1. 08 · Strategies for Canadian Hospitals to Conserve Drugs in Low Supply and Mitigate Drug Shortages During the COVID-19 Pandemic · V2

April 2020

Hospitals in Ontario are already experiencing drug shortages that pose a risk to all hospitalized patients. The purpose of this document is to explore strategies for drug conservation when drug shortages are anticipated and therapeutic alternatives when drug shortages are realized.

Strategies proposed here are suggestions for consideration and may not always represent best practices under ideal conditions. Local implementation will require consultation from users (i.e., front line staff, pharmacy, administrators) where risks, benefits and logistics are considered. Proposed strategies may not be appropriate for all institutions. Proposed strategies focus on drugs used in critical care setting, but conservation attempts and mitigation strategies may apply throughout the hospital.

A more detailed approach to drug shortages from the Canadian Pharmacists Association is described here:

https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/DrugShortagesGuide.pdf

General principles to address drug shortages include asking the following questions:

1. Have you exhausted all supply chain options?
2. How critical is the medication?
3. Is there an interchangeable product available (i.e., same drug but different manufacturer, different routes of administration)?
4. Is there an alternative drug within the same medication class?
5. Is there an alternative drug class that would meet the patient's needs? (i.e., calcium channel blockers instead of beta-blockers for atrial fibrillation)
6. How can we minimize medication wastage (i.e., choosing the appropriate vial size, concentration)?
7. Use the lowest effective dose.
8. Use an escalation strategy (i.e., for ICU sedation and analgesia) whereby oral dosing is preferred in eligible patients followed by intermittent IV dosing and then continuous infusions.

The following 2 tables address strategies for drug conservation in anticipation of drug shortages (Table 1) and then possible therapeutic alternatives should drug shortages be realized (Table 2). During the COVID-19 pandemic essential drugs such as **sedatives**, **analgesics** and **paralytics** are at the greatest risk of shortages and are highlighted. In an effort to prioritize available strategies, those that are 1)easy to implement, 2)logical and practical and 3)have some evidence to support it are identified within. It is also important to consider the impact of conservation strategies on other shortages (i.e., personal protective equipment, IV pumps).

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Table 1: Strategies for Drug Conservation in Anticipation of Drug Shortages

Drug at risk of shortage	Strategies for drug conservation
Essential Drugs at Greatest Risk Of Shortage	
Sedatives - Propofol - Midazolam - Dexmedetomidine - Ketamine	**Strategies to consider first:** • Consider an escalation strategy whereby enteral dosing is preferred followed by intermittent IV dosing followed by continuous infusions. Intermittent clonazepam, lorazepam, diazepam or clonidine instead of continuous infusions of sedatives in patients who only need light sedation. • Analgesia based sedation: mechanically ventilated patients who need only light sedation can receive infusions or intermittent doses of narcotics alone (i.e., hydromorphone, fentanyl) that provide mild sedation. • Adjunctive use of intermittent sedatives (i.e., clonazepam, lorazepam, diazepam, clonidine, ketamine, barbiturates) with sedative infusions require lower doses of the IV infusion. • Nurse managed sedation titration using a validated sedation scale (i.e., RASS) and clearly defined sedation targets
	Other Strategies: • Daily sedative interruption or sedation vacations may reduce sedative requirements in select cases
Analgesics - Hydromorphone - Fentanyl - Morphine	**Strategies to consider first:** • Analgesia vacations/interruptions in patients receiving continuous infusions to ensure the lowest effective dose is being used. • Intermittent enteral dosing of hydromorphone or morphine in patients who can tolerate oral dosing and have minimal analgesic needs instead of continuous infusions. When administered in conjunction with sedative infusions lower doses of the IV infusion will be required. • Multimodal approach to pain using non-narcotic medications such as acetaminophen, pregabalin, NSAIDS, ketamine, lidocaine, and tapentadol can reduce the need for opioids.
	Other Strategies: • Some long acting preparations (i.e., hydromorphone contin, M-Eslon) can be administered via feeding tube

