Ministry of Health

# Mpox Antiviral Guidance for Health Care Providers

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This guidance document provides basic information only. This document is not intended to provide or take the place of medical advice, diagnosis, treatment, or legal advice.

Ontario continues to monitor for cases of mpox (formerly monkeypox) and is working collaboratively with health care providers, Public Health Ontario (PHO), and the Public Health Agency of Canada (PHAC) to address health risk(s). New guidance will continue to emerge as new information becomes available and the epidemiology of this situation evolves.

## Tecovirmat (TPoxx®) Antiviral

TPoxx® is an antiviral medication that inhibits the production of an orthopoxviral envelope protein required for cell-to-cell viral dissemination.

TPoxx® has recently been authorized for sale and use in Canada, for the treatment of human smallpox disease in adults and pediatric patients weighing at least 13 kg based on limited clinical testing in humans. TPoxx® has been approved in other jurisdictions including the European Medicines Agency (EMA) which has authorized TPoxx® for the treatment of mpox, cowpox and smallpox.

It does not have an approved indication for the treatment of mpox in Canada. However, a licensed healthcare professional may request this drug for eligible patients based on their clinical judgement for treating severe mpox infections. Please refer to the eligibility criteria outlined in the next section of this document for more information on which patients may be eligible to receive TPoxx®.

Ontario is able to access TPoxx® through the federal government. All requests for TPoxx® should be made to the Ministry of Health's Emergency Operations Centre (MEOC).

**A very limited supply of TPoxx® is available in Ontario for individuals who are severely ill/disabled due to mpox infection or at high risk for severe disease.**

TPoxx® effectiveness in treating orthopoxvirus infections including mpox has not been studied in humans. Animal studies have shown TPoxx® to be effective in treating orthopoxvirus-induced infection.

Individuals who are hypersensitive to this drug or to any ingredient in the formulation should not receive it. A list of ingredients can be found in the product monograph.

**Careful case-by-case assessment of risks versus potential benefits for any individual mpox case should be undertaken before administering TPoxx® treatment.**

## Use of TPoxx® for Orthopoxvirus Infections in Ontario

TPoxx® is Indicated for the treatment of mpox in adults and pediatric patients weighing **at least 13 kg (29 lbs).** The treatment course for an adult is **600 mg PO BID x 14 days (200 mg/capsule).** Table 1 outlines treatment dosages for adults and children starting at 13 kg.

There is no data on the optimal timing to initiate therapy, although it is likely to be most beneficial if started earlier in the course of infection.

Given the current limited supply of TPoxx®, Ontario is using this product to treat individuals who are severely ill/disabled due to mpox infection or at high risk for severe disease.
TPoxx® should be considered for the following:

- Hospitalized patients with severe disease (e.g., hemorrhagic disease, sepsis, encephalitis, myocarditis, esophagitis, or other conditions requiring hospitalization)
- Persons who may be at high risk of severe disease:
    - Persons who are severely immunocompromised (e.g., individuals with HIV with current CD4 counts $\leq 200/mm^3$ or with uncontrolled viral loads; receiving active treatment for solid tumour or hematologic malignancies such as chemotherapy, targeted therapies, or immunotherapy; recipients of solid-organ transplant and taking immunosuppressive therapy; recipients of hematopoietic stem cell transplant within 2 years of transplantation or taking immunosuppression therapy; autoimmune with immunodeficiency as a clinical component; on treatment with agents such as tumor necrosis factor or high-dose corticosteroids);

- Pediatric populations, particularly patients younger than 10 years of age (see Table 2);
- Pregnant or breastfeeding women (see Table 2);
- Persons with one or more complications (e.g., severe secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities).

- Persons with mpox virus infections with lesions that are leading to significant disability (e.g., proctitis, keratitis or other ocular involvement, pharyngitis/epiglottitis or other breathing/swallowing compromise).

**Table 1: Recommended dosing for pediatric and adult patients**

| **Body Weight** | **Dosage** |
|---|---|
| 13 kg to less than 25 kg | 200 mg twice daily for 14 days |
| 25 kg to less than 40 kg | 400 mg twice daily for 14 days |
| 40 kg and above | 600 mg twice daily for 14 days |

- TPOXX® should be taken within 30 minutes after a full meal of moderate or high fat.
- For more information regarding the recommended adult and pediatric dosage and preparation instructions, see the product monograph.

