

Chapter 5 Antivirals and Vaccine

5.0 INTRODUCTION

The World Health Organization, the Public Health Agency of Canada (PHAC), and the Ministry of Health and Long-Term Care (MOHLTC) all agree that a monovalent influenza vaccine will be a powerful tool for reducing disease, death, and societal disruption during an influenza pandemic. It is not known how effective the vaccine will be against the pandemic strain; however, seasonal influenza vaccines are usually effective in preventing illness in between 70-90% of healthy adults. Antiviral medications will also play an important role in preventing and treating influenza illness during a pandemic. The availability of antiviral drugs will normally precede the availability of influenza vaccine.

The possible roles of antiviral drugs and the feasibility for their widespread use as part of the response to pandemic influenza will depend on a number of issues:

- The availability to the population (production, distribution, stability, potential for stockpiling, cost).
- Extent of effectiveness for prophylaxis or treatment (or both).
- Individual's contraindications to antivirals.
- Possible emergence of drug resistance.

As it is likely that the supply of both antiviral medications and vaccine will be limited during a pandemic, the MOHLTC will control the distribution of both. Use of antivirals for prophylaxis use is currently under development by the federal and provincial governments.

If antiviral medications are approved for prophylactic use, the role of the Niagara Region Public Health Department will be to co-ordinate the storage, handling, and distribution of antivirals among health care organizations and local target groups that have been identified by the MOHLTC.

The Niagara Region Public Health Department will also serve as the primary co-ordinator for the distribution and administration of vaccine in the Niagara region. A vaccine will not be available for at least 4 - 6 months after the pandemic strain is identified and likely will not be available for the first wave. Once vaccine becomes available, there will be a shortage necessitating the use of priority groups based on the Canadian Pandemic Influenza Plan (CPIP) recommendations. When vaccine becomes more readily available, the Public Health Department will organize mass vaccination clinics for the general public.

5.1 GOALS

Minimize serious illness, societal disruptions and overall deaths through the appropriate distribution of antiviral medications, for prophylactic or treatment use, and vaccine, based on the Provincial recommendations for influenza pandemic.

5.2 OBJECTIVES

- Develop a mass immunization clinic plan to include clinic locations, storage, and security of supplies and required resources.
- Develop an efficient plan for antiviral medication distribution and administration.
- Develop a plan for staff education/training for delivery of immunization services and antiviral medication.
- Monitor safety and effectiveness of vaccine programs and antiviral medication use.
- Monitor vaccine and antiviral uptake.

5.3 NIAGARA REGION ANTIVIRAL/VACCINE ACTIVITIES BY PANDEMIC PHASES

| Pandemic Phase | Antiviral/Vaccine Activities |
|---|--|
| <p>Phase 1: No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection is considered to be low.</p> | <ul style="list-style-type: none"> • Continue to actively promote annual universal influenza immunization. • Promote pneumococcal vaccination of the National Advisory Committee on Immunization (NACI) for those aged 65 years and older, and high-risk groups. • Increase annual influenza vaccine coverage among health care workers (HCW) and emergency services workers. • Maintain updated plans to acquire, store, and distribute vaccine and antivirals. • Work with stakeholders to develop plans to redeploy staff to administer vaccine/ antivirals and to provide training. |

| Pandemic Phase | Antiviral/Vaccine Activities |
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| <p>Phase 2: No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease.</p> <p>Phase 3: Human infection(s) with a new subtype, but no human-to-human spread, or at most, rare instances of spread to a close contact.</p> <p>Phase 4: Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.</p> <p>Phase 5: Larger cluster(s) but human-to-human spread still localized, suggesting that the</p> | <ul style="list-style-type: none"> • Maintain antiviral treatment and prophylaxis recommended in “A guide to the control of respiratory infection outbreaks in LTC homes” (MOHLTC, 2004). • Continue Phase 1 activities. • Confirm that security issues with storing and distributing vaccines and antivirals have been addressed. • Distribute priority group enumeration tools to health care organizations to provide estimates of demand for antivirals and vaccines. • Submit estimates to MOHLTC. • Confirm distribution point for vaccination location in each area. • Ensure that list of currently qualified and potential vaccinators is up to date. • Review mass vaccination program and address any problematic issues. • Review/update educational materials on administering vaccines. • Assess current supply of antivirals/vaccines. • Confirm plans for distributing antivirals/ vaccines. • Actively promote annual influenza vaccination. |

| Pandemic Phase | Antiviral/Vaccine Activities |
|--|---|
| virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk). | <ul style="list-style-type: none"> • Review plans for storing, distributing, and administering vaccine/antivirals. • Review estimates of number of people in each priority group for vaccine/antivirals. • Ensure that training of staff and infrastructure is in place to: <ul style="list-style-type: none"> - record a two-dose immunization program - track who receives antivirals for treatment or prophylaxis. • Work with health organizations to train non-traditional vaccinators. |

