

Ebola Virus Disease: What Canadian Hospital Pharmacists Need To Know

The ongoing epidemic of Ebola virus disease (EVD) in West Africa has been the most catastrophic in history, with widespread transmission in Guinea, Liberia, and Sierra Leone.¹ As of March 2015, there had been over 25 000 probable, suspected, or confirmed cases and more than 10 000 deaths.¹ Cases have also appeared in other countries, including the United States.¹ In response to the epidemic, the Public Health Agency of Canada has worked to improve current response measures, which has included forming Ebola Rapid Response Teams, to be deployed to support provincial and territorial health authorities if necessary.² Provinces have also designated specially equipped hospitals for treatment of patients with EVD. As members of the health care team, hospital pharmacists require a working knowledge of EVD and its management, given that travel and health care-related EVD transmission is possible in Canada (Table 1).

Canadian Hospital Pharmacy Preparedness

Canadian hospital pharmacies must establish EVD procedures for the procurement and distribution of medications to maintain staff and patient safety.^{3,5} Pharmacies should ensure that institutional policies and procedures concerning patient isolation include procedures to minimize patient contact when medications are ordered.^{3,5}

For example, the use of paper orders should be avoided in the rooms of patients with EVD.⁵

Procedures for dispensing, delivering, documenting, and disposing of medications for EVD patients in isolation are essential.^{3,5} Health care providers must be able to manipulate packaging and administer medications while wearing personal protective equipment (PPE).³ Disposable medication containers that can be incinerated, without staples or sharp objects, are preferred.³ Other operational considerations, such as unit-dose packaging, with delivery by automated cabinets or a pneumatic tube system in a non-isolation or clean area, and establishment of a satellite pharmacy near the isolation unit, may also be helpful.^{3,5} Usual procedures for documentation of medication administration may have to be adapted for EVD patients in isolation.⁵ Policies for documentation and disposal of controlled substance waste originating from potential or confirmed EVD patients must be established. Also, procedures for replacement of code carts and their contents in EVD isolation rooms are essential.⁵ Furthermore, a process is needed for crediting medications delivered for but not administered to EVD patients.⁵

The hospital pharmacy may be responsible for procuring investigational medications, a situation that would require coordination between the manufacturer, Health Canada, and the institutional research ethics board, in accordance with local policies for investiga-

Table 1. Informational Resources

Resource	Comments	Web Address*
American Society of Health-System Pharmacists: Ebola Resource Center	Ebola and pandemic preparedness checklist for pharmacy	www.ashp.org/menu/PracticePolicy/ResourceCenters/Ebola
Canadian guidelines (CCCS, CAEP, and AMMI)	Clinical management of patients with Ebola virus disease	www.ammi.ca/guidelines/
Centers for Disease Control and Prevention (US)	Information on Ebola virus disease	www.cdc.gov/vhf/ebola/index.html
Government of Canada	Designated Ebola virus disease hospitals in Canada	www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/ebola/treatment-traitement/hospitals-hopitaux/index-eng.php
Public Health Agency of Canada	Information on Ebola virus disease	www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/ebola-eng.php
World Health Organization	Overview of Ebola epidemic	http://who.int/csr/disease/ebola/one-year-report/introduction/en/
	Updates on Ebola research and development: vaccines, therapies, and diagnostics	www.who.int/medicines/ebola-treatment/2015-0130_Ebola_RD_Update.pdf?ua=1

AAMMI = Association of Medical Microbiology and Infectious Disease Canada, CAEP = Canadian Association of Emergency Physicians, CCCS = Canadian Critical Care Society.
*Cited March 28, 2015.

tional drug use, as well as federal and international regulations.³⁻⁵ If EVD is suspected, the provincial public health authority should be notified promptly. Discussions regarding procurement of investigational medications should include the latest results of clinical trials and drug availability. Pharmacists may want to increase their understanding of available manufacturer(s), mechanism(s), and therapeutic use(s) of these agents in both individual cases and larger trials, as part of the institution's preparation for EVD (Table 2).

