Recommendations for Antiviral Post-Exposure Prophylaxis of Highly Pathogenic Avian Influenza A(H5N1)

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Purpose

This document provides recommendations for clinicians on the appropriate prescribing of antiviral post-exposure prophylaxis (PEP) for adults and children exposed to highly pathogenic avian influenza (HPAI) A(H5N1).

Recommendations related to other aspects of PEP management (e.g., infection control practices, testing, diagnostics) are beyond the scope of this document. See the **Additional Resources** section for more information about these topics. For information related to antiviral availability and drug coverage, see the drug availability section of Ontario Health's **Influenza Clinical Guidelines and Resources** webpage.

Recommendations Development

The recommendations in this guidance document are informed by best available evidence identified through a systematic literature search conducted between February and March 2026. The search included peer-reviewed studies, review articles, Canadian guidelines, international guidelines and grey literature. The recommendations were developed by the Ontario Health Infectious Diseases (ID) program's guidance development working group with consensus-based feedback and contributions from Ontario Health's Infectious Diseases Advisory Committee (IDAC). This document was reviewed by multidisciplinary clinicians and health care administrators from Ontario Health's Primary Care Program, Renal Program, Systemic Treatment Program (Cancer Care), Regional Clinical Vice-Presidents and the Chief Medical Executive.

This guidance document shall be updated as needed to align with relevant changes in clinical best practice.

See the **Authorship, Contributors and Acknowledgements** section for additional information about the authors and contributors of this guidance document.

Disclaimer

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Introduction

Epidemiology

HPAI A(H5N1) is a zoonotic viral infection that primarily affects wild and domestic birds.[1] However, HPAI A(H5N1) has been responsible for sporadic infections in humans after close contact with infected animals or animal products, or after exposure to environments contaminated by these animals (e.g., live poultry markets, barns).[1–3] HPAI A(H5N1) may cause severe human illness, with a cumulative historic case fatality rate (CFR) of approximately 50%.[4–6] However, the CFR may be overestimated as asymptomatic or mildly symptomatic infections may go undetected.[7]

British Columbia reported Canada's first domestically acquired human case of HPAI A(H5N1) in 2024 — this country's only confirmed human infection to date.[8] The source of the individual's exposure was not identified. However, genetic sequencing showed that the HPAI A(H5N1) virus matched a strain circulating in local poultry and wild birds in the province at the time.[5] Rare instances of limited human-to-human transmission of HPAI A(H5N1) have been reported after close or prolonged contact with an infected person.[9] Although sustained human-to-human transmission of HPAI A(H5N1) has not been established, there is concern that the virus could pose a pandemic risk because of its virulence, adaptability and the lack of existing population immunity.[10,11]

Goals of Post-Exposure Prophylaxis

The goals of antiviral PEP in an individual exposed to a person or animal with suspected or confirmed HPAI A(H5N1) infection are to:

- Prevent HPAI A(H5N1) infection.[2]
- Limit the risk of person-to-person HPAI A(H5N1) transmission.[4]

Recommendations for HPAI A(H5N1) Post-Exposure Prophylaxis

The use of antivirals for HPAI A(H5N1) PEP should be guided by an individual's level of exposure risk and take into consideration the time since their exposure.[10] See the **Highly Pathogenic Influenza A(H5N1) Exposure Risk Classification** section for a description of the exposure risk categories.

Antiviral PEP is not an alternative for appropriate personal protective equipment (PPE) or other infection prevention and control measures.[11]

See **Figure 1** for a suggested algorithm for HPAI A(H5N1) PEP in adults and children.

- For individuals indicated for antiviral PEP based on their exposure risk[†], it should be started as soon as possible, ideally within 48 hours of the their last exposure, but may be started up to 10 days after their last exposure.[12–15]

- Antiviral PEP is RECOMMENDED for individuals with high exposure risk[†] to HPAI A(H5N1).[4]

- Antiviral PEP MAY BE CONSIDERED for individuals with intermediate exposure risk[†] to HPAI A(H5N1), based on clinical discretion of the individual's underlying medical condition(s) and risk of progression to severe disease.[4]
  - Individuals at higher risk of developing seasonal influenza-related complications (e.g., individuals aged 65 years and older, children aged younger than 5 years, individuals with certain underlying medical conditions) may also be at a greater risk for developing complications associated with HPAI A(H5N1).[16] See Table 2 of Ontario Health's **Recommendations for Antiviral Therapy of Seasonal Influenza** for a list of risk factors that are associated with an increased risk of developing seasonal influenza-related complications.