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Neuromuscular Blockers - Cis-atracurium - Rocuronium	**Strategies to consider first:** • Use the lowest effective dose. Strategies for dose assessment should include a combination of train of four monitoring, observed respiratory effort and/or periodic interruption. • Intermittent NMBA dosing (as opposed to continuous infusion) guided by train of four monitoring and respiratory effort may result in lower total daily dosing
	Other Strategies: • Consider magnesium infusions to boost the effect of neuromuscular blockers in combination with strategies to use the lowest effective dose of the neuromuscular blocker
Vasoactive - Norepinephrine - Epinephrine - Dopamine - Vasopressin - Dobutamine	**Strategies to consider first:** • Stress dose steroid therapy (i.e., hydrocortisone) has been shown to reduce vasopressor requirements in vasopressor-refractory shock • Targeting lowest effective sedation dose can result in lower vasopressor requirements • Concurrent enteral midodrine can reduce IV vasopressor needs
	Other Strategies: • For vasopressor dependent patients consider targeting a lower MAP in patients without a history of uncontrolled hypertension
Cardiac Arrest Cart Meds	**Strategies to consider first:** • Code/Crash Carts & intubation kits should be designated as such; kept in COVID areas so unused drugs can be reused in the same area • Drugs in crash carts and intubation kits could be place in sealed plastic bags to minimize exposure in contaminated rooms
	Other Strategies: • Keeping code/crash carts outside of the room and have the drugs passed in as needed may reduce the risk of contamination
Other Drugs Potentially at Risk of Shortage	
Metered Dose Inhalers	**Strategies to consider first:** • Avoid routine salbutamol and ipratropium dosing, preserving the drugs for patients with evidence of bronchospasm • Patients prescribed MDIs at home could be asked to bring them in to use as "patient's own medication". • Salbutamol and ipratropium could be administered via nebulizer to COVID-negative patients while MDIs reserved for suspected or confirmed diagnoses of COVID-19 including intubated patients

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	• Salbutamol/ipratropium combination nebules could be used in place of individual nebules • Long acting beta-agonists (i.e., salmeterol, formoterol) could be used to reduce the need for salbutamol rescue therapy • Long acting anticholinergic agents (i.e., tiotropium) could be used in place of ipratropium for COPD • Turbuhalers/handihalers may be used by non-ventilated patients with dexterity
	Other Strategies: • Same MDIs theoretically could be used for multiple patients with a spacer device (i.e., aerochamber) that is changed for each patient. The mouthpiece would need to be sterilized between uses. • Respimat inhalers may be considered in lieu of nebulizers • Upon discharge, rather than sending partly used MDIs home with the patient, these MDIs (or canisters) could potentially be redeployed after sterilization • Theophylline/aminophylline could be used in asthmatic patients to reduce the use of salbutamol
Stress ulcer prophylaxis and Acid suppression therapy	**Strategies to consider first:** • Twice daily PPI could be used instead of continuous infusions for the management of gastrointestinal bleeding • Antacids could be used for acute reflux symptom management instead of PPI/H2Ras • Early enteral feeding could allow for shortening the duration of pharmacologic stress ulcer prophylaxis • Discontinuation of stress ulcer prophylaxis therapy in those tolerating enteral feeds or those who are hemodynamically stable with limited risk factors.
	Other Strategies: • Sucralfate could be used for stress ulcer prophylaxis instead of H2Ras and PPIs
Diuretics	**Strategies to consider first:** • Using enteral furosemide can be as effective as IV dosing • Furosemide infusions can be a more efficient way of fluid removal while minimizing the total dose used • Administering furosemide with metolazone can augment diuresis theoretically with lower doses of furosemide

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Antimicrobials - antibiotics antifungals	**Strategies to consider first:** • Ensure durations of antimicrobial therapy adheres to best practice guidelines • Engage with antimicrobial stewardship program where available to assist with antimicrobial therapy • Step down from IV to oral antimicrobials as soon as appropriate

Table 2: Therapeutic Alternatives for Drugs No Longer Available

Drug Therapy	Usual Choices	Other Therapeutic Alternatives
Essential Drugs at Greatest Risk of Shortage		
ICU Sedation	Propofol Midazolam Dexmedetomidine	**Alternatives to consider first:** • Consider an escalation strategy whereby enteral dosing is preferred followed by intermittent IV dosing followed by continuous infusions. • Intermittent clonazepam, lorazepam, diazepam or clonidine instead of continuous infusions of sedatives in patients who only need light sedation. • Analgesia based sedation: mechanically ventilated patients who need only light sedation can receive infusions or intermittent doses of narcotics alone (i.e., hydromorphone, fentanyl) that provide mild sedation. • Ketamine infusions may be considered as an alternative sedative strategy for short term sedation (i.e., 24-48 hours)
		Other potential alternatives: • Phenobarbital can be administered enterally or intravenously in conjunction with benzodiazepines and titrated to provide sedation • Inhaled anesthetics can also be considered in select patients

