When the Antidote Causes Harm: Preventing Errors with Intravenous Acetylcysteine (Table 2 of Safety Bulletin)

TABLE 2. Contributing Factors with Corresponding Recommendations from a Multi-Incident Analysis

Contributing Factors	Recommendations
Design of Acetylcysteine Protocol and Standardized Order Set; Availability of Resources	
Inconsistent and/or unclear terminology in some poison centre protocols and/or hospital/health region standardized order sets increases risk of errors.	**Poison Centres** • Collaboratively develop a pan-Canadian protocol to support a consistent approach to the safe treatment of acetaminophen overdoses. • Incorporate a step in the patient care consultation process to request the hospital or health region's standardized order set and to confirm mutual understanding of the dose being delivered and next steps. **Hospitals and Health Regions** • *Develop standardized order sets according to the following principles:* ◦ With support from an interdisciplinary team, use clear and concise directions and consistent terminology and avoid potentially dangerous abbreviations. ◦ Where applicable, incorporate poison centre protocol and guidance into order sets. For pediatric patients, also consider local pediatric centre guidance. ◦ Ensure consistency with the organization's infusion pump programming terminology and sequence of programming steps. ◦ Include direction for when to contact the local provincial poison centre (https://infopoison.ca/) and steps to access a medical toxicologist and pharmacist for consultation, when applicable. ◦ Incorporate a step in the poison centre consultation process, to provide the hospital/health region's standardized order set and to confirm mutual understanding of the dose being delivered and next steps. ◦ Include dosing tables to provide calculation supports for preparing doses and/or checking the rate/duration of infusions. ◦ Check that smart pump drug libraries include acetylcysteine, with applicable parameters established according to specific directions provided in the standardized order set.
Use of a 1-litre bag of dextrose 5% in water (D5W) for administration of acetylcysteine in lower-weight patients (e.g., toddlers) increases potential for harm.	**Poison Centres, Hospitals, and Health Regions** • *Develop standardized protocols and standardized order sets according to the following principles:* ◦ Clearly differentiate pediatric weight-based volume and infusion directions from instructions for adult patients, to reduce the risk of volume overload and/or overdose. ◦ Ensure that the intravenous (IV) bag size used to prepare the acetylcysteine dose is appropriate for lower-weight patients, who are at increased risk of harm from fluid overload. ◦ Include monitoring parameters for electrolytes and fluid balance. ◦ Include monitoring parameters for early signs of infusion overdose (e.g., headache, confusion, nausea and vomiting, irritability, disorientation, decreased level of consciousness, seizures). • *Additional notes:* ◦ Acetylcysteine is compatible with D5W, 0.9% saline, 0.45% saline, and 0.45% saline + 5% dextrose solutions.[13,31,33] ◦ Re-examine regimens that use 1-litre D5W infusion solutions to administer acetylcysteine in this population; consider use of weight-based infusion volume limits. Consider the osmolarity, tonicity, and total volume of the IV solution (e.g., D5W becomes hypotonic upon infusion).

Lack of user testing of protocols and/or standardized order sets with local prescribers, pharmacists, and nursing staff before implementing a change in the protocols and/or standardized order sets reduces the likelihood that vulnerabilities will be detected and addressed before implementation.	**Hospitals and Health Regions** • *Complete the following steps before finalizing and implementing a standardized order set for IV administration of acetylcysteine:* ◦ User testing of the order set. ◦ Hospital/health region risk assessment, with considerations that include access to real-time pharmacist support, and also the potential for patient transfer to other facilities (with different protocols/standardized order sets). • *Consider the following additional strategies:* ◦ Where available, consider testing order sets and protocols in a simulation laboratory. ◦ Develop a change management approach, including education strategies, for prescribers, pharmacists, and nurses before launching new or changed standardized order sets and/or other clinical supports.
Having out-of-date, confusing, or conflicting clinical resources accessible to health care providers increases the likelihood of errors in prescribing, preparing, and/or administering the infusion.	**Hospitals and Health Regions** • Ensure that the up-to-date poison centre protocol and hospital/health region standardized order set (and other related supports) are readily accessible to any prescriber, pharmacist, or nurse who may need it. • Remove outdated or conflicting resources from patient care areas.
Canadian Product Monograph	
The Canadian Product Monograph(s) do not reflect leading practices (e.g., for the initial infusion rate, and guidance for determining weight-based infusion volume limits), increasing the risk of errors.	**Product Manufacturers (Sponsors)** • Review and update product monographs based on findings and recommendations in this Safety Bulletin.
Decision to Treat and Prescribing of Acetylcysteine	
Lack of real-time access to clinical "decision-to-treat" resources for acetylcysteine infusion increases the likelihood that treatment will be provided when it is not indicated.	**Hospitals and Health Regions** • Provide prescribers with real-time access to clinical "decision-to-treat" and prescribing resources (e.g., clinical pathways including a nomogram, poison centre contact information), as well as access to laboratory resources.[34]
Prescribing acetylcysteine using the order or phrase "as per protocol" without understanding the implications of dosing and fluids administered increases the risk of errors in preparation, administration, and monitoring.	**Prescribers** • Use a standardized order set to reduce the risk of errors associated with IV administration of acetylcysteine and to ensure a mutual understanding among care team members (including prescriber, nurse, pharmacist, poison centre staff, patient, and family) of how acetylcysteine is being provided and monitored. • Avoid using verbal or telephone orders which may lack clarity or be misinterpreted.