- Antiviral PEP is NOT recommended for individuals with low exposure risk[†] to HPAI A(H5N1).[4]

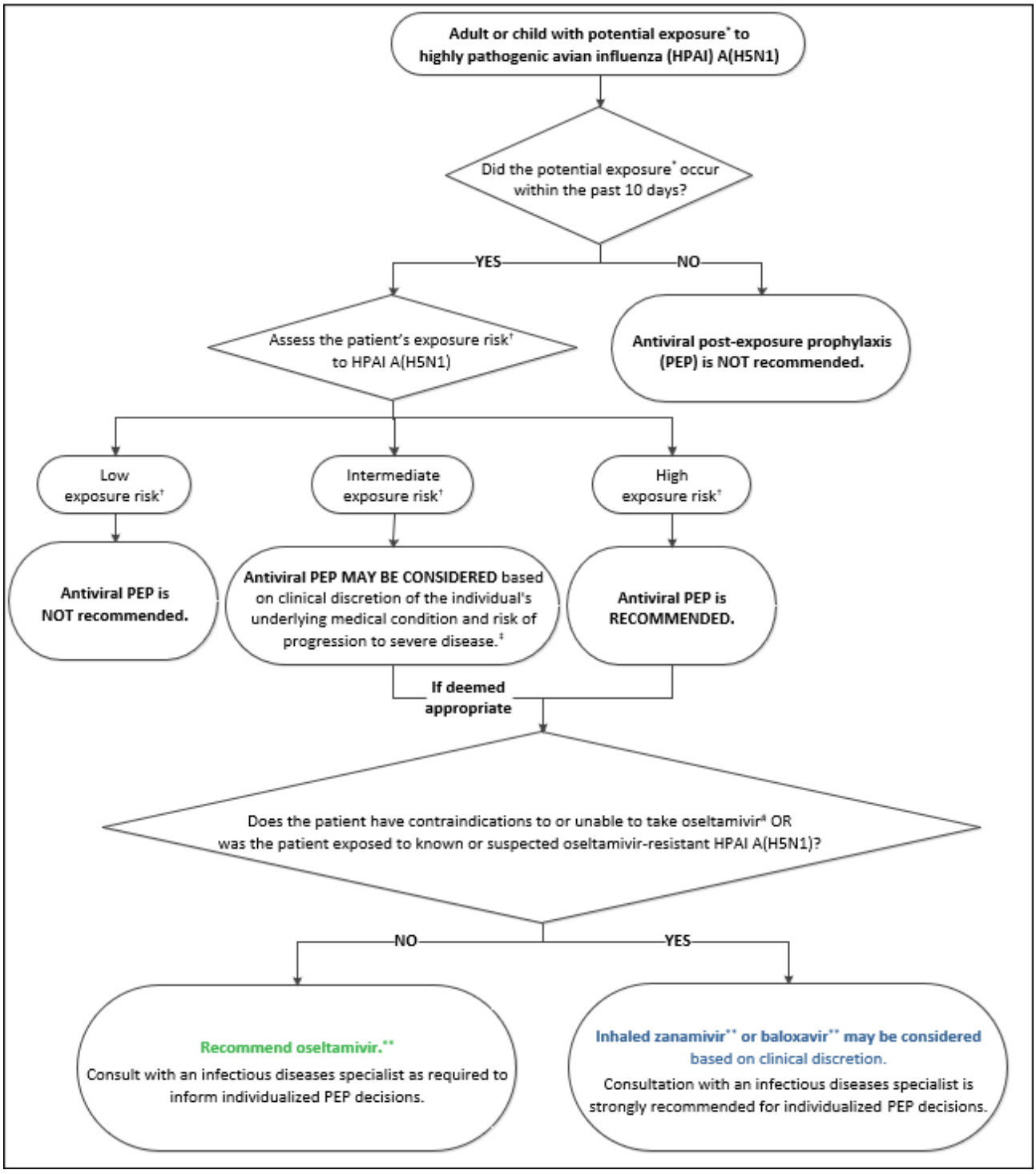
- Oseltamivir[**] is recommended as first-line antiviral medication for HPAI A(H5N1) PEP.[4,17]
  - Consult with an Infectious Diseases (ID) specialist as required to inform individualized treatment decisions.

- For individuals who are contraindicated to or unable to take oseltamivir[#] OR exposed to known or suspected oseltamivir-resistant HPAI A(H5N1):
  - Inhaled (INH) zanamivir[**] OR baloxavir[**] may be considered for antiviral PEP based on clinical discretion.[6]
  - Consultation with an ID specialist is strongly recommended for individualized PEP decisions.

