Ontario Palliative Care Network

# Strategies for Potential Shortages in Medications Relevant to Palliative Care during the COVID-19 Pandemic

During the COVID-19 pandemic, there is a risk that shortages of medications essential to the delivery of palliative care will occur. This risk exists in hospitals, palliative care units, hospice residences, community (home care) settings and long-term care homes. In addition, increased demand for medications which are used for multiple purposes/settings such as palliative care and critical care will exacerbate that risk. Critical shortages of these medications will impact care delivery in all settings and result in reduced quality of care for patients and increased pressures on acute care resources if patients are unable to receive appropriate care in community settings. Preparation for, and mitigation of, these risks will entail:

1. Identification of the essential medications for palliative care during the pandemic
2. Identification of alternate medications that can be utilized if there are shortages of standard first-line therapies
3. Implementation of conservation strategies to ensure efficient use of existing medication stocks
4. Establishment of reliable mechanisms to track supply and utilization of these medications for all settings

Action on these key steps will support consistent availability and delivery of quality palliative care, including end-of-life care, for both the patients who test positive for COVID-19, and the usual population who require palliative care.

The intent of this document is to provide guidance for a) clinicians who are making decisions about medication choices in the face of shortages, b) pharmacists who provide service to the palliative care sector and c) system planners and administrators who may need to establish policies and procedures in the face of shortages.

## Considerations for Routes of Administration in the Context of Medication Shortages

A shortage of a palliative care medication may represent an absolute shortage of that medication or, more often, may represent a shortage of a particular formulation of that medication. Most concern about shortages is focused on parenteral formulations of medications which are commonly required for subcutaneous (SC) or intravenous (IV) delivery at end-of-life when patients are no longer tolerating the oral route of administration. Parenteral formulations may also be used earlier for severe or refractory symptoms. Faced with shortages, delaying or avoiding the switch to parenteral formulations may be a valuable strategy. Continuing or prolonging the use of enteral routes of administration will be an important consideration. This would include oral, sublingual/buccal, rectal and administration by enteral tubes where they are in place. Enteral formulations which include tablets, liquids, sublingual and oral-dissolving formulations, and suppositories need to remain accessible.

## Strategies for Drug Conservation in Anticipation of Drug Shortages

The 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 settings of care. An excellent guide to clinical decision-making in times of drug shortages has been developed by the Canadian Pharmacists Association[1].

Some of the medications in this document (**bolded)** have already been identified as at risk of shortage: https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/covid19-interim-order-drugs-medical-devices-special-foods/information-provisions-related-drugs-biocides/tier-3-shortages.html (As of May 15, 2020)

| **Essential Medications and Alternates[2,3]** | **Strategies for drug conservation and considerations for alternates** |
|---|---|
| Opioid Analgesics<br>• **Hydromorphone (parenteral, enteral)**<br>• **Morphine (parenteral, enteral)**<br>• **Fentanyl (parenteral)**<br><br>Non-opioid Analgesics/Adjuvants<br>• Pregabalin<br>• Gabapentin<br>• Duloxetine<br>• **Dexamethasone** | • Utilize enteral routes of administration for as long as possible. Use of liquid formulations or crushed oral tablets can prolong the ability to use an enteral route.<br>• Use of the rectal route, although likely a choice only when other options are not available, may prolong the ability to utilize short-acting formulations of opioids[4]<br>• If the supply of the primary opioid becomes unavailable, consider rotation to an alternate opioid.<br>• Reserve opioid infusions via CADDs (continuous ambulatory delivery device) for patients with refractory symptoms or for end-of-life care.<br>• For opioid CADDs, utilize smallest volume in cassette to minimize waste (especially |

[1] Drug Shortages: A Guide for Assessment and Patient Management. Canadian Pharmacists Association. 2010. https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/DrugShortagesGuide.pdf

[2] Adapted from Kanji, S. et al. Strategies for Canadian Hospitals to Conserve Drugs in Low Supply and Mitigate Drug Shortages During the COVID-19 Pandemic. The Ottawa Hospital, Critical Care. March 2020.

[3] For suggested drug doses, Pallium Canada has prepared a document with a helpful table and references: https://www.pallium.ca/wp-content/uploads/2020/05/Managing-Potential-Palliative-Care-Medication-Shortages-During-COVID-19.pdf.

