



**BRITISH
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**British Columbia's
Pandemic Influenza Response Plan (2012)
Logistics of Antiviral Distribution**

September 2012

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Writers: Drs. Bonnie Henry, Fawziah Marra, and Timothy Foggin

Reviewers of initial drafts:

1. Dr. Robert Brunham, BCCDC
2. Dr. Nick Foster, BCCDC
3. Dr. David Patrick, BCCDC
4. Medical Health Officers
5. Hospital Pharmacy Directors
6. BC Pharmacy Association
7. College of Pharmacists of BC
8. Pharmaceutical Services Division, Ministry of Health

EXECUTIVE SUMMARY

This document discusses the issues surrounding how antivirals will be moved from the manufacturer to the point from which they will be stored locally in a community and ultimately dispensed to the patient (health care worker, public or emergency service workers).

The major issues addressed in this document are:

1. Steps that should be taken during the pandemic alert period (phases 4 and 5);
2. Triggers that lead to further decentralization of the provincial stockpile; and
3. What steps are required to ensure a continuous supply when and where needed throughout the province during an influenza pandemic (phase 6).

The initial needs of acute care settings will be addressed through an early forward placement that can be available for any early surge in hospital needs. The initial needs of community pharmacies during phases 4 and 5 are met through commercial supply lines, although provincial stockpile can be “loaned” in exceptional circumstances should an entire community be temporarily short of medication.

Basic intelligence about current medication distribution in the province has been gathered; in essence, all prescription medications are channelled through four shared and two private

warehouses. Pharmacies throughout the province have been mapped; many have accounts with multiple warehouses and will need to choose a preferred warehouse for eventual antiviral medication orders. Some redistribution between warehouses will be required.

Remote and isolated communities that lack pharmacy services altogether have also established a process that will ensure early treatment of their population. As these communities have no formal pharmacy services, pre-positioning of antivirals in public health offices, band offices, and nursing stations was found to be the most appropriate method to ensure timely access. During the H1N1 (2009) pandemic, such an approach was taken for over 30 communities in British Columbia.

With respect to phase 6 triggers, once we meet that trigger, the Provincial Health Officer approves the release of the stockpile, where a proportion of the stockpile will be shipped to all community and hospital pharmacies. This trigger will allow all community pharmacies to order more antiviral medications through their chosen warehouse and hospital pharmacies to order from the BC Centre for Disease Control. Such orders will be limited in quantity such that needs are met but individual pharmacy stockpiling will not occur. Pharmacies will be advised that ordering patterns will be monitored and warehouses will report daily.

1. INTRODUCTION

The National Antiviral Stockpile (NAS) was created in the fall of 2004 and contained 16 million doses of Oseltamivir. In February 2006, it was decided that the size (and diversity) of the stockpile should be increased to 55.7 million doses to support a national early treatment strategy, namely, to provide antivirals to all Canadians expected to need treatment during a pandemic. The calculations were based on assumptions of a clinical attack rate of 35 per cent over the course of a pandemic of moderate severity, with half of those clinically ill seeking medical care and receiving a standard five-day course of antiviral treatment. Given the experience of H1N1 (2009) in New Zealand and Australia, those planning assumptions were revised downward as the impact of the virus was lower than anticipated in 2004.

The NAS contains enough antivirals to treat 17.5 per cent of the population. For British Columbia, this translates to just over 7 million treatment doses (700,000 courses) for adults and children. In addition to the NAS stockpile, British Columbia has purchased an additional 3 million doses (300,000 courses), taking the stockpile to 10 million doses.

This component of the provincial pandemic influenza plan speaks to the distribution of the provincial antiviral stockpile from warehouses to points of dispensing. Please refer to different plans to read about assessment and treatment of influenza.

The initial approach in the Canadian Pandemic Plan on treatment with antivirals was to emphasize early treatment to all clients who live in British Columbia and become ill with a novel influenza strain that has been deemed to have pandemic potential (or to have already caused a pandemic). The epidemiology of H1N1 influenza cases indicates that the majority of affected people were below 55 years of age. The illness was mild in the majority of the cases reported

with comparatively few of those infected needing hospitalization. Those requiring hospitalization were mostly between the ages of 15 to 44 years of age, over half had underlying risk conditions, and most had delayed provision of antivirals. Other patients at higher risk of hospitalization or complications included pregnant women, people of any age with chronic medical conditions and young children under the age of two years.