- Antiviral PEP for HPAI A(H5N1) should be limited to discrete exposure[*] events.[17]
  - Prolonged use of antiviral PEP is not recommended.[17]
  - For people who are unable to avoid ongoing exposure to sources of the HPAI A(H5N1) virus, consultation with an ID specialist is recommended for individualized PEP decisions.[4]

See the **Clinical Evidence** section for a detailed description of the evidence summary and rationale that support the clinical recommendations.

Figure 1: Algorithm for Highly Pathogenic Avian Influenza A(H5N1) Post-Exposure Prophylaxis



[*] Exposure is defined as:

- Close contact (within 2 meters) with a confirmed or probable human case of HPAI A(H5N1)[4] **OR**
- Direct or indirect, unprotected close contact (within 2 meters) to wild birds, poultry or other animals with confirmed or presumptive HPAI A(H5N1)[4,18] **OR**
- Direct or indirect, unprotected contact with contaminated environments such as surfaces contaminated with biological tissues from confirmed or presumptive HPAI A(H5N1)-infected animals (e.g., carcasses, feathers, feces, secretions, raw milk)[18] **OR**
- Unprotected exposure to biological material known to contain HPAI A(H5N1) virus in a laboratory setting (e.g., primary clinical specimens, virus culture isolates)[18]

[†] For information on the classification of exposure risk, see the **Highly Pathogenic Influenza A(H5N1) Exposure Risk Classification** section.

[‡] Individuals at higher risk of developing seasonal influenza-related complications (e.g., individuals aged 65 years and older, children aged younger than 5 years, individuals with certain underlying medical conditions) may also be at greater risk for developing complications associated with HPAI A(H5N1).[16] See Table 2 of Ontario Health's **Recommendations for Antiviral Therapy of Seasonal Influenza** for a list of risk factors that are associated with an increased risk of developing seasonal influenza-related complications.

[#] For information about clinically relevant contraindications and administration considerations of oseltamivir, see the supplemental drug information section in Ontario Health's **Recommendations for Antiviral Therapy of Seasonal Influenza**.

[**] HPAI A(H5N1) PEP with oseltamivir, INH zanamivir, or baloxavir is considered off-label use in Canada.

Highly Pathogenic Influenza A(H5N1) Exposure Risk Classification

Table 1 outlines the classification of exposure risk for HPAI A(H5N1).[4]

Table 1: HPAI A(H5N1) Exposure Risk Classification

Exposure Risk Category	Definition[4]
High	- Individuals with unprotected and very close exposure (i.e., within 1 to 2 meters) to a flock or group of infected animals (asymptomatic or sick/dead) or to particular birds or other animals that have been directly implicated in human cases (e.g., farm family member or worker who handled sick or infected animals). - Individuals involved in the handling and slaughtering of live poultry and other animals, such as those in a live animal market, in an area experiencing an HPAI A(H5N1) outbreak or visitors to an area where such activities are being undertaken while unprotected. - Individuals involved in handling infected (asymptomatic or sick/dead) animals or decontaminating affected environments (including animal disposal) as part of outbreak control efforts (e.g., cullers) who did not have, or were wearing insufficient PPE, or had a breach in the use of PPE, during these activities. - Household/family contacts of a suspected or confirmed human HPAI A(H5N1) patient (defined as living under the same roof as the primary case when the case is presumed to be contagious). - Individuals, such as health care workers (HCWs) (i.e., those working in a setting where health care is being provided), who had no PPE in place when in close contact (i.e., within 1 to 2 metres) of a human HPAI A(H5N1) case, or in direct contact with respiratory secretions or other potentially infectious specimens from the case.
Intermediate	- Individuals without PPE who handle single or small groups of animals infected with HPAI A(H5N1) (asymptomatic or sick/dead) in an open-air environment which is not densely populated by animals of the same species as the infected animal (e.g., single wild bird in a park). - Individuals, such as HCWs or laboratory personnel, who might have inadequate or insufficient PPE when in direct contact with a human HPAI A(H5N1) case or specimens/secretions which may contain virus or with laboratory isolates.

Exposure Risk Category	Definition[4]
Low	- Personnel involved in culling non-infected or likely non-infected animal populations as a control measure (e.g., those exclusively culling asymptomatic animals in a control area outside of the infected and primary control zones). - Individuals who handle (i.e., have direct contact with) single or small groups of asymptomatic animal(s) with a possible proximity to a geographic area where HPAI A(H5N1) has recently been identified (e.g., hunters/trappers, bird banders, Indigenous hunters and harvesters). - Personnel involved in handling infected (asymptomatic or sick/dead) animals or decontaminating affected environments (including animal disposal) as part of outbreak control efforts (e.g., cullers) who did have or were wearing sufficient PPE during these activities. - Individuals, such as HCWs, who used appropriate PPE during contact with human HPAI A(H5N1) cases. - Laboratory personnel working with the influenza virus using appropriate laboratory procedures and infection control precautions (e.g., wearing proper PPE).