**Table 2: Use of TPoxx® in Special Populations**

| **Special Population:** | **TPoxx® use indication** |
|---|---|
| **Pediatrics (<13kg)** | No data is available to Health Canada. Health Canada has not authorized an indication for pediatric use in children weighing less than 13 kg. |
| **Pediatrics (≥13kg)** | Health Canada has authorized an extraordinary use indication for pediatric patients weighing ≥ 13 kg. TPOXX® has not been studied in children and adolescents 17 years of age and younger. |

| Special Population: | TPoxx® use indication |
|---|---|
| **Pregnant individuals** | TPoxx® has not been studied in pregnant people. TPoxx® should not be used in pregnancy unless the benefits outweigh the risks. Animal studies suggest no embryo-fetal development toxicity during organogenesis. The background risk of significant congenital disabilities and fetal loss for the indicated population is unknown. |
| **Breastfeeding individuals** | It is unknown if TPoxx® is excreted in human milk. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for TPoxx® and any potential adverse effects on the breastfed child from TPoxx® or the underlying maternal condition. |
| **Geriatrics (≥65 years)** | Clinical studies of TPoxx® did not include sufficient numbers of subjects 65 years of age and over to determine whether the safety profile of TPoxx® is different in this population compared to younger subjects. |

## Precautions

The efficacy of TPoxx® for treatment of smallpox and mpox disease has not been determined in humans because adequate and well-controlled field trials have not been feasible and inducing disease in humans to study the drug's efficacy is not ethical.

Table 3 provides a list of precautions and clinical comments as found in the product monograph.

**Table 3: Precautions related to TPoxx® Usage**

| Precaution | Clinical Comment |
|---|---|
| Endocrine and Metabolism | Co-administration of repaglinide and TPoxx® may cause mild to moderate hypoglycemia. Monitor blood glucose and monitor for hypoglycemic symptoms when administering TPoxx® with repaglinide. |
| Immune Dysfunction | TPoxx® efficacy may be reduced in immunocompromised patients based on studies demonstrating reduced efficacy in immunocompromised animal studies. |
| QTc Interval Prolongation | TPoxx® has been reported to cause prolongation of the QTc interval. Caution should be observed if TPoxx® is administered to patients who are considered to be at high risk of the torsade de pointes arrhythmia, including but not limited to, those with congenital or acquired long QT syndrome, other cardiac disease, electrolyte depletion (e.g., hypokalemia, hypomagnesemia, or hypocalcemia) or conditions that lead to electrolyte depletion, or in situations of concomitant treatment with Class IA or Class III antiarrhythmics or other QTc-prolonging drugs. |
| Reproductive Health - Fertility | There is no data on the effects of TPoxx® on fertility in humans. In male mice, decreased fertility associated with testicular toxicity (increased percent abnormal sperm and decreased sperm motility) was observed at 1000 mg/kg/day (approximately 24 times the human exposure at RHD). |

## Potential Side Effects of TPoxx®

In adults, the most commonly reported side effects were headache and nausea followed by abdominal pain and vomiting.

Less common adverse reactions can include:

- Gastrointestinal: dry mouth, chapped lips, dyspepsia, eructation, and oral paresthesia.
- General pyrexia, pain, chills, malaise, and thirst.

- Investigations: abnormal electroencephalogram, hematocrit decreased, hemoglobin decreased, heart rate increased and QTc prolongation.
- Musculoskeletal and connective tissue: arthralgia and osteoarthritis.
- Nervous system: migraine, disturbance in attention, dysgeusia and paresthesia.
- Psychiatric: depression, dysphoria, irritability, and panic attack.
- Respiratory, Thoracic and Mediastinal Disorders: oropharyngeal pain.
- Skin and subcutaneous tissue: palpable purpura, rash, pruritic rash, facial redness, facial swelling, and pruritus.

## Storage Conditions

Store TPoxx® at room temperature (+15°C to +25°C).