The above experience with H1N1 influenza resulted in recommendations that early treatment with antivirals was only administered to persons with mild illness if they had underlying chronic conditions otherwise it was for those with moderate to severe illness. However, because the epidemiology of a future novel influenza is unknown, the approach should be a more general emphasis of early treatment for all suspected cases until the severity and epidemiology of the disease are well known. Antivirals are not recommended for pre- or post-exposure prophylaxis except in specified outbreak situations. This approach may change as information becomes available during the next pandemic.

For greatest benefit, treatment with antivirals should begin within 48 hours, if not earlier. Thus, timely access to treatment in addition to issues around equity and availability of medication necessitates a provincial approach to the distribution of antivirals within British Columbia and forms the basis of this plan. Finally, an epidemic situation requires a fluid response.

British Columbia finds itself in a unique position inasmuch as it has a limited number of distribution points of medication to community pharmacies and utilizes a central pharmaceutical database (PharmaNet), in which the majority of outpatient prescriptions (i.e., not hospitalized patients or emergency departments) for patients of all ages are entered by pharmacists. This

allows for dispensing of antivirals by pharmacists

and monitoring of its use at a population level.

2. GOAL STATEMENT AND OBJECTIVES

2.1 Goal Description

The purpose of this plan is to guide the distribution of antiviral medication to points throughout the province from which they might

be selectively dispensed during a pandemic alert period (phases 4 and 5) and made widely available during an influenza pandemic (phase 6).

2.2 Objectives

1. Consider pandemic alert period preparations and special circumstances.
2. Establish triggers with regards to distribution from warehouses to dispensing points.
3. Identify preferred distribution mechanisms to enable consistent early treatment.
4. Present clear steps to ensure uninterrupted distribution throughout the province.
5. Discuss operational issues such as cost of distribution, etc.
6. Identify dependencies that arise from this plan.
7. Present regional data to aid detailed local planning.

3. ASSUMPTIONS

General assumptions about pandemic influenza, such as assumed clinical attack rates and duration of illness, are described elsewhere in the provincial plan. The 2009 experience with influenza A/H1N1 demonstrated that even with clearly stated assumptions, much fluidity of response may be required.

Previous planning has made some basic assumptions, including the fact that we will eventually face a moderately severe pandemic. Expectations have been that we would have 1-3 months' notice from the start of the pandemic until it reaches B.C. Much thinking has focused on avian influenza in many jurisdictions. Recent experience with H1N1 (swine) has seen many changes, not only to these assumptions, but also the previously expected responses. Ongoing pandemic planning is important, the risk now no less and possibly even more than prior to H1N1.

For example, experience with the H1N1 (2009) influenza strain in Mexico, the United States, and also during the Southern hemisphere's influenza season, showed that the virus mainly caused mild illness. Most cases were able to self-manage at home without the use of antiviral treatment. As a result, an important assumption for that antiviral plan was that treatment with antivirals be initiated for those at higher risk of complications if influenza was strongly suspected based on clinical presentation.

Therefore, treatment with antivirals was only considered for patients with moderate to severe symptoms, and for those with mild illness who, due to underlying health conditions, were thought to be at high risk for complications. Such health conditions or risks included pregnant women, cardiac or pulmonary disorders (including bronchopulmonary dysplasia, COPD, cystic fibrosis and asthma), diabetes mellitus, other metabolic diseases,

cancer, immunodeficiency or immunosuppression, renal disease, anemia or hemoglobinopathies and conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration.

However, because specific information about the characteristics and epidemiology of a future novel influenza strain is unknown, our assumptions and response need to take into consideration that the scenario could be more severe than what we experienced with H1N1 (2009). Therefore a more general approach that emphasizes early treatment for all cases of suspected pandemic influenza is recommended until the severity and epidemiology of the disease are well known.