Clinical Evidence

Clinical studies have not evaluated antiviral PEP for HPAI A(H5N1) infection in humans using placebo-controlled comparisons.[6,19] Given the sporadic occurrence and limited number of human HPAI A(H5N1) cases, recommendations for antiviral PEP are informed by clinical evidence from seasonal influenza and other novel avian influenza viruses.[20]

Oseltamivir

Oseltamivir is the preferred antiviral for HPAI A(H5N1) PEP based on evidence supporting its use for PEP against other types of avian influenza and seasonal influenza.[4,17]

Two observational studies evaluated the effectiveness of oseltamivir PEP during an outbreak of HPAI A(H7N7) in poultry. In both studies, the workers who handled potentially infected poultry received oseltamivir PEP until 2 days after their last exposure.[21,22] One study found that oseltamivir PEP significantly reduced the rate of laboratory-confirmed HPAI A(H7N7) infection compared with no oseltamivir PEP, while the other study found no significant difference.[21,22] However, a trend towards a lower rate of HPAI A(H7N7) infection was observed in the latter study among the workers who received oseltamivir PEP compared with those who did not.[22]

A randomized controlled trial evaluated the effectiveness of a 7-day course of oseltamivir PEP in household contacts aged 12 years and older exposed to individuals with laboratory-confirmed seasonal influenza within 48 hours of symptom onset.[23] Oseltamivir PEP significantly reduced the risk of symptomatic, laboratory-confirmed seasonal influenza in household contacts within 7 days of oseltamivir initiation compared with placebo.[23] The trial also found that the benefit of oseltamivir PEP was consistent for the outcome of symptomatic and asymptomatic laboratory-confirmed seasonal influenza.[23]

The World Health Organization (WHO) estimates that oseltamivir PEP for avian influenza, including HPAI A(H5N1), could reduce hospitalization by approximately 15 per 1,000 treated individuals and mortality by approximately 3 per 1,000 treated individuals.[20] The estimates are based on extrapolated data from oseltamivir PEP for seasonal influenza and assumed a high incidence of severe infection among those infected.[20] However, the assumptions in the model are based on very low certainty evidence.[20]

Zanamivir

INH zanamivir is listed as an option for HPAI A(H5N1) PEP by the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada).[17] The use of INH zanamivir for HPAI A(H5N1) PEP is based on its use for seasonal influenza PEP as there are no clinical trials evaluating its effectiveness for avian influenza PEP.[20]

The effectiveness of a 10-day course of INH zanamivir PEP was evaluated in two randomized controlled trials of household contacts aged 5 years and older exposed to individuals with laboratory-confirmed seasonal influenza within 36 hours of symptom onset.[24,25] Household contacts were assessed for the development of symptomatic, laboratory-confirmed seasonal influenza within 11 days of INH zanamivir PEP initiation in one trial, and within 14 days of INH zanamivir PEP initiation in the other trial.[24,25] Both trials found that INH zanamivir PEP significantly decreased the incidence of symptomatic, laboratory-confirmed seasonal influenza in household contacts compared with placebo.[24,25] The benefit of INH zanamivir PEP was also consistent for the outcome of symptomatic and asymptomatic laboratory-confirmed seasonal influenza.[24,25]

INH zanamivir PEP utilizing alternative dosing regimens have also been evaluated in clinical studies. One randomized controlled trial compared a 5-day course of INH zanamivir PEP with placebo in household contacts aged 13 years and older exposed to individuals with influenza-like illness within 4 days of symptom onset.[26] No significant difference was found between the two groups for the development of symptomatic, laboratory-confirmed seasonal influenza within 10 days of PEP initiation.[26] However, there was a trend towards benefit for the INH zanamivir group.[26] One limitation of this trial was that index patients were not tested for seasonal influenza, so the true number of household contacts exposed to laboratory-confirmed seasonal influenza was unknown.