[4] Warren ED. Practical Use of Rectal Medications in Palliative Care. J Pain Symptom Manage, 1996. 11(6): p 378-387. https://www.jpsmjournal.com/article/0885-3924(96)00012-7/pdf

| Essential Medications and Alternates[2,3] | Strategies for drug conservation and considerations for alternates |
|---|---|
| | if the anticipated duration of infusion is expected to be short).<br>• Reserve fentanyl for infusion via CADD for severe symptoms refractory to other opioids, refractory opioid toxicity or where these other parenteral opioids are unavailable.<br>• Employ multimodal analgesia, if appropriate and indicated, when patients are able to tolerate enteral medication (i.e. NSAIDs, gabapentinoids, acetaminophen, serotonin-norepinephrine reuptake inhibitors). |
| Alternates - opioid<br>• Oxycodone (enteral)<br>• Methadone (enteral)<br>• Fentanyl (transdermal)<br>• Sufentanil[5]<br>• Tramadol (enteral)<br>• Codeine (enteral)<br><br>Alternates – non-opioid<br>• Nortriptyline<br>• Desipramine<br>• **Ketamine (parenteral)**<br>• Acetaminophen<br>• NSAIDs | • If hydromorphone and morphine resources are scarce, consider oxycodone (including preparations combined with acetaminophen) in stable patients tolerating enteral route.<br>• Methadone (tablets or liquid) can be a good enteral alternative to morphine and hydromorphone but requires consultation with a clinician experienced in using methadone.<br>• Faced with shortages of other parenteral opioids, transdermal fentanyl patches can be considered.<br>• Ketamine can be used for parenteral analgesia particularly for neuropathic pain. Consultation with a clinician experienced in its use would be required.<br>• Codeine and tramadol are weak opioids for enteral use only. They would not be ideal choices for patients who require strong opioids. They are listed here for consideration in the event of severe shortages or where a patient's dose of a stronger opioid is low and there exists an equipotent dose of one of these. |

[5] Availability of sufentanil may vary significantly depending on the setting.

| **Essential Medications and Alternates[2,3]** | **Strategies for drug conservation and considerations for alternates** |
|---|---|
| Neuroleptics/Antipsychotics[6]<br>• Haloperidol (parenteral, enteral) | • Mild or moderate delirium can usually be managed by identifying and managing, where possible, the underlying causes. Nonpharmacological management approaches should occur for all patients.<br>• Medication management should be reserved for those patients who have severe delirium and/or are at risk of harm to themselves or others. |
| Alternates<br>• Olanzapine (enteral, parenteral)<br>• Risperidone (enteral)<br>• Quetiapine (enteral) | • Oral-dissolving tablets (ODT) of olanzapine and risperidone can be a useful alternate. This formulation is generally as effective as the parenteral formulation.<br>• Quetiapine can be useful when oral administration is still possible.<br>• Methotrimeprazine (listed below) can be used enterally or parenterally where some degree of sedation is needed. |
| Sedatives<br>• **Midazolam (parenteral)**<br>• **Lorazepam (parenteral, enteral)**<br>• **Methotrimeprazine[7] (parenteral, enteral)** | • For midazolam infusions via CADD, utilize the smallest volume in the cassette to minimize wastage.<br>• Consider use of intermittent parenteral sedatives (lorazepam, methotrimeprazine) as an alternate. |
| Alternates<br>• Clonazepam (enteral)<br>• **Phenobarbital (parenteral)**<br>• Diazepam (enteral)<br>• Loxapine (parenteral)<br>• **Ketamine (parenteral)**<br>• **Propofol (parenteral)**<br>• **Dexmedetomidine (parenteral)** | • Consider clonazepam for patients requiring only mild sedation and are still tolerating enteral route<br>• Phenobarbital is a good alternate for intermittent IV or SC use.<br>• Benzodiazepines can be used enterally by either the oral or rectal route (see |

[6] In palliative care this class of drugs is primarily used in the management of delirium without the intent of sedation although at end-of-life, management of agitated delirium may require sedation.
[7] Methotrimeprazine could be included in the section on neuroleptics/antipsychotics and can be used in the management of delirium. Usually it is used primarily for its sedating properties, particularly at end-of-life, which is why it has been placed in this section.