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ICU Analgesia	Hydromorphone Fentanyl Morphine	**Alternatives to consider first:** • Intermittent enteral administration of hydromorphone, oxycodone or morphine can used in place of narcotic infusions and titrated to the same pain score (i.e., CPOT) • Fentanyl patches (although less easy to titrate) can be used in place of narcotic infusions.
		Other potential alternatives: • Lidocaine infusions can be used in combination with narcotics for pain
Neuromuscular Blockade	Cisatracurium Rocuronium	**Alternatives to consider first:** • Limited options exist if these agents are no longer available. Succinylcholine could be used for intubation and procedural paralysis.
Anticoagulants	Heparin LMWH Warfarin	**Alternatives to consider first:** • While only one LMWH may be on formulary, several are available (i.e., enoxaparin, tinzaparin, dalteparin) • LMWH could be used in place of heparin and vice versa for therapeutic anticoagulation or DVT prophylaxis • Fondaparinux can be used for DVT prophylaxis and treatment • DOACs can be used for full anticoagulation
		Other potential alternatives: • Argatroban infusions could be used for full anticoagulation • Danaparoid could be used for DVT prophylaxis or treatment
Intubation Drugs	Propofol Rocuronium Succinylcholine Ketamine Fentanyl Phenylephrine	**Alternatives to consider first:** • Etomidate could be used in place of propofol • Norepinephrine or ephedrine can be administered as IV push or epinephrine can be administered IM in place of phenylephrine • Lidocaine IV can be used in place of fentanyl • Succinylcholine can be used for rapid sequence intubation

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Other Drugs Potentially at Risk of Shortage		
Vasopressors	Norepinephrine Epinephrine Dopamine Vasopressin	**Alternatives to consider first:** • Phenylephrine can be administered as intermittent boluses or infusions for patients in distributive shock • Intermittent dosing of oral midodrine can be used in patients in place of low dose vasopressors to improve vascular tone
		Other potential alternatives: • Ephedrine can be used intravenously, enterally or intramuscularly.
Inotropes	Dobutamine Milrinone	**Alternatives to consider first:** • Norepinephrine, epinephrine and dopamine can increase cardiac output via β_1 receptor stimulation
Antimicrobials - antibiotics - antifungals	Penicillins Cephalosporins Carbapenems Fluoroquinolones Aminoglycosides Macrolides Vancomycin Azole antifungals Echinocandins	**Alternatives to consider first:** • For most classes of antibiotics more than one agent is available in Canada (i.e., in the event of a ceftriaxone shortage cefotaxime or ceftazidime could provide similar coverage. • Even for antimicrobials like Vancomycin alternatives exist such as linezolid, daptomycin and Septra. • Antifungals options exist within the same class and between classes (i.e., fluconazole, itraconazole, caspofungin, micafungin, amphotericin, etc.)

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Metered Dose Inhalers	Salbutamol Ipratropium Inhaled corticosteroids	**Alternatives to consider first:** • Patients prescribed MDIs at home could be asked to bring them in to use as "patient's own medication". • Salbutamol and ipratropium can both be delivered via nebulized solutions • systemic corticosteroids could be used in bronchospastic or asthmatic patients • Budesonide is available as a solution for nebulization • long acting beta agonists (formoterol, salmeterol) could be used for maintenance dosing (not rescue therapy). • Combination fluticasone/salmeterol (Advair) is available in MDI
		Other potential alternatives: • Salbutamol is available as oral tablets and could theoretically be used for maintenance dosing in bronchospastic COPD patients
Stress Ulcer Prophylaxis	Proton pump inhibitors H2-receptor antagonists	**Alternatives to consider first:** • Several PPIs (i.e., pantoprazole, lansoprazole, omeprazole, esomeprazole, dexlansoprazole) and H2RA (ranitidine, famotidine, cimetidine) are available in Canada • PPIs and H2Ras could be interchanged for stress ulcer prophylaxis, reflux and management of gastrointestinal bleeding • Antacids could be used in place of PPIs and H2Ras for reflux symptom management
		Other potential alternatives: • Sucralfate is an alternative for stress ulcer prophylaxis
Diuretics	Furosemide	**Alternatives to consider first:** • Ethacrynic acid is another loop diuretic that could be used in place of furosemide • Thiazide diuretics could be used in the event that furosemide is no longer available
		Other potential alternatives: • Low dose dopamine infusions theoretically could augment urine output • Dialysis would be the definitive way to remove fluid in the absence of other pharmacologic options

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Antiarrhythmics	Amiodarone	**<u>Alternatives to consider first:</u>** • Other agents besides amiodarone to consider for the management of atrial fibrillation (I.e., magnesium, procainamide, sotalol, propafenone) • Patients with hemodynamically stable new onset atrial fibrillation can be managed with rate control alone (I.e., beta blockers or calcium channel blockers) • Electrical cardioversion, when successful, can negate the need for antiarrhythmic drugs for hemodynamically unstable atrial fibrillation

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