Two randomized controlled trials of adults and children compared INH zanamivir PEP with placebo in household contacts exposed to an individual with laboratory-confirmed seasonal influenza within 48 hours of symptom onset.[27,28] In both studies, the seasonal influenza treatment dosing regimen was used for INH zanamivir PEP.[27,28] Neither trial demonstrated a significant difference between the INH zanamivir and placebo groups for the development of symptomatic, laboratory-confirmed seasonal influenza.[27,28] However, both trials were underpowered because target enrollment was not reached, which limited the ability to determine the true effect of INH zanamivir.[27,28]

The WHO estimates that zanamivir PEP for avian influenza, including HPAI A(H5N1), could reduce hospitalization by approximately 15 per 1,000 treated individuals and mortality by approximately 3 per 1,000 treated individuals.[20] The estimates are based on extrapolated data from zanamivir PEP of seasonal influenza and assumed a high incidence of severe infection among those infected.[20] However, the assumptions in the model are based on very low certainty evidence.[20]

Intravenous (IV) zanamivir is not included as an option for HPAI A(H5N1) PEP because it has not been studied for this indication. Furthermore, access to IV zanamivir is only available through Health Canada's **Special Access Program**.

Peramivir

Peramivir is not recommended because it has not been studied for HPAI A(H5N1) PEP nor for seasonal influenza PEP.[29–31] Peramivir is not approved by Health Canada for HPAI A(H5N1) PEP and access to the drug is only available through Health Canada's **Special Access Program**.[29]

Baloxavir

The efficacy of baloxavir for avian influenza PEP, including HPAI A(H5N1), has not been studied in clinical trials.[6] However, the Infectious Diseases Society of America and the WHO include baloxavir as an option for HPAI A(H5N1) PEP based on its use for seasonal influenza PEP.[6,9]

The effectiveness of baloxavir PEP compared with placebo was examined in a randomized controlled trial of household contacts within 48 hours of exposure to individuals with laboratory-confirmed seasonal influenza.[32] Baloxavir PEP significantly reduced the risk of symptomatic, laboratory-confirmed seasonal influenza within 10 days of baloxavir initiation compared with placebo.[19,32] This benefit was consistent in adults and children, including the subgroup of patients with underlying risk factors for seasonal influenza-related complications.[32] One limitation of the trial was that it did not capture the time between the index patient's symptom onset and the start of baloxavir PEP in household contacts.[32]

Two small, retrospective studies also evaluated the rate of seasonal influenza infection among close contacts of individuals with seasonal influenza who received baloxavir PEP compared with those who did not.[33,34] Both studies found that close contacts who received baloxavir PEP had a significantly lower rate of seasonal influenza infection compared with those who did not receive baloxavir PEP.[33,34]

The WHO estimates that baloxavir PEP for avian influenza, including HPAI A(H5N1), could reduce mortality by approximately 3 per 1,000 treated individuals and hospitalization by approximately 15 per 1,000 treated individuals.[20] The estimates are based on extrapolated data from baloxavir PEP of seasonal influenza and assumed a high incidence of severe infection among those infected.[20] However, the WHO notes that the assumptions underpinning the model are based on very low certainty evidence.[20]

Amantadine

Although amantadine is approved by Health Canada for the prophylaxis of influenza A infections, it is not recommended for HPAI A(H5N1) PEP due to historically high resistance rates to avian influenza.[4,35] Amantadine is also associated with a higher rate of adverse drug events compared with neuraminidase inhibitors (NAIs) and baloxavir.[4]

Supplemental Information: Antiviral Agents

Oseltamivir

Oseltamivir is the preferred antiviral agent for HPAI A(H5N1) PEP by the Public Health Agency of Canada (PHAC) and AMMI Canada even though it is considered off-label use in Canada.[4,17,36]

Dose and duration recommendations for HPAI A(H5N1) post-exposure prophylaxis

Table 2 outlines age-specific dosing recommendations for HPAI A(H5N1) PEP.

For HPAI A(H5N1) PEP, the oseltamivir dosing used for the treatment of seasonal influenza is recommended rather than the dosing used for seasonal influenza PEP.[4,17] This recommendation is based on limited animal data that support higher dosing for HPAI A(H5N1) virus and to reduce the potential for development of antiviral resistance.[10,37–40] No dose adjustment of oseltamivir is required for obese individuals.[41,42]

Oseltamivir is not approved for use in infants younger than 1 year of age.[36,43] Oseltamivir dosing recommendations for this age group are adapted from national and international guidelines for the treatment of seasonal influenza.[43–46] Due to limited data for oseltamivir use in infants younger than 1 year of age, PEP should only be considered after a thorough risk assessment and in consultation with specialist(s) as required (e.g., ID, pediatrician).[4]

The recommended duration of oseltamivir for HPAI A(H5N1) PEP is 10 days following the last exposure to a source of HPAI A(H5N1).[4,17,20] This extended duration is based on the potentially longer incubation period of avian influenza viruses compared with seasonal influenza strains.[4,47]