Antivirals are not recommended for pre- or post-exposure prophylaxis except in specified outbreak situations.

BC is pursuing a philosophy of timely access to treatment of pandemic influenza. This means that those who fit criteria will benefit most if ill and treated within 48 hours. Such a goal can only be attained if there is equitable access to specific health care (in large part in terms of antiviral medication) across the province. As such, a provincial approach to the distribution of and access to antivirals is essential.

The final assumption is that of the two antivirals stockpiled for use in a pandemic, Oseltamivir (Tamiflu®) would be used widely and Zanamivir (Relenza®) would be kept in reserve in case of resistance.

4. PANDEMIC ALERT PERIOD MEASURES

4.1 Pandemic Phases 4 and 5

Pandemic phases, as per the World Health Organization definition, convey only a general measure of worldwide spread but not of severity of illness at the individual or regional levels.

Despite a growing number of influenza cases, Roche (Oseltamivir—Tamiflu®) and GSK (Zanamivir—Relenza®) are expected to be able to supply pharmacies throughout the province using their usual distribution channels throughout phases 4 and 5, and possibly even in early phase 6. In the event that a given community temporarily runs out of commercial supply, the provincial stockpile may be used as an interim measure until a commercial supply

resumes or stockpiles are officially released. Permission from pharmaceutical companies to supply local pharmacies from the provincial stockpile in such a manner will be granted. As initial hospitalized cases are expected to be few, hospitals are requested to use their current commercial supplies as per usual practice in phases 4 and 5.

In preparation for more widespread needs, all pharmacies are requested in phase 5 to identify their preferred warehouse for eventually placing orders of stockpile antivirals. Stockpiles will subsequently be partially redeployed between two warehouses.

4.2 Pandemic Phase 6

In anticipation of an eventual rapid rise in numbers in phase 6, a small proportion of the provincial antiviral medication stockpile (5 to 10 per cent) will be forward positioned to all hospitals in B.C. and community pharmacies. Some small communities, particularly First

Nations communities, are very isolated and must be given special consideration as many do not have any pharmacy at all. Forward placement to those communities will also take place.

Table 1: Pandemic Alert Period Measures

1.	Pre-position small portion of stockpile in acute care settings.
2.	Pre-position small amounts in most isolated communities.
3.	Monitor for local shortages of commercial supplies.
4.	Identify preferred warehouses based on their pharmacy networks.
5.	Position stockpile in appropriate warehouses.

5. TRIGGERS

5.1 Pandemic Phases 4 and 5

In pandemic phases 4 and 5, there are two triggers for moving a small amount of the centralized provincial stockpile peripherally.

The first trigger—seeing a novel influenza virus spread across the continent and begin taking hold in the province—should lead to the forward positioning of a small proportion of the stockpile to acute care sites across the province. This trigger is likely to occur in phase 4 and/or phase 5.

A second trigger for further decentralizing a small proportion of the stockpile, also in phase 4 and/or phase 5 (and possibly early phase 6), is for community-wide shortage of commercial supply. In this instance, warehouses will be authorized to distribute to select community-based pharmacies some of the stockpile on a temporary basis even if it has not yet been widely made available. This is intended as a temporary measure until commercial supply is replenished. Reporting back to BCCDC of such interim measures is nonetheless expected.

5.2 Pandemic Phase 6

The third trigger will be when a worldwide declaration of an influenza pandemic (phase 6) is declared and accompanied by national/provincial recognition of a significant increase in incidence or severity within our borders, or in bordering states. Such a situation would warrant final preparations for further shipments to hospitals and/or community pharmacies. A first step in this regard is to ensure the stockpile in the two

warehouses is in accordance to previously designated preferences that were indicated by pharmacies. All warehouses are then placed on standby for further distribution.

Community pharmacies will be asked to indicate their preferred distributor (from among two chosen warehouses). The purpose of this is to remove barriers to ordering antiviral

medications as much as possible (from a community pharmacy perspective).

