



INTERIM GUIDELINES NO. 1
CLINICAL MANAGEMENT and the USE OF ANTI-VIRALS FOR INFLUENZA A (H1N1)
VIRUS INFECTION

The outbreak of Influenza A (H1N1) is evolving rapidly, and countries from different regions of the globe have been affected. In order to understand the spectrum of severity of the disease caused by Influenza A (H1N1) virus infection, standard clinical case descriptions are provided, which includes the mild form of influenza like illness (ILI) and the more severe forms.

Based on the World Health Organizations (WHO) guidance for the surveillance of human infections of Influenza A (H1N1), the following case definitions are described for the purpose of reporting probable and confirmed cases of Influenza A (H1N1) and for differentiating the application of clinical management and anti-viral use.

I. CASE DEFINITIONS FOR INFECTIONS WITH INFLUENZA A (H1N1):

Clinical Case Description:

Acute febrile respiratory illness (fever >38°C) is the common feature in all probable cases. The spectrum of disease ranges from influenza-like illness to pneumonia.

1. A **Suspected Case of Influenza A (H1N1)** virus infection is defined as an individual with influenza like illness who has a close contact with an ill confirmed case of Influenza A (H1N1) virus infection; **OR**

A person with influenza like illness with a recent history of contact with an animal with confirmed or suspected Influenza A (H1N1) virus infection; **OR**

A person with influenza like illness who has traveled to an area where there are confirmed cases of Influenza A (H1N1) within 7 days of onset of illness.

2. A **Probable Case of Influenza A (H1N1)** virus infections is defined as an individual with an influenza test that is positive for Influenza A, but is non-subtypable by reagents used to detect seasonal influenza virus infection; **OR**

An individual with a clinically compatible illness or who died of an unexplained acute respiratory illness who is considered to be epidemiologically linked to a probable or confirmed case.

3. A **Confirmed Case of Influenza A (H1N1)** virus infection is defined as an individual with laboratory confirmed Influenza A (H1N1) virus infection by one or more of the following tests:

- Real-time RT-PCR
- Viral culture

- Four-fold rise in influenza A (H1N1) virus specific neutralizing antibodies

II. USE OF ANTI-VIRAL AGENTS:

Under pandemic conditions, antiviral agents are highly important on the first wave of infection, when vaccines are not yet available. In the absence of vaccines, anti-virals are the only medical intervention for providing both protection against disease and therapeutic benefit in persons who are ill.

During a pandemic, antiviral agents may be not enough to meet the demands of many countries. When the attack rate is so high that the antiviral agents on national stockpile, the option is to provide the antiviral agents to areas where the first cases of pandemic influenza are seen.

III. RECOMMENDATION FOR PROPHYLAXIS:

A. Priority groups to receive antiviral agents for prophylaxis are those who have potential contact with droplets from a patient without having an adequate PPE will be the following:

- Health Workers
- First responders
- Workers providing essential services

B. Other people like household contacts of probable or confirmed case

IV. GUIDELINES ON CLINICAL MANAGEMENT OF INFLUENZA A (H1N1)

- Take respiratory and blood specimens for laboratory testing for influenza and other infections as clinically indicated.
 - Treat with a neuraminidase inhibitor such as oseltamivir (75 mg orally, twice daily for 5 days) as early in the clinical course as possible. The benefits of oseltamivir, the optimal dosage and schedule for later-stage intervention in severe influenza illness are unknown.
 - If clinically indicated, hospitalize patients under appropriate infection control precautions as described in a separate section.
 - Provide supportive care. Monitor oxygen saturation and treat desaturation with supplemental oxygen as required.
 - As nebulizers and high-air-flow oxygen masks have been potentially implicated in the nosocomial spread of severe acute respiratory syndrome, use these measures only if clinically justified and apply them under strict infection control, including airborne transmission precautions.
 - Take respiratory and blood specimens serially to check for possible bacterial infection.
 - Consider intravenous antibiotic therapy to control secondary bacterial infections as required.
- a. Antibiotics are not indicated in the treatment of uncomplicated influenza, although its use may be necessary for the treatment of associated bacterial respiratory complications.

- b. If the patient's condition worsens or is not getting better within 72 hours or shows signs of secondary lung infection, an antibiotic may be prescribed.
- c. Antibiotics may be prescribed earlier for the elderly or other patients identified to be at risk of complications.
- d. When treating a secondary lung infection, the risk of *Staphylococcus aureus* infection should be considered, and oxacillin may be indicated alongside with other antibiotics.
 - o Decision on the choice of antibiotics should be based on prevalent bacterial strains and resistance patterns.

