

DRUG ANTIVIRALS

TREATMENT AND PROPHYLAXIS OF INFLUENZA IN CHILDREN AND ADULTS IN THE CONTEXT OF COVID-19

This optimal use guide is intended for health professionals. It is provided for information purposes only and should not replace the judgment of the clinician who performs activities reserved under an act or a regulation. The recommendations in this guide were developed using a systematic process and are supported by the scientific literature and the knowledge and experience of Québec clinicians and experts. In the context of the COVID-19 public health emergency, INESSS is constantly on the lookout for any new data that might warrant changes to this guide. For further details, go to inesss.qc.ca.

GENERAL CONSIDERATIONS

- The clinical recommendations in this guide concern the treatment and prophylaxis of influenza in children and adults in the context of the COVID-19 health emergency.

INFLUENZA-LIKE ILLNESS (ILI)

Anyone with symptoms consistent with ILI, gastroenteritis or COVID-19 should follow [the public health authorities' recommendations](#).

INFLUENZA-LIKE ILLNESS	
TYPICAL SYMPTOMS	OTHER SYMPTOMS AND ASPECTS
Most common symptoms: Fever ¹ ($\geq 38.5^{\circ}\text{C}$) OR cough (dry) of sudden onset AND at least one of the following symptoms: ▶ Sore throat ▶ Joint pain ▶ Muscle pain ▶ Prostration ² or extreme fatigue	In adults: ▶ Headache In children: ▶ Gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea and abdominal pain) <i>N.B.: In very young children, the symptoms may be mild or non-specific, such as rhinorrhea, a decline in the child's overall state of health, the refusal to eat or drink, and decreased interest in activities.</i> In the elderly: ▶ Cough sometimes of late onset ▶ Geriatric fever ³ or sometimes no fever

1. Temperature taken rectally in young children. In children, fever is defined as $\geq 38.3^{\circ}\text{C}$.

2. Prostration: a state of extreme physical and psychological exhaustion, weakness and total inactivity.

3. Geriatric fever is defined as any of the following criteria: a) a single oral temperature measurement $> 37.8^{\circ}\text{C}$ or b) repeated oral temperature measurements $> 37.2^{\circ}\text{C}$ or repeated rectal measurements $> 37.5^{\circ}\text{C}$ or c) a single temperature measurement (oral, tympanic, axillary or rectal) $> 1.1^{\circ}\text{C}$ above the individual's baseline temperature (measured previously via the same route).

ILI SEVERITY		
MILD	MODERATELY SEVERE	SEVERE
Typical symptoms sometimes accompanied by diarrhea and vomiting	<p>Typical symptoms AND more serious signs or symptoms:</p> <ul style="list-style-type: none"> ▶ Chest pain ▶ Mild hypoxia ▶ Cardiopulmonary insufficiency (e.g., hypotension) ▶ Mild central nervous system impairment (e.g., confusion and altered mental status) ▶ Severe dehydration ▶ Exacerbation of existing chronic conditions 	<p>Signs and symptoms associated with the following conditions:</p> <ul style="list-style-type: none"> ▶ Respiratory failure requiring oxygen therapy ▶ Central nervous system abnormalities (e.g., encephalitis and encephalopathy) ▶ Complications of hypotension (e.g., shock and organ failure) ▶ Myocarditis or rhabdomyolysis ▶ Invasive secondary bacterial infection (e.g., persistent high fever and other symptoms beyond 3 days)

RISK FACTORS FOR INFLUENZA COMPLICATIONS

RISK OF COMPLICATIONS	HIGH RISK OF COMPLICATIONS
<ul style="list-style-type: none"> ▶ Child under 2 years of age¹⁻² ▶ Person 75 years of age or older ▶ Resident of a residential and long-term care centre, a seniors' home or an intermediate resource, whether public or private ▶ Person with a chronic illness or a condition that requires a regular medical follow-up (e.g., a cardiac, pulmonary, renal, hepatic, hematologic or neurological disease, cancer, immunocompromise and severe obesity) ▶ Child or adolescent (age < 18 years) on prolonged aspirin therapy ▶ Healthy pregnant woman in the 2nd or 3rd trimester OR pregnant woman with a chronic illness or condition, regardless of the stage of pregnancy ▶ Person living in a remote or isolated community³ 	<p>Based on clinical judgment, certain people may be considered to be at high risk for influenza complications, such as:</p> <ul style="list-style-type: none"> ▶ Immunocompromised individuals (e.g., recipients of a recent allograft or solid organ transplant and patients on chemotherapy) ▶ Individuals with severe pulmonary disease ▶ Individuals with multiple comorbidities

1. Children under 6 months of age are at greatest risk for influenza complications, followed by children 6 to 23 months of age, then by those 2 to 4 years of age.

