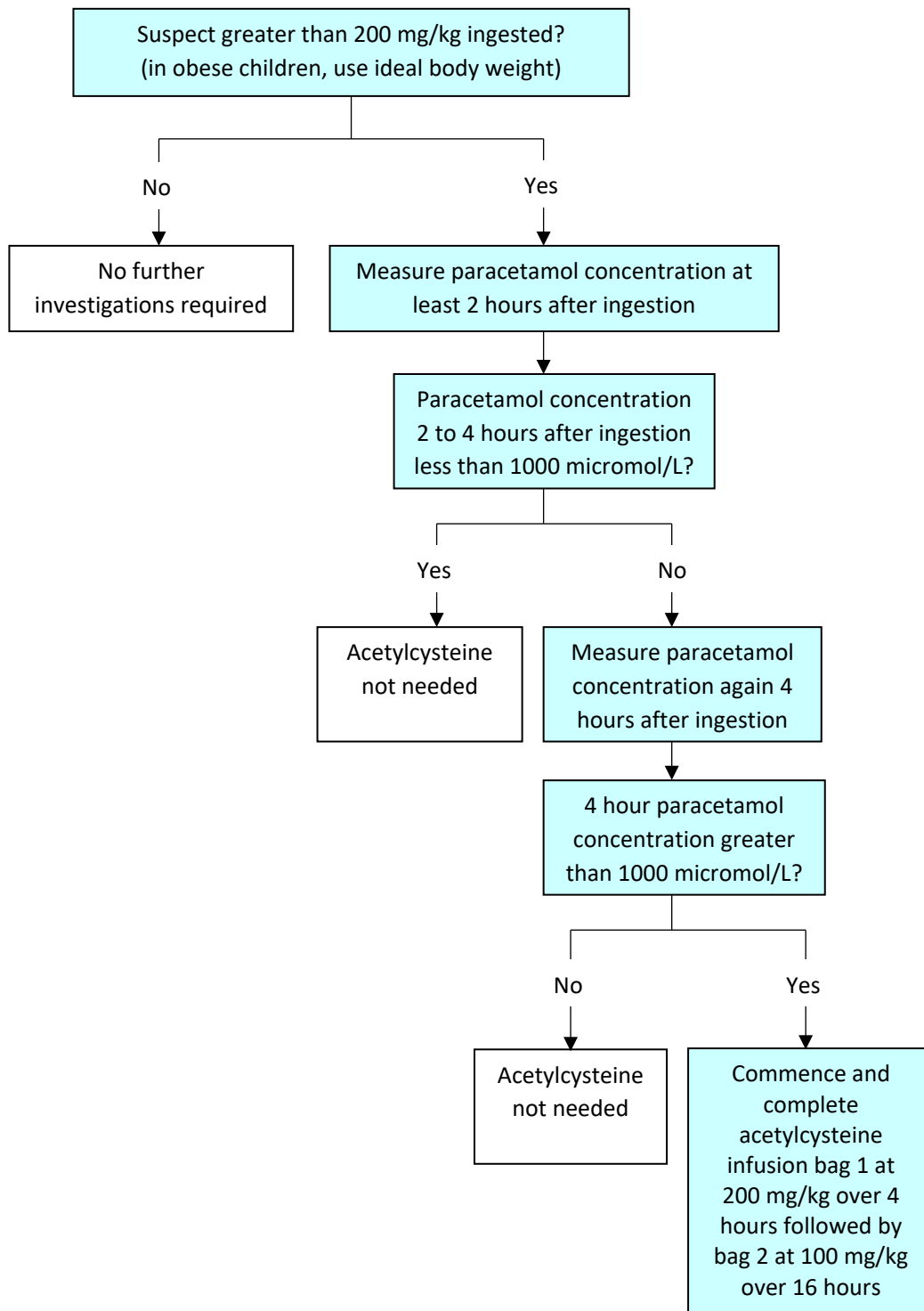
## Acetylcysteine in paracetamol overdose

Flowchart 4: Modified release (MR) paracetamol ingestion



## Acetylcysteine in paracetamol overdose

Flowchart 5: Liquid paracetamol ingestion in less than 6 years of age<sup>5</sup>



NB: Only use to guide management in a healthy child less than 6 years of age

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### 2. Criteria for ceasing acetylcysteine infusion

- 2.1. Acetylcysteine infusion can be ceased once all the criteria for cessation are met as per flowcharts. If acetylcysteine is required beyond 2 bags, it can be ceased once all criteria for cessation are met as per Box 1.

