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Propofol 2% (20 mg/mL): Safety Considerations for Introducing a Novel Product into Hospitals

Some Canadian hospitals will need to begin using an imported double-strength (2% or 20 mg/mL) propofol 100 mL product because there is a shortage of the 1% (10 mg/mL) propofol 50 mL and 100 mL products. To mitigate the risks associated with introducing this novel product into medication-use systems, the following preliminary considerations (from Table 1) are provided:

- *Reserve the use of propofol 2% for maintaining sedation via continuous infusion in critical care areas (ideally only in the intensive care units) for adult patients who are mechanically ventilated.*
- *Consider if both the 1% (which continues to be available as a 20 mL vial) and 2% products are required in the same patient care area.*
- *Engage interdisciplinary staff in developing the implementation process, as a way to gain insight into critical aspects of providing safe care, including at transitions of patient care.*
- *Use medium- and higher-leverage strategies (e.g., alerts, forcing functions) in electronic systems (e.g., prescriber order entry, automated dispensing cabinets, infusion pump drug libraries).*
- *Create a go-live plan, including activation of communication and education plans and of updated drug libraries and alerts for infusion pumps.*
- *Supplement prescriber and staff education with information posters at the point of care in affected care areas.*
- *Only the propofol 1% product (20mL) should be drawn up into syringes; best practices for syringe labelling should be followed. It is envisioned that there will be no need to withdraw propofol 2% into a syringe.*
- *If the concentration of a propofol infusion needs to change (e.g., as a result of a patient transfer between care areas), prime new intravenous tubing with the new concentration.*

Drug shortages are one of the critical issues arising from the COVID-19 pandemic. The increased worldwide demand for high-alert drugs used in the care of intubated and mechanically ventilated patients has heightened the risk of a shortage of these products. To address any shortage that does occur, an alternative product (typically the same drug in a different concentration, strength, packaging format, or dosage form) may be substituted for the medication that is unavailable. The introduction of new products into the medication-use system must be carefully managed to mitigate risks, such as the potential for medication errors.[1]

REPORTED CONCERN

Due to an impending shortage of the propofol 1% (10 mg/mL) 50 mL and 100 mL products in Canada, some hospitals may need to use a double-strength (2% or 20 mg/mL) product that is now being imported from Europe (Figure 1). **Propofol 2% is a product unfamiliar to Canadian practitioners and thus carries a risk of 2-fold overdose. A multipronged systems approach, including interprofessional communications and technical safeguards, is required to avoid errors with this product. Errors may also arise once the shortage is resolved and hospitals can again stock propofol 1% 50 mL and 100 mL products.**

Figure 1. Propofol 2% 100 mL product imported from Europe under a Health Canada Interim Order (photograph courtesy of Fresenius Kabi Canada).

BACKGROUND

Health Canada has issued an *Interim Order Respecting Drugs, Medical Devices and Foods for a Special Dietary Purpose in Relation to COVID-19* to expedite procurement and maintain an adequate supply of necessary medications and products during the pandemic. Patients with severe COVID-19 may require treatment, including intubation, in a critical care unit. Medications used to support patients in critical care include sedatives (e.g., propofol), analgesics (e.g., fentanyl), vasopressors (e.g., norepinephrine) and neuromuscular blocking agents (e.g., cisatracurium); these agents represent the majority of medications being imported under the interim order.[2]

The US Food and Drug Administration (FDA) is also authorizing importation of the European 2% product. *The FDA has restricted propofol 2% for "maintaining sedation via continuous infusion in patients 16 years and older who require mechanical ventilation in an intensive care unit (ICU) during the COVID-19 pandemic."*[3] While the product does not have the same restrictions in Canada, hospitals planning to use the propofol 2% product are considering the FDA guidance.

Propofol, a short-acting general anesthetic/sedative, is approved in Canada for sedation during intensive care and other procedures, as well as for induction and maintenance of general anesthesia.[4] The demand for propofol is exceeding supply during the pandemic, and some hospitals have switched to alternative agents for specific indications. However, other hospitals that are treating a large number of intubated patients must have access to a continuous supply of propofol. The temporary importation of propofol 2% from Europe is intended to fill this need, but its introduction to the Canadian market carries certain risks. Not only is the 2% product **double** the strength of the 1% product familiar to Canadian practitioners, but it is also not currently supported by medication systems, including infusion pump drug libraries. A 2-fold overdose of propofol can result in hemodynamic instability, cardiovascular collapse, and death.

