

Part D. MEDICAL COUNTERMEASURES: ANTIVIRAL PREPAREDNESS AND RESPONSE

NC Department of Health and Human Services, Division of Public Health

The antiviral armamentarium for chemoprophylaxis and treatment of influenza includes two main classes of antiviral agents, the adamantanes (amantadine and rimantadine) and the neuraminidase inhibitors (zanamivir and oseltamivir). The Centers for Disease Control and Prevention (CDC) recommends against the use of adamantanes for treatment or prophylaxis of seasonal influenza because of the potential development of antiviral resistance.

A. Background

The adamantanes are only active against influenza A, while the neuraminidase inhibitors have activity against both influenza A and B. Recent evidence indicates that amantadine has no, or limited, activity against the H5N1 avian influenza A strains. While the adamantanes are much less expensive and in greater supply compared to the neuraminidase inhibitors, current evidence suggests that the neuraminidase inhibitor oseltamivir is recommended to stockpile for chemoprophylaxis and treatment during the next influenza pandemic. However, both adamantanes and neuraminidase inhibitors may play a role in chemoprophylaxis and treatment depending on the following factors:

- Susceptibility of the pandemic influenza strain to currently available antiviral medications
- Prophylactic and therapeutic efficacy of the respective antiviral agents against the strain
- Number of doses of the respective antiviral agents available via the public and private sectors
- Size of the target populations recommended to receive chemoprophylaxis or treatment
- Cost and reimbursement

The main goals of influenza chemoprophylaxis and treatment are to reduce morbidity, mortality, and the infection rate associated with the pandemic strain. Reduction of the infection rate via chemoprophylaxis is the last preventive option and should follow implementation of other recommended or indicated preventive efforts (e.g., restrictions on travel and communal events, isolation of ill persons, quarantine of exposed persons, implementation of infection control measures such as the use of masks and diligent hand washing, and vaccination).

B. Assumptions Regarding Antiviral Distribution

1. In the event of insufficient supplies, antiviral agents will be prioritized for treatment.
2. Antiviral agents will be distributed in limited supply through the activation of the CDC Strategic National Stockpile (SNS).

C. Investigation Interval

(Characterized by surveillance for novel virus and human-to-human spread of previous animal influenza)

1. The NC Division of Public Health (NC DPH) will provide technical assistance to local health departments for planning and policy development to include:
 - a. Sharing CDC guidelines and recommendations for chemoprophylaxis and treatment, including criteria for identification and prioritization of specific priority groups
 - b. Assistance in the calculation and review of county-specific priority groups considered to be high-risk
 - c. Assistance in the calculation and review of county-specific priority groups necessary to ensure maintenance of healthcare capacity and quality as well as the maintenance of public health and safety
 - d. Assistance in the calculation and review of county-specific antiviral doses required for chemoprophylaxis or treatment of identified priority groups

- e. Education and training on the request, receipt, handling, transport, storage, security, and tracking of antiviral medications
 - f. Review and assessment of county plans for request, receipt, handling, transport, storage, security, and tracking of antiviral medications
 - g. Review and assessment of county delivery/distribution plans for antivirals to hospitals, private healthcare providers, clinics, and other points of care
 - h. Review and assessment of distribution plans for antivirals to tribal authorities and bordering counties and states (mutual aid agreements)
2. Review the current NC DHHS *Strategic National Stockpile Distribution Plan* and update it as necessary for receipt and distribution of influenza antivirals.
 3. Develop a distribution plan that delivers antivirals to counties based on CDC guidelines and recommendations for antiviral chemoprophylaxis and treatment, number of doses of antivirals allocated or available to NC, and county-specific priority group calculations.
 4. Review, and modify as necessary, existing legal framework for distributing/dispensing antivirals as determined necessary by the state health director or other designee. This framework should include provisions for the use of standing orders (by the local health director or other designee) for chemoprophylaxis and/or treatment with FDA-approved antivirals, as well as antivirals available via Emergency Use Authorization of other compassionate care programs.
 5. Consider the indications and feasibility of:
 - Procurement and maintenance (including availability of antivirals, shelf life/expiration date issues) of local or state stockpiles of antiviral drugs
 - Establishment of institutional stockpiles in healthcare facilities
 - Emergency purchase from private sector distributors

D. Recognition Interval

(Characterized by the identification of clusters of novel influenza cases and the confirmation of sustained and efficient human-to-human transmission)