Preparation and Administration of Acetylcysteine for Infusion	
Having nurses prepare the infusion bag(s) without the benefit of pharmacist order verification and preparation reduces the likelihood that a dosing error will be detected and prevented.	**Hospitals and Health Regions** • Ensure that clear instructions for preparation and administration of acetylcysteine infusion are readily available. • Consider having the pharmacy prepare the IV bag for maintenance acetylcysteine doses, and possibly the loading dose, if this can be done in a timely fashion. • Implement an independent double-check process for determining/verifying doses and dose preparation.
Inability of nurses to easily and quickly check to confirm doses/rates for an acetylcysteine infusion reduces the likelihood that an error will be detected and prevented.	**Hospitals and Health Regions** • Add clinical advisories that appear during infusion pump programming to help guide a check of the pump settings. • Designate acetylcysteine as a high-alert medication requiring an independent double check when initiating and adjusting IV pump settings. • Provide initial and ongoing education to the nursing team who will manage delivery of medications via pumps.
Transfer of care between staff (e.g., covering breaks, moving between units) and between facilities (e.g., with potentially different protocols) without mutual understanding of the acetylcysteine treatment in progress increases the risk of errors.	**Nurses** • At any transfer of care, ◦ assess the prescriber's order, the step of the standardized order set in progress (i.e., loading or maintenance dose), and ensure that IV infusion dose rate/duration has been programmed correctly, ◦ assess that infusion pumps and equipment at the receiving facility are compatible with the standardized order set used, and ◦ ensure a mutual understanding of the key monitoring parameters.
Infusion Pump Programming	
Choosing "no drug selected", "other drug", "drug X", "basic mode", or a generic "IV fluids" setting (depending on the pump model) bypasses a smart pump's drug error reduction software and reduces the likelihood that a programming error will be detected and prevented.	**Hospitals and Health Regions** • Include acetylcysteine in infusion pump drug libraries and build specific regimens for adults and pediatric patients. ◦ Develop a timely process to support nurses when incorrect or missing drug library settings are identified, as well as a clear process to remedy the concern. • Review instances of "no drug selected" and pump override reports to identify quality improvement opportunities.[35]

Delivery of a loading dose and maintenance dose from the same infusion bag increases the risk of errors. • Use of pumps that allow the dose to be programmed repeatedly (e.g., with a "continue" option) increases the risk if a one-bag (2-step, 2-infusion rates) single-concentration regimen is used.	**Hospitals and Health Regions** • Do not administer loading doses from the IV bag containing the maintenance dose if the smart infusion pump does not have the option to program and automatically switch from delivery of the loading/bolus dose to delivery of the continuous maintenance infusion with a separate dose limit for each. If such pumps are not available prepare a separate bag for the loading dose and maintenance dose infusions.[1] • Design the standardized order set to ensure consistent guidance for the administration of acetylcysteine in all areas to support the ability to safely transfer and care for patients. **Poison Centres** • Design a pan-Canadian protocol that can be safely implemented regardless of the type of infusion pump available in the hospital or health region.
Delays in IV infusion pump upgrades may increase the risk of errors.	**Hospitals and Health Regions** • Prioritize IV infusion pump upgrades that are designed to include additional safety features.
Monitoring of Acetylcysteine Infusions	
Lack of timely recognition by physicians and nurses of the patient's signs and symptoms associated with acetylcysteine infusion overdose reduces the likelihood that an infusion overdose will be detected and appropriate interventions provided.	**Care Teams** • Ensure that patient monitoring includes assessment for signs and symptoms of concern and actions to be taken if they occur. ◦ Signs and symptoms of acetylcysteine infusion overdose occur early and may include various symptoms that are also associated with hyponatremia, such as confusion, irritability, restlessness, headache, intractable vomiting (despite treatment with an antiemetic such as ondansetron), altered level of consciousness, and/or seizure. • Ensure laboratory testing that captures indices relevant to acetylcysteine therapy and fluid management are performed according to the standardized order set, and review results promptly to ensure patient treatment is progressing as anticipated and/or to identify concerns. • If over-infusion is suspected, contact the local poison centre to speak with a toxicologist, and seek expertise in fluid management.
Patient and Family Engagement	
Lack of patient/family engagement in the treatment plan, including monitoring parameters, reduces the likelihood that errors will be detected and shared with health care providers.	**Hospitals and Health Regions** • Engage the patient/family in the plan of care, including the plan for loading and maintenance dose infusions with anticipated timelines. During discussion, describe signs and symptoms of concern to bring to the attention of a health care provider, including confusion, irritability, restlessness, and intractable vomiting.