A fourth trigger to watch for will be when there is significant activity of influenza in the local region. At that time, the B.C. Provincial Health Officer will allow a pre-determined amount of the stockpile (based on per capita) to be released to community and hospital pharmacies. This movement will allow community and hospital pharmacies to be free to reorder antiviral medications from the provincial stockpile. Community pharmacies are only allowed to order from the one warehouse they have previously indicated as their preferred distributor and will have restrictions on the amounts they can order, pending review of evolving epidemiology.

Warehouses report daily what orders have been placed. Monitoring of pharmacy orders is likely to be conducted along with monitoring of PharmaNet data to watch for unusual ordering patterns. Hospital pharmacies will reorder from BCCDC Pharmacy, as will remote First Nations communities.

If the epidemiology of the influenza pandemic changes such that a high proportion of people are requiring hospitalization or intensive care, further recommendations about expanded antiviral use may be warranted, and controls may be put in place regarding community pharmacy orders, in order to preserve a certain amount for hospital use. The situation will be monitored.

Table 2

Triggers	Responses
1. Novel influenza taking hold locally.	Forward position 0.5% of stockpile to acute care sites.
2. Isolated local community shortage of antiviral meds.	Acute care pharmacies to “loan” from their stockpile.
3. Increasing local spread or severity.	Position stockpile in two warehouses.
4. Shortage of commercial supplies in > 30% of community pharmacies in given health authority or HDSA.	Warehouses can ship to affected HDSA, authorized to take orders from pharmacies in that HDSA.
5. Changing epidemiology, more hospitalizations, more intensive care requirements.	Consider some controls on community pharmacy orders to “preserve” certain amount for hospitals.

6. PREFERRED DISTRIBUTION MECHANISM

6.1 Antiviral Medications

Ongoing dialogue with between the Ministry of Health (PharmaCare) and antiviral medication manufacturers is essential to ensure continued

commercial supply to community pharmacies as long as possible. This is unlikely to be possible beyond early phase 6 at the latest.

6.2 Provincial Stockpile

Calculations for the needed provincial stockpile assumed that 35 per cent of the population would be infected with a novel influenza strain, with half of those seeking medical attention.

Thus, antiviral medications for 17.5 per cent of the population were purchased. The current and planned provincial stockpile composition is shown in the table below.

Table 3: Provincial Stockpile Summary (Current And Planned)

	Adult (doses)	Pediatric (doses)	Adult (planned)	Pediatric (planned)
Tamiflu	7,148,140	443,470	1,118,340	480,000
Relenza	1,349,750	---		
Subtotals	8,497,890	443,170	1,118,340	480,000

6.3 Pharmacy Warehouses

For the next pandemic, there will be two warehouses serving the 1,000+ hospital and community pharmacies throughout the province.

The provincial stockpile is currently stored in these two warehouses.

6.4 Distribution Points

There will be three main distribution points for the antivirals: community pharmacies, hospital pharmacies and remote communities. Due to surveillance and monitoring requirements, it is deemed important that most of the antivirals be dispensed from a community pharmacy, as they have access to PharmaNet. Dispensing of antivirals for hospital inpatients and patients in the emergency department will not be recorded in PharmaNet, as “back-entering” of this data by BCCDC Pharmacy is prohibited by the College of Pharmacists of BC. Similarly, if alternative assessment sites and alternative care sites (i.e., “fever clinics” and “temporary flu hospitals”) are utilized and dispensing of antivirals occurs from these points, the data on usage will not be captured in PharmaNet.

Hospital Pharmacies

An initial forward positioning of the adult antiviral stockpile (0.5 per cent) will occur, followed by further distribution of the pediatric antivirals. As the need for more becomes evident based on usage (prescriptions filled), further courses can be ordered and shipped to hospital pharmacies directly from BCCDC. Hospitals will provide electronic or manual usage reports of antivirals to BCCDC prior to reordering fresh supplies.

As more antivirals are distributed to these and other distribution points, some mechanism is required to “reserve” a certain proportion of the overall stockpile for hospital use in more severe cases. With this understanding in mind, should supplies run low in the community, hospitals have relationships with community-based pharmacies so that temporarily at least one community pharmacy can be locally supplied; alternatively, pharmacies in such communities could request temporary supplies from BCCDC.