1. The DPH will maintain regular electronic and/or phone contact with CDC, WHO, and other organizations as necessary for updates on the epidemiology of emerging or re-emerging strains as well as antiviral efficacy against the strains.
2. Obtain from CDC the most current recommendations on antiviral dosage and duration of therapy for treatment and chemoprophylaxis. Provide this guidance to hospitals, healthcare providers, local health departments, and other key stakeholders.
3. Enhance education and training at the state and local levels with hospitals and healthcare providers so that roles and responsibilities are well understood.
4. Implement communications plan to assure that the medical community and public are knowledgeable on the following topics:
 - a. The role of antivirals in responding to pandemic influenza
 - b. The need to prioritize the use of limited supplies of antivirals for treatment and chemoprophylaxis
 - c. The rationale for identified priority groups
 - d. The importance of appropriate use to minimize the development of drug resistance.
5. Refine and revise antiviral distribution plan based on stockpiles and on updates to priority group recommendations.
6. Purchase antivirals from US DHHS, if available, for state stockpile.

E. Initiation and Acceleration Intervals

(The initiation interval is characterized by a lab-confirmed case of defined novel influenza A in the county, region, or state. The acceleration interval is characterized by an increasing number of cases of pandemic influenza.)

1. DPH will maintain regular electronic and/or phone contact with CDC, WHO, and other organizations as necessary for updates on the epidemiology of the pandemic strain, antiviral availability and efficacy against the strain, and vaccine development timetable.

2. Review the county-specific priority group data, amending the list if analysis of early epidemiologic and morbidity and mortality data suggest other high-risk groups.
3. Coordinate with the Immunization Branch to assess preparedness and response capacity for vaccination of priority groups and the general public once vaccine is available.
4. Determine the available supplies of indicated antiviral medication(s) in the public (SNS, state, and any local stockpiles) and private sectors.
5. Implement antiviral distribution plan to address preparedness at the state and local levels for receipt, transport, storage, security, tracking, and delivery/distribution of antivirals.
6. Implement pandemic influenza antiviral chemoprophylaxis and treatment plan based on information obtained from 1 through 5 above.
7. Develop and distribute educational materials to appropriate state agencies, local health departments, hospitals, private healthcare providers, and the public.

F. Acceleration and Peak Intervals

(Characterized by sustained and extensive transmission of the influenza virus in the community)

1. DPH will maintain daily electronic and/or phone contact with CDC, WHO, and other organizations as necessary for updates on the epidemiology of the pandemic strain, antiviral availability and efficacy against the strain, and vaccine development timetable.
2. Assure delivery/distribution of antivirals to counties based on the most current federal (HHS/CDC) and state guidelines.
3. Assist local health departments in the redistribution of antiviral medications as needed and available.
4. Review available epidemiologic and clinical data on the efficacy of chemoprophylaxis and treatment. Increase surveillance for resistance to antivirals associated with treatment or chemoprophylaxis. Encourage hospitals and healthcare providers to obtain specimens from patients who develop severe disease while receiving treatment or chemoprophylaxis.
5. Encourage healthcare providers to report adverse reactions to medications via FDA's MedWatch.
6. Review available safety data from CDC and FDA (i.e., type and frequency of any reported adverse reactions and epidemiologic evidence for causal association) and communicate relevant information to hospitals, healthcare providers, local health departments and the public.
7. Reassess antiviral plan accordingly based on efficacy and safety issues in 4 and 5 above.

G. Deceleration Interval

(Characterized by declining rates of pandemic influenza cases)

1. If available and epidemiologic and clinical data indicate antiviral medications were efficacious in reducing infection and/or reducing morbidity and mortality, re-order antiviral medications as available utilizing experience gained from the initial wave.
2. Redistribute antivirals according to plan and experience gained from the first wave.

H. Resolution Interval

(Characterized by influenza cases that are sporadic and decreasing in occurrence, nearing pre-pandemic levels)

1. Determine total amounts of antivirals ordered, shipped, administered, and wasted (if possible).
2. Determine type and frequency of any reported adverse reactions, and review epidemiologic evidence for causal association.
3. Review epidemiology of the pandemic and data on the efficacy of antiviral chemoprophylaxis and treatment.
4. Update antiviral plan based on 2 and 3 above.
5. Recover, if possible, unused antivirals, or produce guidelines on future use or disposal of expired drugs.