| Essential Medications and Alternates[2,3] | Strategies for drug conservation and considerations for alternates |
|---|---|
| | footnote #3 as well as previous note about the lower desirability of this route).<br>• For use of parenteral loxapine consultation with clinicians experienced in its use is advised.<br>• Ketamine, while potentially useful as an analgesic, could also be used as a sedative.<br>• Use of ketamine, propofol, dexmedetomidine will usually only occur in hospital and only by clinicians familiar with the use of these drugs and in appropriate settings. |
| Anti-emetics<br>• Metoclopramide (parenteral, enteral)<br>• Ondansetron (parenteral, enteral) | • Provincial drug coverage for ondansetron is reserved for those receiving certain cancer treatments; in this instance patients would need to self-pay or have supplemental insurance. |
| Alternates<br>• Haloperidol<br>• Prochlorperazine<br>• Methotrimeprazine<br>• Dimenhydrinate | • Prochlorperazine and dimenhydrinate can be given rectally. |
| Anti-secretagogues[8]<br>• Glycopyrrolate (parenteral)<br>• Scopolamine (parenteral) | • Employ educational strategies for families around end-of-life upper airway secretions.<br>• Utilize positioning and non-pharmacologic strategies as the first approach in management. |
| Alternates<br>• Hyoscine butylbromide (parenteral)<br>• Atropine 1% drops (for enteral use)<br>• Scopolamine (transdermal) | • Consider atropine ophthalmic drops applied sublingually in event of scarcity of glycopyrrolate or scopolamine.<br>• Consider hyoscine butylbromide (Buscopan©) as an alternative if glycopyrrolate or scopolamine are scarce. |

[8] These drugs may be used at the end-of-life to manage excessive upper airway secretions.

| Essential Medications and Alternates[2,3] | Strategies for drug conservation and considerations for alternates |
|---|---|
| | • Consider use of scopolamine transdermal patches where available. |
| Metered Dose Inhalers (MDI)[9]<br>• **Salbutamol**<br>• Ipratropium<br>• Inhaled corticosteroids | • Consider long acting beta agonists (i.e. salmeterol, formoterol) to minimize use for short acting salbutamol.<br>• Consider long acting anticholinergics (i.e. tiotropium) in COPD to minimize use of ipratropium.<br>• Consider systemic corticosteroids for bronchospasm.<br>• Consider delivery of salbutamol or ipratropium by nebulizer in COVID-19 negative patients to reserve MDI for COVID-19 positive/suspected patients.<br>• In the hospital setting, encourage patients to bring in their own MDI from home ("patient's own medication") if they were already prescribed at baseline.<br>• Discuss institutional ability to share MDI between patients with spacer devices and sterilization procedures.<br>• Discuss institutional ability to reuse partially used MDI after sterilization.<br>• Consider theophylline/aminophylline in patients with asthma to reduce use of salbutamol.<br>• At end-of-life, managing shortness of breath due to bronchospasm may be managed with opioids and, if needed, sedation. |

## Other Considerations for Conservation of Parenteral Medications at the System Level

- There is considerable waste of medication generated when doses prescribed do not account for the volume of an entire vial. Unused medication in the vial will be discarded. Providing prescribers information about vial sizes and concentrations can assist in maximizing the use of single-dose vials.

[9] These drugs can be important for the palliative care of certain populations, particularly those with COPD. Given that there are know shortages, they are included in this table.

- In institutional settings, pharmacy policy and procedures may be revised to maximize utilization of multi-dose vials by employing strategies such as preparation of single dose syringes to prevent medication discarded from accessed vials. These practices would need to be aligned with guidelines established by the Institute of Safe Medication Practices Canada (ISMP).
- When it is not possible or feasible to maximize use of medication in multi-dose vials, attempt to access vials of the smallest volume to minimize discarded waste.
- Due to potential discard from incomplete use of small volume medication vials (that cannot be accessed as a multi-dose vial for a future dose), when prescribing intermittent medications, it may be helpful to divide total daily doses in larger/less frequent doses, rather than smaller/more frequent doses which may require opening more vials and lead to more waste.
- There may be contributions to medication conservation related to the equipment used for medication administration whether by intermittent injection or continuous infusion. These may include specific infusion devices as well as the type of tubing and connectors[10]. These are areas that will need further review and investigation.

