

Stratégies antivirales contre la pandémie de grippe 2009

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Stratégies antivirales

- Prophylaxie
 - Pré-exposition et post-exposition
 - En établissement de santé et à domicile
- Traitement préventif
 - Personnes à risque élevé et à faible risque
 - Post-exposition et premiers stades de la maladie
- Traitement actif
 - Monothérapie et traitement d'association
 - Infection confirmée et infection soupçonnée

Facteurs à considérer concernant la chimioprophylaxie contre la grippe

- Mortalité
- Hospitalisations
- Cas de grippe prévenus
- Événements indésirables graves (non liés à un médicament)
- Événements indésirables liés à un médicament
- Pharmacorésistance
- Rapport coût-efficacité*

Source : Lignes directrices de l'OMS concernant les antiviraux, 20 août 2009

Facteurs à considérer concernant le traitement actif contre la grippe

- Mortalité
- Hospitalisations
- Complications
- Événements indésirables graves (non liées à un médicament)
- Pharmacorésistance
- Rapport coût-efficacité*

Table 1 - Antiviral (Anti-Influenza) drugs currently approved for use in Canada

Drug	Trade Name & Manufacturer	Class	Authorized Indications (as per product monograph)	Formulation(s)	Shelf Life/Stability	Proposed Use(s) During Pandemic
Oseltamivir	Tamiflu®, Hoffmann-La Roche Inc.	Neuraminidase Inhibitor	Treatment of influenza A and B in persons 1 year of age and older who have been symptomatic for no more than 2 days Prevention of influenza A and B in persons 1 year of age and older after close contact with an infected individual for post-exposure prophylaxis (10 days)	Capsules (30 mg, 45 mg and 75 mg): 10 capsules per blister pack Powder for oral suspension (12 mg/mL when reconstituted): 900 mg per bottle (volume of 75 mL in a 100-mL glass bottle)	Shelf life of capsules: 7 years for new government stockpile orders (previously 5 years) Shelf life of powder for suspension: 2 years Stability: Once reconstituted, 10 days in refrigerator (at 2°-8° C)	Capsules (adult and paediatric) for early treatment of ill persons and for outbreak control (treatment and post-exposure prophylaxis) in health care and other closed facilities where high-risk persons reside Oral suspension not included in the national stockpile
Zanamivir	Relenza®, GlaxoSmithKline	Neuraminidase Inhibitor	Treatment of influenza A and B in persons 7 years of age and older who have been symptomatic for no more than 2 days Prevention of influenza A and B in persons 7 years of age and older (post-exposure prophylaxis and up to 28 days' pre-exposure prophylaxis)	ROTADISK® consisting of a circular foil disk with four blisters each containing 5 mg of zanamivir. A DISKHALER® inhalation device is provided to administer the medication (through inhalation). One box contains 5 disks, which is equivalent to one treatment course	Shelf life: 5 years	Early treatment of ill persons and outbreak control (treatment and prophylaxis) in health care and other closed facilities where high-risk persons reside Preferred treatment for pregnant and nursing women
Amantadine	Symmetrel® syrup, Bristol-Myers Squibb <i>Generic amantadine manufacturers: Dominion Pharmacal, GenPharm, Medican Pharma, Pharmel, Pharmascience</i>	M2 ion Channel blocker (cyclic amines or adamantanes)	Treatment of influenza A in persons 1 year of age and older Prevention of influenza A in persons 1 year of age and older	Capsules (100 mg/capsule): bottles of 100 capsules Syrup (10 mg/mL): bottles of 500 mL	Shelf life of capsules: 3.5 to 4 years depending on manufacturer* Shelf Life of syrup: 2 years	For use as combination therapy (with a neuraminidase inhibitor) for the treatment of severe disease Prophylaxis if strain is known to be susceptible to amantadine

Source : Annexe E, Plan canadien de lutte contre la pandémie d'influenza dans le secteur de la santé : Utilisation des médicaments antiviraux pendant une pandémie, 12 mai 2009