5.4 ANTIVIRALS

5.4.1 ANTIVIRAL MEDICATIONS

There are three drugs available to prevent and treat influenza: Amantadine, Oseltamivir, and Zanamivir. Oseltamivir (Tamiflu® - Roche Pharma) and Zanamivir (Relenza® - GlaxoSmithKline) belong to a class of antiviral drugs called neuraminidase inhibitors. Neuraminidase inhibitors can be used to treat or prevent influenza. When used to treat influenza, they must be started within 48 hours of onset of symptoms. These drugs do not kill the influenza virus, but rather decrease the virus' ability to continue to grow in the body. By doing this, the neuraminidase inhibitors result in an improvement in symptoms 1 – 1 ½ days earlier than if the drug were not used. There is some evidence that neuraminidase inhibitors also decrease the risk of influenza complications when used for treatment.

Prophylaxis Use:

The neuraminidase inhibitors can also be used to prevent influenza symptoms. In order to prevent influenza, they must be taken on a daily basis during the time when influenza is circulating. Taking the neuraminidase inhibitor for prevention does not prevent the virus from entering the body but allows the body to develop an immune response to the virus. Instead, the neuraminidase inhibitor prevents the virus from growing in the body, and thereby prevents the development of influenza symptoms and decreases the chances that the virus will spread to others.

Prophylaxis with antivirals may play a key role in maintaining critical services (i.e. preventing infection in, and providing reassurance to, people caring for individuals with influenza as well as workers in critical industries) until a vaccine becomes available.

Neuraminidase inhibitors can also be used for prevention after an exposure (called “post exposure prophylaxis”). An example of its use in this way would be to provide the drug to the remainder of the family, when a family member is diagnosed with influenza. This has been shown to decrease the risk of illness in exposed family members who do not yet have symptoms.

i) Amantadine

Amantadine is an older drug that has troublesome side-effects and is complicated to use. Amantadine is effective for influenza A only, whereas neuraminidase inhibitors are effective for both influenza A and B viruses. The influenza virus also has demonstrated the ability to become easily resistant to Amantadine. The recent outbreak of avian influenza (H5N1) has been shown to be resistant to Amantadine in the lab. Amantadine is, however, significantly less expensive than the newer neuraminidase inhibitors.

ii) Oseltamivir (Tamiflu)

Oseltamivir can be used for treatment if given within 48 hours after onset of symptoms and possibly even later. It decreases the severity of the illness; and may also decrease complications such as pneumonia, hospitalization, and death. Treatment with Oseltamivir will also decrease the ability of the ill person to spread influenza to others. For treatment of seasonal influenza, Oseltamivir is given as 75 mg twice daily for five days. Oseltamivir is taken by mouth and comes as a capsule or liquid. It is safe, effective, and easy to use. It does not interact with the vast majority of other drugs. Some adjustment of the dose is required for individuals known to have kidney disease. In Canada, it is licensed for treatment for ages one and older. For prevention, it is licensed for those 13 years of age and older. Unfortunately, Oseltamivir is relatively costly, and is only made by one manufacturer (Roche Pharma), located in Switzerland.

A few instances of the influenza virus developing resistance to Oseltamivir have been documented. Because of its mechanism of binding to the influenza virus, the development of resistance to Zanamivir is felt to be more unlikely than the development of resistance to Oseltamivir. The development of resistance to the neuraminidase inhibitors is being closely monitored, but still appears to occur infrequently.

Prophylaxis Use:

For prevention, Oseltamivir can be used for a prolonged period of time (up to eight weeks in some studies) and will provide up to 90% protection against influenza illness while the drug is being taken. Oseltamivir can also be given as post-exposure prophylaxis and will provide good protection as long as the drug is being taken. For prevention, 75 mg of Oseltamivir is taken once daily for as long as influenza infection is a risk.

iii) Zanamivir (Relenza)

Zanamivir is produced by GlaxoSmithKline. It has been less popular than Oseltamivir because it is taken by inhalation using a Diskinhaler device. This method of delivery poses a problem for some elderly individuals (particularly in long-term care facilities) who are not able to coordinate the use of the inhaler. Zanamivir should not be used in individuals with asthma or with chronic lung disease as it may worsen these conditions. It is only approved in Canada for treatment and only for individuals 12 years of age and older. For treatment, two puffs twice a day for five days are currently recommended. It must be started within 48 hours of onset of symptoms and will decrease the duration of symptoms by 1 – 1 ½ days. It may also decrease the development of complications from influenza. Health Canada has recently approved Zanamivir for prophylaxis of contacts of cases.

iv) Monitoring Adverse Reactions

The Ontario Health Plan for an Influenza Pandemic (OHPIP) Committee is responsible for setting standards and acceptable rates for adverse antiviral drug reactions. The PHAC and the MOHLTC are responsible for developing, maintaining, and enhancing routine and national surveillance activities for adverse antiviral drug reactions.