Table 2. Oseltamivir Dose Recommendations for HPAI A(H5N1) Post-Exposure Prophylaxis[††]

Age and Weight Group	Dose
13 years and older, AND weight greater than 40 kg	75 mg orally (PO) or by oro/nasogastric tube (OG/NG) twice daily[4]
13 years and older, AND weight less than or equal to 40 kg	60 mg PO/OG/NG twice daily[15]
1 to 12 years, AND weight greater than 40 kg	75 mg PO/OG/NG twice daily[4]
1 to 12 years, AND weight greater than 23 to 40 kg	60 mg PO/OG/NG twice daily[4]
1 to 12 years, AND weight greater than 15 kg to 23 kg	45 mg PO/OG/NG twice daily[4]
1 to 12 years, AND weight less than or equal to 15 kg	30 mg PO/OG/NG twice daily[4,44]
Full-term infants 9 months to younger than 12 months	3.5 mg/kg/dose PO/OG/NG twice daily[‡‡,43,44]
Full-term infants younger than 9 months	3 mg/kg/dose PO/OG/NG twice daily[43,44]
Premature infants, AND older than 40 weeks postmenstrual age (PMA)	3 mg/kg/dose PO/OG/NG twice daily[43,44]
Premature infants, AND 38 through 40 weeks PMA	1.5 mg/kg/dose PO/OG/NG twice daily[43,44]
Premature infants, AND younger than 38 weeks PMA	1 mg/kg/dose PO/OG/NG twice daily[43,44]

[††] The dosing recommendations are adapted from the dosing used to treat seasonal influenza.[4,17]

[‡‡] The American Academy of Pediatrics recommends 3.5 mg/kg orally twice daily instead of 3 mg/kg orally twice daily for infants in this age group to achieve target oseltamivir exposure for the treatment of seasonal influenza.[44,48] It is unknown whether the higher dose will improve efficacy or prevent the development of antiviral resistance.[31] However, there is no evidence that the 3.5 mg/kg dose increases adverse events in infants from this age group.[31]

Dose adjustment for renal impairment

Table 3 provides dosage recommendations for adults with renal impairment.

Table 3: Oseltamivir Dose Recommendations for HPAI A(H5N1) Post-Exposure Prophylaxis for Adults with Renal Impairment††

Creatinine Clearance (mL/min) or Renal Replacement Modality	Oseltamivir Dose
Greater than 60	No dose adjustment necessary[49]
Greater than 30 to 60	30 mg PO/NG/OG twice daily[49]
Greater than 10 to 30	30 mg PO/OG/NG once daily[49]
Less than or equal to 10 AND not on dialysis	75 mg PO/OG/NG for 1 dose[50,51]
Intermittent hemodialysis (IHD)	75 mg PO/OG/NG for 1 dose, then 75 mg after each dialysis session[50,52]
Continuous ambulatory peritoneal dialysis (CAPD)	30 mg PO/OG/NG on day 1 and day 7[49]

†† The dosing recommendations are adapted from the dosing used to treat seasonal influenza.[4,17]

Table 4 provides dosage recommendations for children with renal impairment.

Table 4: Oseltamivir Dose Recommendations for HPAI A(H5N1) Post-Exposure Prophylaxis for Children with Renal Impairment††

Estimated Glomerular Filtration Rate (mL/min) or Renal Replacement Modality	Oseltamivir Dose
60 and above	No dose adjustment necessary[45]
30 to less than 60	Give 40% of the age and weight-based dose in Table 2 twice daily[45]
10 to less than 30	Give 40% of the age and weight-based dose in Table 2 once daily[45]
Less than 10	Oseltamivir is not recommended[45]
Children receiving IHD, AND weight greater than 40 kg	The first dose is based on age and weight as listed in Table 2, then 30 mg PO/OG/NG after each dialysis session[46]
Children receiving IHD, AND weight greater than 23 kg to less than or equal to 40 kg	The first dose is based on age and weight listed in Table 2, then 15 mg PO/OG/NG after each dialysis session[46]
Children receiving IHD, AND weight greater than 15 kg to less than or equal to 23 kg	The first dose is based on age and weight listed in Table 2, then 10 mg PO/OG/NG after each dialysis session[46]
Children receiving IHD, AND weight less than or equal to 15 kg	The first dose is based on age and weight listed in Table 2, then 7.5 mg PO/OG/NG after each dialysis session[46]

†† The dosing recommendations are adapted from the dosing used to treat seasonal influenza.[4,17]

Dose adjustment for hepatic impairment

No dose adjustment is necessary for patients with mild to moderate hepatic impairment.[36] The safety and efficacy of oseltamivir in patients with severe hepatic impairment has not been studied.[36]

Other drug-related information

For information related to administration considerations, pregnancy, breastfeeding/chest-feeding, clinically relevant contraindications, drug-drug interactions and adverse drug effects, see the supplemental drug information section for oseltamivir in Ontario Health's **Recommendations for Antiviral Therapy of Seasonal Influenza**.