Antiviraux contre la grippe (2009)

As of June 2009, the antiviral susceptibilities of circulating viruses are:

	Oseltamivir	Zanamivir	M2 inhibitors
Pandemic A(H1N1) 2009	Susceptible ^a	Susceptible	Resistant
Seasonal A (H1N1)	Mostly resistant	Susceptible	Mostly susceptible
Seasonal A (H3N2)	Susceptible	Susceptible	Resistant
Influenza B	Susceptible	Susceptible	Resistant
Avian influenza (H5N1)	Susceptible	Susceptible	Variable resistant

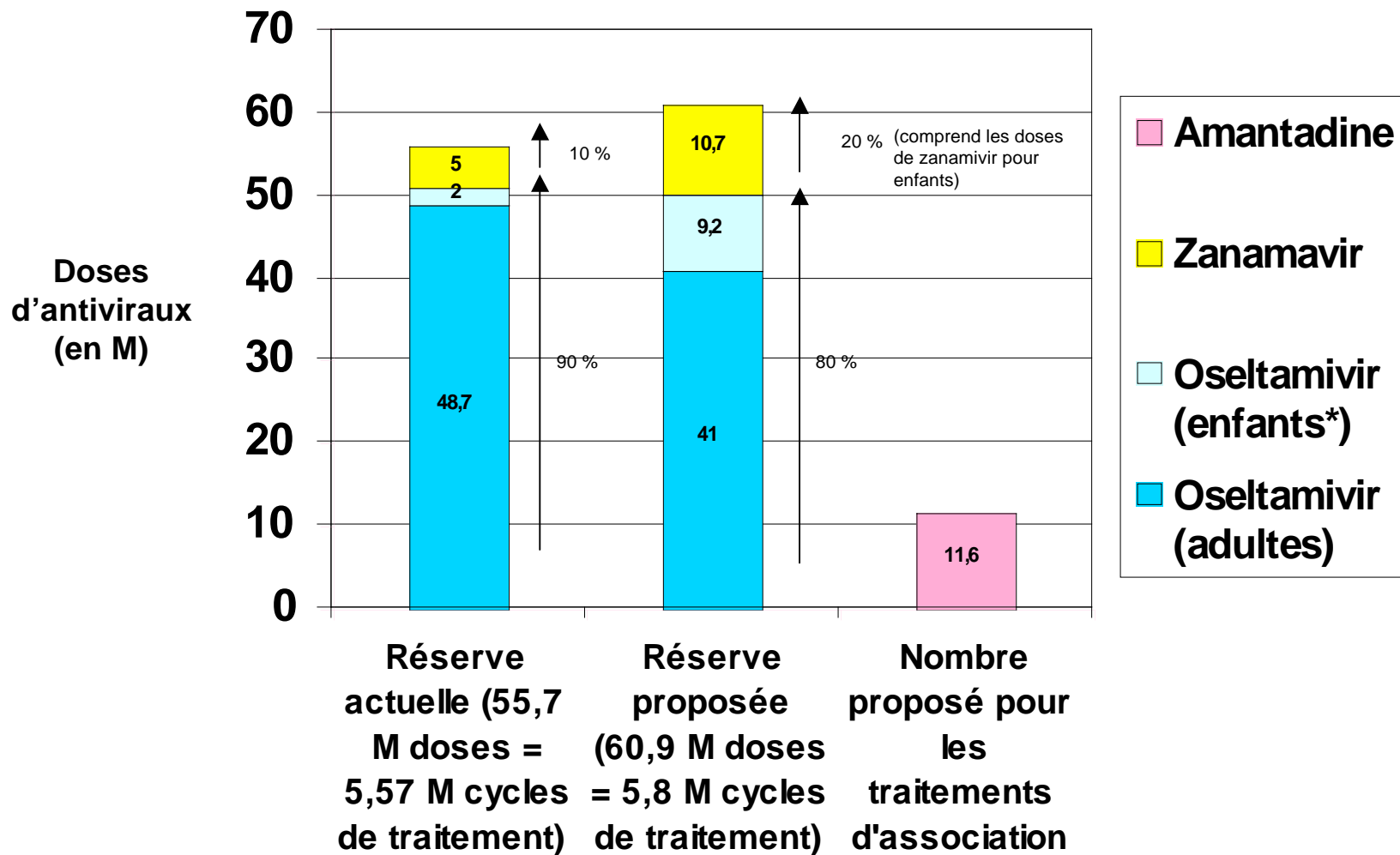
a A small number of isolated cases of resistance to oseltamivir have been reported