5.4.2 ALLOCATION PLANS

Although antiviral agents are effective for the treatment and prophylaxis of influenza, the primary and preferred means of influenza prophylaxis during a pandemic will be vaccines.

Under the present circumstances, the supply of antiviral drugs would be well below the anticipated demand during an influenza pandemic.

Oseltamivir (Tamiflu) is the drug of choice for both treatment and prophylaxis. It is estimated that up to 25% of the Canadian population may be infected, which is equivalent to 20 million doses of Oseltamivir for the Province of Ontario. The goal of the PHAC is to stockpile enough Oseltamivir to provide treatment to those infected with the pandemic virus. It is estimated that by January 2008, the MOHLTC hopes to meet the goal of stockpiling 24 million doses set aside for treatment of pandemic influenza cases in Ontario. Based on the 25% attack rate for the Province of Ontario and Niagara Region's population of approximately 430,000, it is assumed that the Region will receive enough antiviral medications to treat 107,500 Niagara residents. Since one individual requires 10 doses for treatment purposes, the number of treatment doses required in Niagara would be 1,075,000.

Since the first priority is to stockpile enough doses for treatment purposes, there will not be enough antivirals to stockpile for prophylaxis use for everyone. CPIP guidelines for use of antivirals for prophylaxis use are presently under development. In the event a decision is made to stockpile antivirals for prophylaxis use, the PHAC and the MOHLTC will identify and prioritize target groups of people who are to receive antiviral drugs for prophylaxis. That process must consider the impact the drugs will have on maintaining essential health care services, and critical infrastructure.

5.5 NIAGARA REGION HEALTHCARE/ESSENTIAL SERVICE WORKERS

As directed by the MOHLTC in the Fall of 2005, each Public Health Department collected enumeration data of health care and essential service workers in their local region. Based on the enumeration survey conducted in Niagara, it has been estimated that approximately 15,000 health care and essential service workers have been identified from the following groups:

- Emergency Responders (Fire, Police).
- Emergency Responders (EMS).
- Public Health Department.
- Acute Care hospitals.
- Long-term Care Facilities.
- Physicians/Clinics.
- Community Agencies.

There are other critical infrastructure services that have not yet been enumerated which include, but are not limited to, the following:

- Food and Water.
- Electricity.
- Gas and Oil.
- Transportation.
- Telecommunications.
- Financial Institutions.
- Public Safety and Security.
- Continuity of Government.

This data may be useful for administering vaccine and/or antiviral medication for both treatment and prophylaxis purposes for priority target groups identified by the PHAC.

5.6 PERSONAL AND CORPORATE STOCKPILES

Due to limited supplies of antiviral medication, many services will need to rely on public health measures to prevent influenza until a vaccine becomes available. This has led some individuals and workplaces to consider stockpiling antiviral drugs. The shelf life of Oseltamivir is currently four years.

i) Personal Stockpiles

Personal stockpiles pose concerns for several reasons outlined below:

- Antivirals may be obtained on the internet without a prescription.
- It may be difficult for an individual, without consultation from a health care provider, to determine when they are experiencing influenza and therefore when to take the drug for treatment.
- Stockpiling is costly.
- Inappropriate use of Oseltamivir may promote the development of drug resistance.
- The demand for drugs in the private market may hinder governments from stockpiling the drugs as part of their pandemic planning process.
- Since some people will be able to afford the drug and others will not, stockpiling creates inequities in access to health care.

ii) Corporate Stockpiles

Depending on the upcoming CPIP guidelines regarding antivirals for prophylaxis use, some workplaces may be eligible for publicly provided antiviral medications because of the nature of their work. Since Roche Pharma currently has the patent on Oseltamivir until 2016, there are ongoing discussions on how to meet the increasing demands for the drug with only one world-wide supplier.

The PHAC and the MOHLTC have the right to retrieve corporate Oseltamivir stockpiles from one business to provide it to another workplace that has been identified as an essential service. In the event businesses have stockpiled Oseltamivir through non-government funding and have had their stockpile retrieved, they likely will be compensated for their cost.

5.7 DISTRIBUTION PLANS

It is anticipated that the Niagara Region Public Health Department will receive the allocation of antiviral medications and vaccine for the Niagara Region. Antiviral medications may then be distributed to dispensing sites in the community, based on OHPIP directives and the local need.

A Public Health Department medical directive has been developed to address the use of Oseltamivir for treatment and prophylactic use. A medical directive has also been developed for use of Influenza vaccine during a pandemic, once available.