OPPORTUNITY FOR PROACTIVE SYSTEM RESPONSE

Several professional organizations, licensing bodies, group purchasing organizations, and governments have previously developed guidelines for managing drug shortages. Table 1 (page 4) consolidates concepts, human factors, and safety principles from these sources. The table highlights safety considerations for hospitals ***after*** a decision has been made to introduce the propofol 2% product into the medication-use system.

When implementing changes to support safe use of a new product, consider medium- and higher-leverage system-based strategies, such as alerts and forcing functions, to complement person-based interventions such as staff education and communications.[5] As an example, Figure 2 depicts a concept clinical advisory alert that forces nurses to stop and acknowledge the product selected from the pump library. Fresenius Kabi Canada has developed a product alert poster. This poster can be placed in care areas to supplement existing education and other strategies.

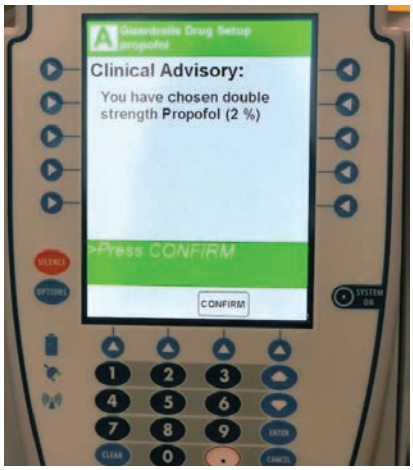

Figure 2. Example of a clinical advisory alert for infusion pump library (courtesy of Sinai Health).

If errors or near misses do occur, or if there are other concerns related to the adoption of the double-strength (2%) propofol product, they should be reported through the usual reporting mechanism, to Health Canada, and to the Canadian Medication Incident Reporting and Prevention System, to support further learning.

ISMP Canada invites all hospitals to share their implementation procedures and documents. These may be shared on the ISMP Canada website (with permission), to supplement the preliminary recommendations in this bulletin, for the benefit of other hospitals and practitioners. Please send documents and comments to info@ismpcanada.ca.

(Table 1 follows on page 4)

ACKNOWLEDGEMENTS

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Table 1. Safety Considerations for Introduction of Double-Strength (2% or 20 mg/mL) Propofol

Safety Considerations for Introduction of Double-Strength (2% or 20 mg/mL) Propofol

Interdisciplinary Planning

- Identify a decision-making and communications group or committee to introduce the new product, to coordinate ongoing communication and education, and to monitor the supply situation, including availability of the product being replaced and use of the replacement product.
- Determine any limitations on product use.
  - Reserve the use of propofol 2% for maintaining sedation via continuous infusion in critical care areas (ideally only in the intensive care units) for adult patients who are mechanically ventilated.
  - Consider if both the 1% (still available as a 20 mL vial) and 2% products are required in the same patient care area.
  - It is envisioned that there will be no need to withdraw propofol 2% into a syringe.
- If a patient requires transport to another location, or internal transfer to another care area, ensure that the receiving facility/area, as well as any transport service, is aware of the new product and is capable of using it safely.
  - If propofol 2% is restricted to the ICU, consider the possibility that a patient may require transfer to another service/unit (e.g., the operating room), where staff may be familiar with only the 1% product.
  - If the concentration of a propofol infusion needs to change (e.g., as a result of a patient transfer between care areas), prime new intravenous tubing with the new concentration.
- Prepare a plan to safely remove propofol 2% and reintroduce propofol 1% when the time-limited shortage ends. Use the safety considerations provided in this table.

Procurement

- Determine the risk of ordering either the old or the new product but receiving the alternative product in error.
  - Currently, propofol 2% is available through a controlled-release procurement process to limit accidental ordering and procurement.
- Create a product file in relevant hospital information systems to allow for documentation and management of the new product.
  - Once the stock of the propofol 2% product is received, add an alert to propofol product files to note the availability of 2 strengths.