V. ANTI-VIRAL:

A. Use of antiviral Agents for chemoprophylaxis and Treatment:

1. During Seasonal Epidemics

Research has shown that antiviral drugs are effective for both the prevention (chemoprophylaxis) and early treatment of influenza, if administered within 48 hours following the onset of illness. During seasonal epidemics, anti-virals are adjuncts to vaccination as a strategy for reducing the medical and economic burden of influenza. Their use can reduce the duration of uncomplicated disease and the likelihood of complications requiring antimicrobial treatment and possibly hospitalization. Though studies are not adequate, antiviral agents are seen to reduce serious complications and mortality in groups at highest risk, including the elderly and persons with underlying disease.

2. During the pre-pandemic period when a new virus has emerged

Antiviral in the outbreak foci could reduce opportunities for adaptive mutation and reassortment and thus possibly prevent the virus from establishing efficient human-to-human transmission.

3. When there is no evidence of human to human transmission

At the phase when no human-to-human transmission has been documented, antivirals would be used for the prophylaxis of persons at high risk of exposure, the protection of teams investigating the outbreak, and the early treatment of symptomatic persons. Prophylaxis of groups at high risk should be combined with administration of vaccine protective against circulating strains of influenza virus to reduce the risk of re-assortment

4. When there is limited human to human transmission

At the phase where there is limited human-to-human transmission has been confirmed, the use of anti-virals will be used on clusters of cases with the objective of reducing further human cases and thus preventing or at least delaying further spread. Targeted and aggressive use of anti-virals might also limit opportunities for the virus to improve its transmissibility through adaptive mutation during continuing chains of transmission. Anti-virals would be used for the early treatment of suspected cases, prophylaxis of contacts, including health care workers, and around a limited number of small, well-defined clusters.

5. During a pandemic

Under pandemic conditions, antiviral agents are highly important on the first wave of infection when vaccines are not yet available. In the absence of vaccines, antivirals are the only medical intervention for providing both protection against disease and therapeutic benefit in persons who are ill. During a pandemic, antiviral agents may be not enough to demands of many countries. Priority groups to receive antiviral agents will be health workers and first responders and workers providing essential services for prophylaxis. For treatment, priority will be the patients considered at high risk of severe disease. For this purpose, clinical predictors of serious outcomes would be needed to better target the use of limited supplies.

6. Use during pregnancy

Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these drugs should be used during pregnancy only if the potential benefit outweighs the potential risk to the embryo or fetus.

B. ANTI-VIRAL TREATMENT

Anti viral treatment should be given to:

1. Confirmed case
2. Probable case
3. Suspected case at high risk of severe disease

C. Timing and Duration:

If antiviral therapy is contemplated, it should be given within the first 48 hours of illness to reduce the duration of uncomplicated influenza. High risk or severely ill patients seen after 48 hours may still be given an antiviral agent. Treatment should be continues for 5 days or for 24 to 48 hours after acute symptoms resolve in immunocompetent patients. Antiviral treatment may be prolonged for immunocompromised patients.

Recommended Daily Dosage of Antiviral Agents for Chemoprophylaxis and Treatment:

Antiviral Agent	Formulation	Approved Ages & Dosage	
		Treatment	Prophylaxis
Oseltamivir	75 mg / capsule	13 year-old & older: 75 mg BID x 5 days	1 capsule once daily x 10 days
	12 mg/ml solution	Children 1 – 12 years old: 15 kg or less: 30 mg BID x 5 days	
		16 – 23 kg: 45 mg BID x 5 days	
		24 – 40 kg: 60 mg BID x 5 days	
		>40 kg: 75 mg BID x 5 days	
Zanamivir	5 mg powder blisters (Inhaler)	>7 years-old: 10 mg BID x 5 days	Not approved for prophylaxis

Side Effects and Adverse Reactions of Antiviral Agents:

1. Oseltamivir

Nausea and vomiting more frequent among adults receiving oseltamivir for treatment of prophylaxis, less severe if taken with food.

2. Zanamivir

Bronchospasm, respiratory function deterioration after inhalation for patients with underlying airway disease. Hypersensitivity reaction, oropharyngeal or facial edema, diarrhea, nausea, sinusitis, bronchitis, cough, dizziness, ear, nose and throat infections.

For treatment, priority will be the patients considered at high risk of severe disease. (Clinical predictors of serious outcomes—to be announced as soon as determined by international experts from initial cases—would be needed to better target the use of limited supplies.)

VI. DISCHARGE GUIDELINES

Until further notice is available, WHO recommends that infection control precautions for adult patients remain in place for 7 days after resolution of fever. Previous human influenza studies have indicated that children younger than 12 years can shed virus for 21 days after onset of illness. Therefore, infection control measures for children should ideally remain in place for this period. Where this is not feasible (because of lack of local resources), the family should be educated on personal hygiene and infection control measures (e.g. hand-washing and use of a paper or surgical mask by a child who is still coughing). Children should not attend school during this period.

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