2. In children with mild ILI, antiviral treatment is not recommended if age is the only risk factor for influenza complications.

3. Defining an isolated or remote area is done by the public health authorities concerned.

TREATMENT-RELATED LABORATORY TESTS

- ▶ The recommendations regarding the appropriate use of the tests for the different respiratory viruses (SARS-CoV-2, influenza and respiratory syncytial virus) during the influenza season in the context of the COVID-19 pandemic are available [here](#).

PHARMACOLOGICAL TREATMENT

PRINCIPE DE TRAITEMENT

- !** Consideration should be given to influenza treatment or prophylaxis, regardless of the person's vaccination status, when:
 - The [influenza activity index](#) shows the presence of influenza type A or B viruses that are susceptible to the available therapeutic options OR
 - The test result shows the presence of influenza type A or B viruses that are susceptible to the available therapeutic options
- When indicated, initiate antiviral therapy as soon as possible upon clinical suspicion and ideally within 48 hours of symptom onset **without waiting for confirmation of influenza virus infection.**

PROPHYLAXIS

Antiviral prophylaxis against influenza is **generally not recommended**.

- It may, however, be considered as a control measure when an [outbreak in a health-care facility is suspected or confirmed](#).

PRESUMPTIVE TREATMENT

Presumptive antiviral treatment for influenza **is recommended** in:

- A person at high risk for influenza complications who has had close contact with an infected individual or an individual with ILI, i.e., who was in the same room for 4 hours or longer OR in contact with respiratory secretions as a result of direct exposure without adequate protection.

TREATMENT

Treatment for the influenza virus **is recommended** on the basis of ILI severity and the target population as follows:

ILI severity	Target population	Treatment approach
Mild	<ul style="list-style-type: none"> ► Child 1 year of age or older¹ with a risk factor for influenza complications (in addition to age) ► Person under 75 years of age with a risk factor for influenza complications ► Person who lives in the same household as someone at risk for influenza complications or who looks after such an individual at his/her home 	<ul style="list-style-type: none"> ► Initiate an antiviral if the person has had symptoms for 48 hours or less
	<ul style="list-style-type: none"> ► Person 75 years of age or older ► Person at high risk for influenza complications 	<ul style="list-style-type: none"> ► Initiate an antiviral even if the person has had symptoms for more than 48 hours
Moderately severe	<ul style="list-style-type: none"> ► Anyone 1 year of age or older¹ 	<ul style="list-style-type: none"> ► For non-hospitalized persons, consider hospitalization if the symptoms are moderately severe or severe
Severe		
Regardless of severity	<ul style="list-style-type: none"> ► Resident of a residential and long-term care centre, a seniors' home or an intermediate resource, whether public or private ► Person hospitalized with influenza 	<ul style="list-style-type: none"> ► Initiate an antiviral even if the person has had symptoms for more than 48 hours

1. If necessary, and depending on the resources available at the facility, consideration may be given to treating, on a case-by-case basis, children under 1 year of age after discussion with a pediatric specialist or an experienced colleague.

CHOOSING THE ANTIVIRAL

When influenza treatment or prophylaxis is indicated, choose the appropriate antiviral based on the following table:

POPULATION	OSELTAMIVIR 1 ST CHOICE	ZANAMIVIR 2 ND CHOICE ¹
Children 1 to < 7 years of age	✓	✗
Children ≥ 7 years of age	✓	✓
Adults	✓	✗
Persons ≥ 1 year of age with an underlying pulmonary disease	✓	✓
Pregnant or breastfeeding women	✓	✓

1. For confirmed or strongly suspected cases of influenza type B in adults and if there are no contraindications, preference should be given to zanamivir. If treatment with oseltamivir has already been initiated on the outside, there is no need to switch to zanamivir.