Pharmacy Preparation, Storage, and Dispensing

- Determine, using pictures, labels, and product monographs of the new product whether additional information is required to safely integrate the product.
  - Consider whether an auxiliary warning label needs to be affixed to the 2% product. Example statements include:

    CAUTION:
    DOUBLE-STRENGTH PROPOFOL
    For ICU use ONLY

  - The imported propofol 2% product does not have a drug identification number (DIN); therefore, consider any impact on pharmacy verification processes, such as dispensing.
  - The imported propofol 2% product is labelled with an international bar code that may not be readable by existing Canadian barcoding systems; therefore, if bar coding is used, be aware that a unique, product-specific bar code may need to be created and uploaded into computerized systems.[6]
- Review the new product for the potential for look-alike confusion (i.e., with other strengths of the same medication or with other drug products).
  - Pictures of select propofol 1% 100 mL products available in Canada:

  - Consider segregation or signage in storage areas to differentiate the 1% and 2% products.
- Consider allergies, contraindications, and population limitations (e.g., elderly or pediatric patients, renal or hepatic function) relevant to the new product.
  - Avoid use of propofol 2% in patients who are hypersensitive to peanuts or soy due to the presence of soybean oil in the formulation.[7]
  - Carefully consider the use of propofol 2% in pregnant patients because the formulation includes medium-chain triglycerides.[7]*

Computer Systems

Computerized Alerts

- Work with prescribers and nursing staff to determine the design and duration of computerized alerts in the computerized prescriber order entry system.[8]
  - When selecting a propofol product, an alert should indicate the availability of 2 concentrations. Example statements[9] include:

    > ***There are 2 propofol concentrations: 1% (10 mg/mL) and 2% (20 mg/mL)***
    > ***Propofol 2% (20 mg/mL) is to be used in intensive care units ONLY***
    > ***Confirm the selected concentration of propofol is appropriate for the care area***

  - For propofol 2% products, activate alerts to capture cautions in pregnant patients and contraindications for patients with hypersensitivity to peanut or soy.*

Order Sets

- Update paper and electronic order sets to reflect the new product, while recognizing that some care areas may not be using the new product. Protocols specific to individual units may be required.

Intravenous Pump Programming

- Review all pump libraries to determine the updates and alerts required, including optimization of the drug error reduction software.
  - Present propofol options in the pump library in a way that mitigates selection errors.
  - Create alerts in the pump library to notify users that the double-strength (2%) product has been selected (Figure 2).

- Work with nursing staff to ensure that additional steps (e.g., calculations) are not required for the pump programming process.
- Emphasize the need for independent double checks at the bedside,[10] at initiation, during pump reprogramming, and whenever care is transferred to another care provider.

General Considerations

- Determine additional updates that might be required for any of the following hospital electronic systems or processes:[11]
  - computerized physician order entry
  - hospital formulary, infusion pump drug library, intravenous drug guides, and other drug information resources
  - electronic health records
  - electronic medication administration records (eMARs)
  - automated dispensing cabinets/units
  - pharmacy compounding and intravenous workflow systems
  - medication reconciliation at transitions of care
  - pharmacy, materials management, and finance systems
- Identify opportunities afforded by electronic systems to create forcing functions (e.g., bar coding to prevent inadvertent selection of the wrong product).

Go-Live Date

- Prepare a plan for pumps to be updated and circulated into action for the go-live date or for when the new drug libraries will be activated.
- Update protocols that will include the new product and inactivate those using the old product.
- Consider appropriate timing of the changeover to the new product for individual patients.
  - If the propofol infusion needs to be changed, prime new intravenous tubing with the new concentration to address dead volume in the tubing.

Education and Communication

- Update policies, procedures, and protocols, and provide additional guidance as required.
- Share the education and communication plan with all hospital stakeholders.
  - Include propofol 2% product information in education sessions for all staff, including new and temporary staff (e.g., agency nurses, students, and residents).
  - Communicate changes during unit-based safety huddles.
- Consider additional signage in appropriate places (e.g., automated dispensing cabinets, storage cupboards) to communicate information about the new product. Provide a picture of the product, labels, and product information to care areas that will be receiving the new product.
  - Fresenius Kabi Canada has developed a product alert poster.[12] This resource is being distributed to hospitals that have purchased the propofol 2% product.

Additional Considerations

- Ensure ready availability of information about managing inadvertent overdose.
- To detect potential errors, implement more frequent assessment and monitoring (e.g., vital signs, pump settings) at initiation, at each replacement, and with each order change.
- Follow best practices for labelling of syringes containing propofol 1% used for procedures.
  - Although it is envisioned that there will be no need to withdraw propofol 2% into a syringe, it is essential that syringes are always labelled.

*The original version of this bulletin has been updated to read "Carefully consider" (instead of "Avoid") and "cautions in pregnant patients" (instead of "contraindications in pregnant patients")—*June 12, 2020*

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Système canadien de déclaration et de prévention des incidents médicamenteux

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