Pharmacy staff members have an obligation to familiarize themselves with institutional EVD policies and procedures. Departments should estimate the increased number of dispensary and clinical pharmacy staff needed per EVD case. Clinical pharmacists who will participate in direct care of patients with EVD must be identified in advance, must receive PPE training, and must have a clear understanding of their role in patient care.³

Role of Canadian Hospital Pharmacists

Hospitals with EVD patients may need additional dedicated pharmacy staff to facilitate procurement, preparation, and distribution of therapy. Although all Canadian hospital pharmacists need to have an understanding of EVD, those working in critical care, infectious diseases, and the emergency department will likely play the largest roles in clinical management of this disease.³ Investigational drug services pharmacists may also be involved in procuring and managing investigational EVD therapies, including inventory control and ensuring all regulatory requirements are met.³

Treatment

As of early spring 2015, no medications had been approved for the prevention or treatment of EVD.^{6,7} Supportive care may allow time for the development of adequate antibody response. Adminis-

Table 2. Investigational Medications for Ebola Virus Disease (EVD)⁶⁻⁸

Medication	Manufacturer	Mechanism of Action	Dosing and Use to Date	Comments
Not readily available in Canada				
Brincidofovir	Chimerix	Unknown for EVD	200 mg PO × 1, then 100 mg twice weekly × 2 weeks (total 5 doses) Used in 5 patients (United States)	Brincidofovir is a lipid conjugate of cidofovir. No safety or efficacy data exist for the use of this drug in treating EVD in humans or animals. Chimerix recently stopped participation in a clinical trial involving Médecins Sans Frontières in Liberia because of a significant decrease in the number of EVD cases diagnosed in 2015. ⁹
Favipiravir	Fuji Film/ Toyama Chemical	Nucleotide analogue that inhibits RNA polymerase and causes lethal mutagenesis following incorporation into viral RNA	150 mg/kg PO bid × 14 days (influenza dosing) Used to treat 1 patient with EVD (France)	Favipiravir, which is currently in the late stages of testing against influenza, has also been tested in cell cultures and small-animal EBV models. The doses required to treat Ebola are likely to be 2–5 times higher than those for influenza. The drug may have teratogenic and embryotoxic effects. Large amounts are available, as the drug is in phase 3 influenza studies.
TKM-Ebola	Tekmira	Small interfering RNA that hinders 3 out of 7 Ebola proteins (L, VP24, and VP35 proteins)	2.4 mg/kg per IV dose	TKM-Ebola showed promise after initial studies in nonhuman primates. The phase 1 trial was put on hold because of adverse effects (increased cytokine levels, headache, dizziness, and tachycardia).
ZMapp	Mapp Biopharmaceutical Inc.	Combination of 3 humanized monoclonal antibodies that bind and coat the viral envelope.	Dosing unknown Used in 7 patients, of whom 5 survived	Derived from the <i>Nicotiana benthamiana</i> tobacco plant, ZMapp has shown survival benefits in nonhuman primates infected with EBV. It has been used emergently to treat 7 human patients. The production process is complex, and the supply of the drug is currently exhausted.
Readily available in Canada				
Amiodarone, chloroquine, clomiphene, dronedarone, verapamil	Brand-name and generic manufacturers available (except for dronedarone [brand name only])	Inhibits entry of virus into host cells	Dosing unknown In vitro studies only	The Emergency Amiodarone Study against Ebola (EASE) trial is a randomized, open-label study underway in Sierra Leone to compare the combination of amiodarone and best supportive care with best supportive care alone. ¹⁰
Lamivudine	Brand-name and generic manufacturers available	Cytosine analogue that inhibits RNA polymerase	Dosing unknown Used by one Liberian doctor in 15 patients, of whom 13 are reported to have survived	The Scientific and Technical Advisory Committee on Ebola Experimental Interventions of the World Health Organization stated that available data did not show lamivudine to have antiviral activity against Ebola. The committee does not currently recommend its use for Ebola treatment. However, the drug is listed as a potential option for further investigation. ¹¹

tration of IV fluids, replacement of electrolytes, treatment of concurrent infections and secondary bacterial infections, nutritional support, administration of antiemetics and analgesics, and management of bleeding are essential aspects of care for those with EVD.⁶ As clinical trials are conducted, investigational treatments for EVD may play a larger role. Investigational medications include brincidofovir, favipiravir, TKM-Ebola, ZMapp, amiodarone, chloroquine, clomiphene, dronedarone, lamivudine, and verapamil (Table 2).^{6,7} Therapies based on blood products obtained from convalescing EVD patients and vaccines, including the VSV-EBOV vaccine developed by the National Microbiology Laboratory of the Public Health Agency of Canada, are also being assessed for their potential use in treating and preventing EVD.⁶

Conclusion

Given the important role of hospital pharmacists on the front lines of patient care, an understanding of EVD management and the development of EVD-specific hospital pharmacy policies and procedures are essential.

References

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