## Symptom Relief Kits (SRKs)

Symptom relief kits (also referred to as symptom management kits or pain and symptom management kits) are commonly used in community settings (home, hospice residences). SRKs are a stock of medications dispensed for a particular patient in anticipation of the emergence of symptoms, particularly at end-of-life, where a delay in prescribing and delivery of medication would result in significant patient distress. Practices around these kits vary across the province in terms of 1) the medications that are included in the kits, 2) the amounts of medications that are dispensed and 3) the guidelines as to how the medications are intended to be used. Generally, SRKs contain multiple parenteral medications, some of which will be at risk during the pandemic. It is likely that a substantial amount of the medications in these kits are not used and are discarded after the patient dies or is admitted to an alternative setting, resulting in significant wastage.

General considerations for SRKs in the context of drug shortages

- Consider delaying the dispensing of kits until the patient is approaching the end-of-life phase of their illness.
- Consider an approach that allows for customizing kits for specific patients based on their needs.
- Only dispense as much medication as might be needed to get through a 12 – 24 hour period until an appropriate prescriber can arrange for a specific prescription and supply of medication.
- Consider alteration of SRKs to include oral/sublingual/buccal medications as alternatives to parenteral ones. Some examples are included below:

[10] There has been some work in Ontario utilizing elastomeric infusors for continuous infusions rather than CADD pumps. Further work on their role in drug conservation will be valuable.

## Alternatives for consideration in SRKs

| Indications/medications | Considerations |
|---|---|
| Opioid Analgesics<br>• **Morphine liquid (1mg/mL)**<br>• Hydromorphone liquid (1mg/mL) | • For patients who can be still be managed with oral opioids, or, at end-of-life, where small volumes of liquid may still be manageable late in the illness. |
| Nausea/vomiting<br>• Olanzapine ODT (oral disintegrating tablet)<br>• Dimenhydrinate (rectal suppository)<br>• Ondansetron ODT | • Oral dissolving tablets can be effective when patients have increased difficulty swallowing<br>• Dimenhydrinate suppositories are not eligible for ODB coverage but are available over-the-counter.<br>• Ondansetron is not eligible for ODB coverage. |
| Agitation/Sedation<br>• Olanzapine ODT<br>• Risperidone ODT<br>• Lorazepam SL | • All are eligible for ODB coverage |
| Upper Airway Secretions<br>• Hyoscine butylbromide SC<br>• Atropine 1% eyedrops<br>• Scopolamine (transdermal patch) | • Scopolamine patches are applied every 72 hours. They are not eligible for ODB coverage but are available over the counter. |

## Monitoring and managing the drug supply

Managing the supply of key medications in the hospital and cancer care sectors has been a well-established process. This involves activities at both provincial and federal levels and includes reliable and regular monitoring of drug utilization patterns, the drug supply and its distribution chain and mitigation strategies when risks to specific drug supplies emerge. This has not been as true of the community care sector, including long term care, where a large amount of palliative care is delivered. Currently, there is no systematic approach to monitoring supply and utilization patterns in community and long term care sectors. Even in the hospital sector, there has not been a clear process to monitor medications which are used predominantly by palliative care clinicians. As a result, drugs such as methotrimeprazine or the anti-secretagogues may not be identified as potential at-risk medications. Demand for medications that are utilized by both palliative care and other practitioners (e.g. opioids, midazolam) may result in allocation of these drugs to critical care or operating room settings during times of shortage thus limiting access within hospital-based palliative care, community and long term care settings. Ensuring the supply of medications in all palliative care settings will require:

- Robust mechanisms to monitor the supply of medications used in palliative care in all setting where palliative care is delivered.
    - Ensure that palliative care medications are included in the existing processes in acute care settings.
    - Establish similar monitoring and reporting processes for pharmacies providing medications to home care programs and long term care homes.
- Where the supply of specific palliative care medications is determined to be at risk, ensure that this is identified within the federal Tier 3 Assignment process and that mitigation strategies are activated to manage the risk.
- Where there is risk to palliative care medications that are shared by palliative care and other care settings, utilize an allocation process that is based on an ethics framework, to allocate these medications in the most effective manner. Such a framework was developed in 2012 within the Ministry of Health[11].

## Development of the document

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[11] http://www.health.gov.on.ca/en/pro/programs/drugs/supply/docs/ethical_framework.pdf