Legend ✓ Recommended ✗ Not recommended

GENERAL INFORMATION ON ANTIVIRALS

	OSELTAMIVIR	ZANAMIVIR
Contraindications	► History of allergic reaction to oseltamivir	► History of allergic reaction to zanamivir or milk protein ► Underlying respiratory disease, severe respiratory insufficiency or coordination problems preventing the proper administration of zanamivir via the Diskus®
Precautions	► None	► Young children ► The elderly
Route of administration	► None	► Inhalation (Diskus®)
Most common drug adverse effects	► Nausea ► Vomiting	► Bronchospasm
Most significant drug interactions	► Attenuated live influenza vaccine: can reduce vaccine immunogenicity	

DOSAGE

	OSELTAMIVIR				
	Adults	Adults with renal impairment (RI)		Children \geq 1 year ¹	
	Dosage	Estimated creatinine clearance (CrCl)	Dosage	Weight	Dosage
Prophylaxis		If no recent (\leq 2 years) CrCl measurement and no suspicion of chronic advanced RI, use the adult dosage.		If RI, dosage adjustments may be considered based on clinical judgment ² .	
75 mg QD x 10 days	CrCl 31 to 60 ml/min	30 mg QD x 10 days	\leq 15 kg	30 mg QD x 10 days	
	CrCl 11 to 30 ml/min	30 mg q2d x 10 days	> 15 kg to 23 kg	45 mg QD x 10 days	
	CrCl \leq 10 ml/min	Consult an experienced colleague	> 23 kg to 40 kg	60 mg QD x 10 days	
Treatment or presumptive treatment	75 mg BID x 5 days	Person on dialysis		> 40 kg	75 mg QD x 10 days
		CrCl 31 to 60 ml/min	30 mg BID x 5 days	\leq 15 kg	30 mg BID x 5 days
		CrCl 11 to 30 ml/min	30 mg QD x 5 days	> 15 kg to 23 kg	45 mg BID x 5 days
		CrCl \leq 10 ml/min	75 mg in a single dose in consultation with an experienced colleague	> 23 kg to 40 kg	60 mg BID x 5 days
		Person on dialysis	Consult an experienced colleague	> 40 kg	75 mg BID x 5 days

1. Oseltamivir is not approved by Health Canada for use in children under one year of age. Treatment may be considered on a case-by-case basis and on the basis of symptom severity. If necessary and depending on the resources available at the facility, consult a pediatric specialist or an experienced colleague for dosage adjustment.

2. If necessary, and depending on the resources available at the facility, consult a pediatric specialist or an experienced colleague.

	ZANAMIVIR	
	Adults	Children \geq 7 years
Prophylaxis		10 mg (two 5-mg inhalations) QD x 10 days
Treatment or presumptive treatment		10 mg (two 5-mg inhalations) BID x 5 days

FOLLOW-UP

SITUATION	FOLLOW-UP
1. 1. If the test result is negative for influenza and another diagnosis is made	► Discontinue the antiviral treatment
2. If the test result is negative for influenza and no other diagnosis is made	► Consider investigating further and discontinuing the antiviral treatment
3. If the signs and symptoms persist or worsen after 48 to 72 hours of antiviral treatment	► Consider further investigation (e.g., to identify a bacterial co-infection) or consult an experienced colleague
4. If a person receiving oseltamivir prophylaxis develops ILI or confirmed influenza	► Discontinue the prophylaxis and initiate treatment with oseltamivir OR zanamivir

RÉFÉRENCES

Pour consulter toutes les références : voir le rapport en soutien au guide d'usage optimal.

For the symptoms of COVID-19, go to <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/signs-symptoms-severity.html>

For the public health authorities' recommendations, go to <https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/instructions-for-people-with-covid-19-symptoms/>

For the definitions of isolated or remote area (only available in French), go to https://www.inspq.qc.ca/sites/default/files/publications/2473_communautes_elongees_vaccination_influenza.pdf

For the recommendations concerning the use of laboratory tests, go to <https://www.inesss.qc.ca/covid-19/investigation-procedures-diagnostiques/utilisation-pertinente-des-analyses-pour-la-detection-des-virus-respiratoires-durant-la-saison-grippale-en-contexte-de-pandemie.html>

For the influenza activity index (only available in French), go to <https://www.msss.gouv.qc.ca/professionnels/maladies-infectieuses/grippe/>

For the recommendations concerning outbreaks in health-care facilities (only available in French), go to https://www.inspq.qc.ca/sites/default/files/publications/2628_virus_respiratoires_situation_eclosion.pdf