Community Pharmacies

Community pharmacies across the province form the basis for widespread antiviral access for British Columbians. During pandemic phase 6, ongoing shipment of antiviral medications to community pharmacies is through routine ordering by the pharmacies from the warehouses. The antivirals will be shipped in the midst of other non-antiviral medications.

A daily report on the dispensing of antivirals by each community pharmacy will be forwarded to BCCDC such that usage at a population level may be evaluated.

“Fever Clinics”

Some health authorities are planning to establish “fever clinics”, depending on the severity of the epidemic. These would function as a satellite of a hospital pharmacy. Thus, medications would be supplied to these clinics through their associated hospitals and pharmacy departments. The hospital pharmacies, in turn, would receive their antivirals from BCCDC.

Long-term Care Facilities

Long term care facilities would access their supplies to antiviral medications in the usual manner. Thus, facilities associated with hospitals would receive their stock for early treatment and prophylaxis of contacts through the hospital pharmacy department, while private facilities would receive their supply from their associated community pharmacy.

Remote First Nations and Non-First Nations Communities

Communities not currently served by the warehouse(s) need to be served in an alternate timely manner. Special consideration is therefore needed for remote local health areas and isolated communities. In a first round of identifying such isolated communities, 30 First Nations communities were identified in collaboration with First Nations and Inuit Health and provisions have been made to forward position a percentage of the provincial stockpile to those communities.

For remote non-First Nations communities, dispensing of antivirals will occur by nurses. Antivirals will be picked up by these nurses from health clinics present in these communities. These clinics are supplied with antivirals by a hospital pharmacy department, which in turn receives stock from BCCDC.

7. STEPS TO ENSURE CONSTANT SUPPLY

For acute care settings initial forward placement will take place. Hospital pharmacies have established further links with BCCDC. Reordering of hospital supplies will occur through the Pharmacy Department at BCCDC.

For community pharmacies there will be an initial percentage of antivirals that are forward positioned, then reordering will take place through their primary warehouse supplier. Using only one warehouse per pharmacy will

prevent double ordering and facilitate ongoing surveillance of antiviral usage throughout the province.

Forward placement of antivirals will also occur for remote First Nations communities; reordering of supplies will then occur through the Pharmacy Department at BCCDC. Since these communities are remote, a week lead time must be given to BCCDC for shipment.

8. OPERATIONAL ISSUES

8.1 Protocols

Hospitals will report antiviral use for their inpatients and some will also report on any dispensing that occurs through emergency departments (this activity is to be minimized but

may need to occur from time to time). Similarly, use of antivirals in remote First Nations communities will be reported to BCCDC Pharmacy.

When local prescribing or dispensing patterns suggest a pharmacy in an affected community has less than a two-day supply of antivirals on hand, it should place an order from the warehouse it identified as its preferred supplier. Parameters of such orders need to be determined. Pharmacies are allowed to order 50 treatment courses of the adult 75mg, 10 treatment courses of the 30mg and 5 treatment courses of the 45mg dose forms on a weekly basis. Reordering that takes place within the timeframe or above the limits need to be authorized by BCCDC Pharmacy, who in turn check the PharmaNet utilization reports.

Warehouses should report daily to BCCDC to whom and how much they have shipped.

8.2 Security Issues

Security is addressed in large part through 1) cutting down steps between warehouse and pharmacy (no intermediary); 2) mixing antivirals

Pharmacies are already mapped by GIS. A time series created from such a daily accounting could help visualize where the provincial stockpile is being deployed over time; such an approach was discussed with a GIS specialist. This is being done on the Pharmacare utilization report and not on the shipments out.

PharmaNet data is supplied daily to BCCDC. If a particular pharmacy is dispensing disproportionately more than neighbouring pharmacies, some queries might be deemed appropriate. Even if antivirals are changed from prescription-based to non-prescription based, such a surveillance mechanism would remain in force.

with routine shipments; and 3) shipping more frequent but smaller allotments.

9. DEPENDENCIES

This plan has taken the antiviral from manufacturer to warehouse to pharmacy (or pharmacy proxy) and is dependent on

dispensing and treatment plans. These plans must be seen as a unit.