Ontario

Ministry of Health

Mpox Antiviral Guidance for Health Care Providers

Version 3.0 – September 16th, 2024

Highlights of Changes:

- Addition of Clade I and II information (p.1)
- Update to the tecoviromat antiviral section to include clinical trial link (p.2)
- Removal of special access program requirement: Form C

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

The virus that causes mpox is distinguished by two separate genetic clades:

- **Clade I**: Sub-clade Ia is endemic to Central Africa and causes more severe illness and deaths than clade II. Sub-clade Ib emerged in the Democratic Republic of Congo (DRC) in 2023 and is spreading through direct contact, primarily through heterosexual networks.
- **Clade II:** This clade is endemic to West Africa and is associated with less severe illness and deaths than clade I. Sub-clade IIb was responsible for the 2022 global mpox outbreak that primarily affected adults who identified as men who have sex with other men.

Ontario continues to monitor for cases of mpox, (clade I and II), 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). Guidance will be updated as new information becomes available and epidemiology evolves.

Information related to mpox and vaccination in this document is based on the current epidemiology in Ontario and evidence related to clade II.

Tecovirmat Antiviral

The anti-viral drug tecovirimat (TPoxx®) is a medication authorized for smallpox that inhibits the production of an orthopoxviral envelope protein required for cell-to-cell viral dissemination.

TPoxx® is available for mpox patients who are severely ill due to mpox infection or at high risk of experiencing severe disease.

The efficacy of TPoxx® in the treatment of mpox has not been formally evaluated in clinical trials, but use is reasonable on the basis of its efficacy against smallpox, animal data, and unpublished data in humans with mpox.

A clinical trial to evaluate the effectiveness and safety of TPoxx® for the treatment of Mpox infection compared to placebo is underway in Canada and internationally. The study is also collecting information about the feasibility and acceptability of conducting this type of trial for non-hospitalized patients with Mpox in Canada. For more information visit: https://www.hivnet.ubc.ca/study/ctn-338-platinum-can/

All requests for TPoxx® should be sent to the Office of Chief Medical Officer of Health, Public Health at vaccinesupplyandlogistics@ontario.ca. There is a limited supply of TPoxx® available in Ontario, as such, TPoxx® requests will be evaluated on a case-by-case basis.

Use of TPoxx® for Orthopoxvirus Infections in Ontario

TPoxx® is authorized for use for the treatment of smallpox.

Use for mpox treatment is for 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 per smallpox treatment authorization
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.
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.

Special Population:	TPoxx® use per smallpox treatment authorization
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 person's clinical need for TPoxx® and any potential adverse effects on the breastfed child from TPoxx® or the underlying condition of the individual.
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 individuals.

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.

There are efforts underway internationally and in Canada to better understand the effectiveness and safety of Tpoxx® as a treatment for mpox.

For Tpoxx ® requests received, the ministry of health will consult with infectious disease specialists in the field prior to approving orders. 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.

Precaution	Clinical Comment
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 (+15ºC to +25ºC).

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.

How to Order TPoxx®

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 Office of Chief Medical Officer of Health, Public Heatlh at vaccinesupplyandlogistics@ontario.ca See **Appendix A** for the information that needs to be provided as part of the request.

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

Dose Requested _____

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