The Niagara PHD currently utilizes the BIOS database system to monitor the vaccine inventory and distribution in the Niagara Region. A similar database could be used to monitor the inventory and distribution of antiviral medication. An inventory of immunization clinic supplies currently exist.

Clerical staff from the Vaccine Preventable Program will be responsible for monitoring, ordering, and stocking supplies required for mass vaccination clinics.

Security of supplies will be essential. A secure on-site location for storage of supplies has been designated in the Public Health Department.

The Public Health Department will arrange for transportation and security of antiviral medication to dispensing sites and of supplies to immunization clinic sites. Transportation and security have yet to be determined.

5.8 ANTIVIRAL MEDICATION DISTRIBUTION

i) Treatment

For influenza treatment purposes, antivirals must be started within 48 hours of the onset of symptoms to be effective. To provide timely treatment, Niagara Region must have an effective distribution system for antivirals. Designated Community Assessment/ Treatment Centres will be the source of antiviral treatment for outpatients who suspect they may have influenza. Organization of clinic plans for Community Assessment/ Treatment Centres is being developed.

Should a pandemic occur before Ontario's stockpile is complete, antivirals for treatment will be distributed according to the available epidemiological evidence (e.g. priority may be given to those likely to develop complications from influenza) and in accordance with the OHPIP ethical framework for decision-making.

ii) Prophylaxis

Issue in utilizing antiviral medications for prophylaxis use is currently being re-addressed. OHPIP will develop a provincial policy on the use of antivirals for prophylaxis, based on the national policy which is currently under development. The Niagara Region has not made plans for distribution of antivirals for prophylaxis use. Once federal and provincial policies are developed regarding prophylactic antivirals, the Niagara Region will develop antiviral medication distribution plans based on OHPIP directives.

iii) Antiviral Medication Eligibility

In order to distribute antiviral medications, mechanisms to ensure that they are given only to individuals who are eligible to receive antiviral medication for treatment or prophylactic use will need to be developed. In the event the PHAC and MOHLTC support the use of antiviral medication for prophylaxis use, target groups of essential services and health care services will be identified and antivirals will be distributed for prophylactic use in order of priority.

Each employer of an essential service organization identified in the priority groups will then be given a designated number of eligibility forms. The employer will distribute these forms to eligible employees within their organization who will then bring the forms to a designated community distribution centres. These forms will have unique identifiers in order to ensure that they are being used appropriately, and an inventory system will be established to track the distribution and return of these forms.

This process will only be implemented with PHAC and MOHLTC approval in using antiviral medication for prophylaxis purposes.

iv) Antiviral Prophylaxis Distribution Centres

In the event the PHAC and the MOHLTC develop a policy for prophylactic use of antiviral medication, local community distribution centres will be developed and operated in a manner similar to vaccination clinics.

An Oseltamivir fact sheet will be given to every client who will receive this antiviral medication.

The number of Clinics, locations, and hours of operation will be determined based on the needs of the people who will be picking up antiviral medications. The following factors must be taken into consideration:

- Infection control measures will be required since some individuals picking up antiviral medications may be ill and infectious.
- Support of pharmacists at these centres will also be necessary to assist in the provision of counselling and drug information. A pharmacist available for consultation during the hours of operations of the distribution centres will therefore be required.
- Security personnel will also be necessary with clear protocols in the event that non-eligible individuals seek to obtain antiviral medication.

Details for Clinic operations in distributing prophylactic antiviral medications will only be developed if the PHAC and the MOHLTC develop a policy supporting the use of antivirals for prophylaxis.

5.9 VACCINES

To immunize the entire province, Ontario would require 24 million doses based on two doses per person, over approximately four months. The Niagara Region has developed a mass vaccination plan in order to implement this goal.

5.10 NEXT STEPS

The following are topics currently being developed:

- Add post-vaccination care instruction sheet to the appendix.
- Compare the Niagara Region Public Health Antiviral/Vaccine Pandemic plan with the newly released December 2006 PHAC plan.
- Explore the potential role of pharmacist in preparing standard labels for dispensing antiviral medication and their role in antiviral drug distribution further.
- Security of supplies, medications, and vaccines at storage sites, immunization clinic sites, and antiviral dispensing sites.
- Secure transportation of supplies, medications and vaccines.
- Database to keep track of eligibility forms, and secure inventory management and distribution system of supplies, vaccines, and antivirals.
- Update enumeration data of essential services and health care services as directed by OHPIP.
- Develop policy for antiviral medication use for prophylaxis based on PHAC and MOHLTC recommendations.
- Medical directives, documentation protocols, policies and procedures, and Clinic locations and operations, need to be developed for antiviral medication distribution centres.
- Monitor and disseminate information to community stakeholders from the PHAC and MOHLTC regarding eligibility for antivirals and vaccines and regarding antiviral medication stockpiling for personal and corporate use.