Source : Lignes directrices de l'OMS concernant les antiviraux, 20 août 2009

Recommandations canadiennes actuelles concernant l'utilisation d'antiviraux contre la grippe

- Période de pandémie (phase 6)
 - Se concentrer sur le traitement précoce des personnes atteintes de grippe et non sur la prophylaxie post-exposition des contacts proches de ces personnes
 - Assurer un accès rapide aux antiviraux et un traitement rapide aux travailleurs des infrastructures essentielles afin de réduire au minimum les perturbations sociales
 - Utiliser les antiviraux pour lutter contre les éclosions
 - notamment par le traitement des personnes atteintes et par la prophylaxie de leurs contacts proches, dans les établissements de soins de santé fermés et d'autres établissements fermés où résident des personnes à risque élevé
 - Ne pas utiliser d'antiviraux des réserves gouvernementales à des fins de prophylaxie pré-exposition

Composition de la Réserve nationale d'antiviraux



*Englobe les gélules de 30 et de 45 mg

Table. Settings and strategies for antiviral drug use during an influenza pandemic and rationales.

Setting and target population	Antiviral strategy	Rationale	Pandemic response goals addressed by antiviral strategy	Estimated number of regimens (million)
<i>Recommendations for antiviral drugs from public sector stockpiles</i>				
Initial pandemic outbreaks overseas and in the U.S.	Treatment; PEP, targeted prophylaxis	-- Effective containment of the initial outbreak of a novel influenza virus strain may prevent the pandemic -- Quenching efforts overseas and in the U.S will slow pandemic spread and provide more time for preparedness	Slow pandemic spread	6
Exposed travelers entering the U.S. early in a pandemic	PEP	-- Contributes to a risk-based policy to reduce the entry of infected persons and delay U.S. outbreaks	Slow pandemic spread	
Persons with pandemic influenza illness	Treatment	-- Reduces influenza complications, hospitalization, and death -- Reduces duration of illness and transmission of infection -- Meets patient and provider expectations for medical care	Reduce health impacts	79*
Outbreak control in closed settings (e.g., nursing homes, prisons)	PEP	-- High risk of illness and death when outbreaks occur in closed settings -- Documented success of PEP for seasonal outbreaks -- Consistent with accepted public health practice -- Protects those in whom vaccination may be less effective	Reduce health impacts	5
<i>Recommendations for antiviral drugs primarily from private sector stockpiles</i>				
Healthcare and emergency service workers	Outbreak (pre-exposure) prophylaxis for workers with high-risk exposure	-- Reduces infection and absenteeism in a critical workforce -- Protects those at highest occupational risk -- Reduces chance of transmitting infection to high-risk patients with illnesses other than influenza	Reduce health impacts Minimize societal disruption	103
	PEP given exposure of other workers			
Persons who are severely immunocompromised	PEP	-- High risk for severe complications and mortality from pandemic influenza, if infected -- Antiviral drugs are the only option for disease prevention	Reduce health impacts	2
TOTAL NUMBER OF ANTIVIRAL DRUG REGIMENS FOR FULL IMPLEMENTATION				195

Source : CDC Guidance on Antiviral Drug Use during an Influenza Pandemic, déc. 2008

Table. Health impacts, antiviral drug requirements, and cost-effectiveness of antiviral treatment and household post exposure prophylaxis strategies.