This medicine should not be used after the expiry date shown on the bottle.

## Informed Consent

The *Health Care Consent Act, 1996* provides specific information on the consent required for treatment. According to the HCCA, the College of Nurses of Ontario (CNO) and the College of Physicians and Surgeons of Ontario (CPSO) standards, nurses and physicians are accountable for obtaining consent when providing treatment. Therefore, it is the responsibility of the health practitioner proposing the treatment to take reasonable steps to ensure that informed consent for that treatment is obtained. According to the HCCA, consent to treatment for a capable person is informed if, before giving the consent:

a. the person received the information about the treatment that a reasonable person in the same circumstances would require to make a decision; and
b. the person received responses to their requests for additional information about the treatment.

**This information must include:**

- The nature of the treatment
- The expected benefits of the treatment
- The material risks of the treatment
- The material side effects of the treatment
- Alternative courses of action

- The likely consequences of not having the treatment

**The elements required for consent to treatment include:**

- The client must have the capacity to consent
- The consent must relate to the treatment
- The consent must be informed
- The consent must be given voluntarily
- The consent must not be obtained through misrepresentation or fraud

**Evidence of Consent:**

Although the HCCA states that consent to treatment may be expressed or implied (i.e., written or verbal), the CNO and CPSO strongly advise nurses and physicians to document that consent was obtained from the client. Examples include: (1) a signed consent form and/or (2) documented consent in the client's health records.

Initial doses of TPoxx® have been acquired through Health Canada's Special Access Program (SAP) which **requires all health care providers requesting this drug to get written informed consent from the patient or their substitute decision maker prior to starting the treatment course.**

## How to Order TPoxx®

TPoxx® will initially be provided to clinicians as part of Health Canada's Special Access Program (SAP). Given the limited supply of TPoxx® available in Ontario, TPoxx® should be prescribed based on the eligibility criteria described above.

Clinicians need to request TPoxx® by contacting the Vaccine Policy & Programs Branch (VPPB) at vaccinesupplyandlogistics@ontario.ca.See **Appendix A** for the information that needs to be provided as part of the request.

Health Canada's SAP has mandatory reporting requirements for clinicians using the Follow-Up Form (Form C) including treatment response outcomes. This form should be returned to the VPPB at vaccinesupplyandlogistics@ontario.ca.The VPPB will send the forms back to SAP on behalf of the clinician.

## Reporting Adverse Events

To comply with Health Canada's SAP, any adverse reactions or events due to TPoxx® must be recorded on Form C and submitted tothe VPPB at vaccinesupplyandlogistics@ontario.ca,, in addition to any other reporting processes used to report adverse events to drugs.

## Additional Resources

European Centre for Disease Prevention and Control - Factsheet for health professionals on mpox (monkeypox)

Ontario Ministry of Health - Mpox Virus

Public Health Agency of Canada - Mpox (monkeypox)

Public Health Ontario – Mpox (formerly known as monkeypox)

United States Centers for Disease Control - Mpox

World Health Organization – Mpox (monkeypox) Key Facts

World Health Organization - Mpox (monkeypox)

# Appendix A

Clinicians must provide the following information for each patient that has consented to receive TPoxx® at the time they are submitting their request. Failure to provide the information below in full may result in requests being delayed or denied.

## A. REQUESTER INFORMATION

**Name of requesting clinician:** _____

**Contact information of requesting clinician:** _____

## B. PATIENT INFORMATION

**Age:** _____ **Sex and gender:** _____

**MPOX test date:** _____

**Test status:** ☐ positive ☐ pending ☐ negative/not tested

**Current disposition:** ☐ hospitalized ☐ outpatient

**Clinical indication for treatment (see eligibility above):** _____

_____

_____

_____

## C. DELIVERY INFORMATION

**Primary contact name:** _____

**Primary contact number:** _____

**Secondary contact name:** _____

**Secondary contact number:** _____

**Name of delivery site:** _____

**Delivery site address:** _____

**Delivery hours:** _____

**Special instructions:** _____

_____

_____

**Please send above information to:** vaccinesupplyandlogistics@ontario.ca