Drug availability and coverage

For information related to oseltamivir availability and drug coverage, see the drug availability section of Ontario Health's **Influenza Clinical Guideline and Resources** webpage.

Zanamivir

The use of INH zanamivir for HPAI A(H5N1) PEP is considered off-label use in Canada.[53] Consultation with an ID specialist is strongly recommended prior to initiating zanamivir for HPAI A(H5N1) PEP.

Dose and duration recommendations for HPAI A(H5N1) post-exposure prophylaxis

AMMI Canada recommends using zanamivir treatment dosing for seasonal influenza when it is used for HPAI A(H5N1) PEP based on limited data that support higher dosing for HPAI A(H5N1) virus and to reduce the potential for development of antiviral resistance while receiving PEP.[10,17] Table 5 outlines age-based dosing recommendations for INH zanamivir adapted from the treatment of seasonal influenza because zanamivir has not been studied for HPAI A(H5N1) PEP.[20] No dose adjustment of INH zanamivir is required for obese individuals.[50]

The recommended duration of zanamivir for HPAI A(H5N1) PEP is 10 days following the last exposure to a source of HPAI A(H5N1).[17,20] This extended duration is based on the potentially longer incubation period of avian influenza viruses compared with seasonal influenza strains.[4,47]

Table 5: Inhaled Zanamivir Dose Recommendations for HPAI A(H5N1) Post-exposure Prophylaxis[##]

Age	Dose
7 years and older	10 mg INH twice daily[17] (A second dose should be administered on the first day of treatment whenever possible, provided there is at least 2 hours between doses. On subsequent days, doses should be 12 hours apart at approximately the same time each day.)[53]
Younger than 7 years	Health Canada has not approved INH zanamivir for use in this age group.[***,53]

[##] The dosing recommendations are adapted from the dosing used to treat seasonal influenza.[17]

[***] AMMI Canada and PHAC do not have dosing recommendations for INH zanamivir in children younger than 7 years of age.[4,50] However, some countries have approved the use of INH zanamivir for seasonal influenza based on limited efficacy data for children aged 5 to 7 years.[15,54,55] The safety and effectiveness of INH zanamivir have not been assessed in pediatric patients younger than 5 years of age.[53]

Dose adjustment for renal impairment

No dosage adjustment is provided for INH zanamivir in the manufacturer's labelling for individuals with renal impairment.[53]

Dose adjustment for hepatic impairment

No dose adjustment is provided for INH zanamivir in the manufacturer's labelling for individuals with hepatic impairment.[53]

Other drug-related information

For information related to administration considerations, pregnancy, breastfeeding/chest-feeding, clinically relevant contraindications, drug-drug interactions and adverse drug effects, see the supplemental drug information section for zanamivir in Ontario Health's **Recommendations for Antiviral Therapy of Seasonal Influenza**.

Drug availability and coverage

For information related to zanamivir availability and drug coverage, see the drug availability section of Ontario Health's **Influenza Clinical Guidelines and Resources** webpage.

Baloxavir

Baloxavir is not approved for HPAI A(H5N1) PEP in Canada.[56] Consultation with an ID specialist is strongly recommended to inform individualized treatment if it is considered for off-label use.

Dose and duration recommendations for HPAI A(H5N1) post-exposure prophylaxis

Standardized baloxavir dosing regimens for HPAI A(H5N1) PEP have not been established because the drug has not been studied for this indication.[6] In the absence of direct evidence, recommendations for baloxavir dosing are informed by expert opinion and by dosing principles used for NAIs in HPAI A(H5N1) PEP. Canadian and international guidelines recommend using seasonal influenza treatment dosing when NAIs are used for HPAI A(H5N1) PEP based on limited data suggesting that higher dosing may be required for HPAI A(H5N1) and to minimize the risk of antiviral resistance during PEP.[10,14,15,17] **Table 6** outlines baloxavir dosing recommendations for HPAI A(H5N1) PEP adapted from treatment dosing used in a clinical trial of severe seasonal influenza in patients aged 12 years and older.[57]

Table 6. Baloxavir Dose Recommendations for HPAI A(H5N1) Post-exposure Prophylaxis for Individuals Aged 12 Years and Older†††

Weight	Dose
40 kg to less than 80 kg	40 mg PO on day 1 and day 4‡‡‡,[57]
80 kg or greater	80 mg PO on day 1 and day 4‡‡‡,[57]

††† The dosing recommendations are adapted from the dosing used to treat severe seasonal influenza.