Parameter	Treatment alone	Household PEP alone	Treatment and Household PEP
Number of deaths prevented	144,000	155,000	288,000
Number of hospitalizations prevented	1.845 million	838,000	2.427 million
Number of antiviral regimens	79.4 million	106.4 million	167.1 million
Cost per death prevented*	\$11,200	\$14,000	\$11,800
Cost per hospitalization prevented*	\$900	\$2,600	\$1,400

*Average cost per regimen based on Federal contract price for oseltamivir and zanamivir, the relative proportions of each agent targeted for acquisition for the national stockpile, rounded to the nearest \$100

Source : CDC Guidance on Antiviral Drug Use during an Influenza Pandemic, déc. 2008

Table R1: Use of antivirals for treatment of influenza

Population	Pandemic (H1N1) influenza virus 2009	Multiple co-circulating influenza A sub-types or viruses with different antiviral susceptibilities	Sporadic zoonotic influenza A viruses including H5N1
Mild to moderate uncomplicated clinical presentation			
At-risk ^a population	oseltamivir or zanamivir (04)	Zanamivir, or oseltamivir plus M2 inhibitor ^b (10)	oseltamivir or zanamivir
Otherwise healthy ^c	Need not treat (03)	Need not treat (09)	oseltamivir
<p>a Infants and children aged less than 5, the elderly (>65 years), nursing home residents, pregnant women, patients with chronic co-morbid conditions such as cardiovascular, respiratory or liver disease, diabetes, and those with immunosuppression related to malignancy, HIV infection or other diseases.</p> <p>b Amantadine should not be used in pregnant women (recommendation 12).</p> <p>c All those not covered by the at-risk definition above.</p>			
Severe or progressive clinical presentation^d			
At-risk ^a population	Oseltamivir (01) (zanamivir should be used where virus is known to be resistant to oseltamivir, or if oseltamivir unavailable) (02)	oseltamivir plus M2 inhibitor ^b , or zanamivir (05,06, 07)	oseltamivir plus M2 inhibitor
Otherwise healthy ^c			
d See section 2 Case Description. Would include all patients requiring hospitalization.			

Source : Lignes directrices de l'OMS concernant les antiviraux, 20 août 2009

Grippe compliquée ou grave

- Signes cliniques (difficulté respiratoire, tachypnée, hypoxie)
- Signes radiologiques de maladie des voies respiratoires inférieures
- Autres complications directes
 - Rhabdomyolyse, myocardite, encéphalopathie, déshydratation sévère
- Complications secondaires
 - Insuffisance rénale, insuffisance multiviscérale, choc septique
- Exacerbation de maladies chroniques sous-jacentes
 - Asthme, MPOC, insuffisance hépatique ou rénale chronique, diabète, autres affections cardiovasculaires
- Hospitalisation pour prise en charge clinique
- Tout signe d'évolution de la maladie

Utilisation d'antiviraux à des fins chimio prophylactiques

- Conditions
 - D'autres mesures d'atténuation (p. ex., prévention des infections) sont en place
 - Les mécanismes d'administration des médicaments et leurs coûts sont acceptables
 - Une vaccination est prévue
- Contexte
 - Situation à risque élevé
 - Avantages nombreux pour un groupe donné
 - Personnes à risque particulièrement élevé

Tableau récapitulatif des recommandations relatives à l'utilisation d'antiviraux à des fins chimioprophylactiques

Risk		Recommendation	Population	Strength of recommendation
Transmission	Complications			
High	High	If drug available and virus susceptible, use either neuraminidase inhibitor or M2 inhibitor	Defined target population Individual patients Healthcare workers	weak weak weak
High	Low	chemoprophylaxis not recommended	Individual patients Healthcare workers	weak weak
Low	High	If drug available and virus susceptible, use either neuraminidase inhibitor or M2 inhibitor	Individual patients Healthcare workers	weak weak
Low	Low	chemoprophylaxis not recommended	Individual patients Healthcare workers	strong strong

Source : Lignes directrices de l'OMS concernant les antiviraux, 20 août 2009

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