#### Box 1: Criteria for ceasing ongoing treatment with acetylcysteine

<ul style="list-style-type: none"> <li>• In patients who required acetylcysteine beyond 2 bags, acetylcysteine can be ceased if ALL of these criteria have been met:           <ul style="list-style-type: none"> <li>○ ALT or AST are decreasing</li> <li>○ INR less than 2</li> <li>○ Patient clinically well</li> </ul> </li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>• For modified release ingestions and patients with initial paracetamol concentration <math>\geq</math> double the nomogram line, paracetamol concentration less than 66 micromol/L</li> </ul>
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### 3. Poisoning short stay unit (SSU) admission (Adult)

<b>DIAGNOSTIC CRITERIA</b>	
<ul style="list-style-type: none"> <li>• Paracetamol poisoning requiring treatment with acetylcysteine</li> </ul>	
<b>SSU ADMISSION CRITERIA</b> <ul style="list-style-type: none"> <li>• Paracetamol poisoning</li> <li>• Toxic paracetamol concentration indicating need for acetylcysteine treatment</li> <li>• 4 hour loading dose of acetylcysteine commenced in ED</li> <li>• Admission discussed with and approved by clinical toxicologist on-call</li> <li>• Supra-therapeutic ingestions</li> </ul>	<b>SSU EXCLUSION CRITERIA</b> <ul style="list-style-type: none"> <li>• Discuss each case with a toxicologist if in doubt</li> <li>• Evidence of hepatotoxicity (elevated INR or acidaemia, renal impairment)</li> <li>• Complicated paracetamol poisoning (massive greater than 1 g/kg)</li> <li>• Unstable vital signs</li> <li>• Uncooperative with treatment</li> <li>• Recommended patient</li> </ul>
<b>BASELINE INVESTIGATIONS</b> <ul style="list-style-type: none"> <li>• UEC, LFTs</li> <li>• ECG</li> <li>• Paracetamol concentration</li> <li>• Blood alcohol as indicated</li> <li>• Urine or serum HCG as indicated</li> </ul>	<b>SUBSEQUENT INVESTIGATIONS</b> <ul style="list-style-type: none"> <li>• As indicated in PROMPT guidelines for paracetamol poisoning</li> </ul>
<b>PRESCRIBING</b> <ul style="list-style-type: none"> <li>• As required for specific overdose</li> </ul>	
<b>HOME DISCHARGE CRITERIA</b> <ul style="list-style-type: none"> <li>• SSU team to consult clinical toxicologist prior to medical clearance (if no clear discharge plan in place)</li> <li>• Stable vital signs</li> <li>• Safe psychosocial situation</li> <li>• Discharge letter, certificates</li> </ul>	<b>HOSPITAL ADMISSION CRITERIA</b> <ul style="list-style-type: none"> <li>• In discussion with toxicologist</li> <li>• Likely to need prolonged acetylcysteine course</li> <li>• Evidence of significant hepatotoxicity on presentation</li> <li>• Deteriorating / decreased GCS</li> <li>• Cardiac instability / need for cardiac monitoring</li> <li>• Development of SSU EXCLUSION CRITERIA</li> </ul>

# Acetylcysteine in paracetamol overdose

## BACKGROUND

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**Medication Class:** Antidote for paracetamol toxicity.

**Pharmacokinetics:** Rapidly and extensively metabolised in the liver. Acetylcysteine undergoes de-acetylation and then follows the normal metabolic pathway of the amino acid cysteine.

**Actions:**

- Precursor for glutathione synthesis; glutathione and acetylcysteine bind to reactive metabolite of paracetamol; repletion of glutathione also directly reduces oxidative cell injury.
- Acetylcysteine may also improve hepatic perfusion in established liver injury due to paracetamol.

**Adverse reactions:**

- Adverse reaction rates to acetylcysteine have been quoted to be as low as 6% to as high as 40%.

Adverse reactions are usually dose and rate dependent and range from minor urticarial to life threatening anaphylaxis.

**Pregnancy:** Pregnancy category B2; benefits probably outweigh risks.

**Breastfeeding:** Safe to use.

## KEY STANDARDS, GUIDELINES OR LEGISLATION

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- [Labelling of Medicines, Fluids and Lines procedure](#)
- [Medication Administration procedure](#)
- [Medication Ordering \(Electronic Medical Record \(EMR\)\) procedure](#)
- [Medication Prescribing Medication Chart procedure](#)

## REFERENCES

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1. Australian Medicines Handbook, accessed online April 2020
2. MIMS Online, accessed April 2020
3. The Society of Hospital Pharmacists of Australia, Australian Injectable Drugs Handbook, 8<sup>th</sup> Edition, accessed online April 2020
4. Therapeutic Guidelines, Toxicology, accessed online April 2020
5. Chiew AL, Reith D, Pomerleau A, Wong A, Isoardi KZ, Soderstrom J, Buckley NA. Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. *Med J Aust* 2020;212(4):175-183.
6. Chiew AL, Fountain JS, Graudins A, Isbister GK, Reith D, Buckley NA. Summary statement: new guidelines for the management of paracetamol poisoning in Australia and New Zealand. *Med J Aust* 2015;203(5):215–218.

## KEYWORDS

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## Acetylcysteine in paracetamol overdose

Parvolex, NAC, N-acetylcysteine

<b>Document Governance</b>	
<b>Supporting Policy</b>	<a href="#">Medication management (Operational)</a>
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<b>Consumer Review</b> <b>Yes or No</b>	No
<b>This Procedure has been endorsed by an EMR Subject Matter Expert (SME)</b>	There are no Order Set or Quick Reference Guides linked