‡‡‡The oral suspension formulation of baloxavir is not marketed in Canada and access to the drug is only available through Health Canada's **Special Access Program**.

Dose adjustment for renal impairment

No dose adjustment for baloxavir is provided in the manufacturer's labelling for individuals with renal impairment.[56] The safety and efficacy of baloxavir have not been established in patients with renal impairment.[56] As baloxavir is primarily excreted through the fecal pathway, renal impairment is unlikely to have a significant impact on its clearance.[56]

Dose adjustment for hepatic impairment

No dose adjustment is required in patients with mild (Child-Pugh class A) to moderate (Child-Pugh class B) hepatic impairment.[56] Baloxavir has not been studied in patients with severe hepatic impairment.[56]

Other drug-related information

For information related to administration considerations, pregnancy, breastfeeding/chest-feeding, clinically relevant contraindications, drug-drug interactions and adverse drug effects, see the supplemental drug information for baloxavir in Ontario Health's **Recommendations for Antiviral Therapy of Seasonal Influenza**.

Drug availability and coverage

For information related to baloxavir availability and drug coverage, see the drug availability section of Ontario Health's **Influenza Clinical Guidelines and Resources** webpage.

Supplemental Information: Immunization

HPAI A(H5N1) Vaccine

Health Canada has approved a vaccine to prevent HPAI A(H5N1) infection for adults and children aged 6 months and older. However, it is currently unavailable in Ontario.[58,59] For the latest information regarding access to the vaccine, contact the **local public health unit**.[60]

Seasonal Influenza Vaccine

Seasonal influenza vaccination continues to be recommended for all individuals aged 6 months and older, irrespective of their risk of exposure to HPAI A(H5N1), provided no contraindications exist.[5,61] Although the seasonal influenza vaccine does not protect against HPAI A(H5N1) infection, it may reduce the severity of seasonal influenza illness and decrease the risk of co-infection and genetic reassortment.[5,62,63]

For more information about the seasonal influenza vaccine, see the Ministry of Health's **Influenza Immunization** webpage.[61]

Additional Resources

- Ontario Health:
  - Influenza clinical guidelines and resources

- Ontario Ministry of Health:
  - Ontario public health standards - influenza disease protocol
  - Avian influenza

- Public Health Ontario:
  - Laboratory testing for respiratory viruses
  - Ontario respiratory virus tool

- Public Health Agency of Canada:
  - Guidance on human health issues related to avian influenza in Canada
  - Avian influenza A(H5N1) for health professionals
  - Pandemic risk scenario analysis for influenza A(H5N1)

- Association of Medical Microbiology and Infectious Disease Canada:
  - Statement on antiviral therapy for HPAI and reported oseltamivir resistance in Canada
  - Update on influenza: management and emerging issues

- International guidelines:
  - Infectious Diseases Society of America: antivirals for novel influenza A virus infections
  - U.K. Health Security Agency: guidance for the management of people exposed to birds or other animals infected with influenza A(H5)
  - U.S. Centers for Disease Control and Prevention: interim guidance for follow-up of close contacts of persons infected with novel influenza A viruses associated with severe human disease or with potential to cause severe human disease, and use of antiviral medications for post-exposure prophylaxis
  - U.S. Centers for Disease Control and Prevention: oseltamivir emergency use instructions
  - World Health Organization: clinical practice guidelines for influenza

- Product monographs:
  - Baloxavir product monograph
  - Oseltamivir product monograph
  - Peramivir product monograph
  - Zanamivir (inhaled) product monograph
  - H5N1 influenza vaccine (Arepanrix) product monograph

Questions

For any questions on the contents of this document, please contact the Provincial Drug Reimbursement Programs (PDRP) at OH-CCO_InfoPDRP@ontariohealth.ca.

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Infectious Diseases Advisory Committee (IDAC)

About IDAC

IDAC provides Ontario Health with timely evidence-based clinical and health system guidance on infectious diseases matters. It is a multidisciplinary committee comprised of health care professionals practising throughout Ontario who specialize or have a focus in treating infectious diseases in the hospital or community setting.

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Disclosures

Ontario Health ID program staff and IDAC members must disclose conflicts of interest. Depending on the nature of the disclosure, Ontario Health will develop and implement a mitigation plan with strategies to address the disclosure.

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