

**CLINICAL MANAGEMENT OF PANDEMIC
(H1N1) 2009 VIRUS INFECTION**

(For the Eastern Mediterranean Region Countries)

Interim Guidance from Expert Consultation

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Medical experts working in the field of chest disease, epidemiology, paediatric infectious disease, internal medicine, intensive care, public health, pulmonary medicine, microbiology and virology participated in this expert consultation meeting in the capacity of their own professional standings and repute.

This interim guidance on clinical management of pandemic (H1N1) 2009 virus infection has been reviewed by these experts and updated following the recommendations of the consultation meeting.

The list of experts who contributed to developing this interim guidance is on the annex.

1. Introduction and purpose of the guideline

The pandemic influenza situation in the Eastern Mediterranean Region of WHO warrants the need for the health authorities in the Region and in particular, the health care facilities adopt and follow standardized treatment protocol for clinical management of patients infected with pandemic (H1N1) 2009 influenza virus. Treatment of suspected or probable cases of human infection with pandemic (H1N1) 2009 virus constitutes a challenge due to the existing knowledge gaps on several aspects of the clinical manifestations of the disease. At the same time, however, medical community's understanding of the disease is evolving leading to improved practices for clinical management of pandemic (H1N1) 2009 virus infection. Clinical evidences are beginning to emerge that such best treatment practices, if applied timely and correctly, can lead to reduced mortality from the current pandemic influenza virus.

In view of the above, this interim guidance has been developed by WHO-EMRO in order to provide recommendations to the countries of WHO Eastern Mediterranean Region on clinical management of human cases infected with pandemic (H1N1) 2009 influenza virus.

It is expected that this interim guidance will help the Member States of WHO Eastern Mediterranean Region to standardize their national clinical management protocols for pandemic (H1N1) 2009 virus infection. It is intended for use in the health care settings only- be it primary, secondary or tertiary level health care center. The algorithm (treatment flow chart) proposed in this interim guidance can be used as a decision tree by the clinicians in exercising their clinical judgement for treatments of patients with either suspected, probable or confirmed pandemic (H1N1) influenza virus infection.

This interim guidance will be revised and updated as new information on the clinical manifestations of the disease as well as epidemiological and virological characteristics of virus become available, and as the current evidence of the clinical management effectiveness with the cases increases.

2. Case Definitions

This interim guidance on clinical management of pandemic (H1N1)2009 virus infection will use the following six case definitions of influenza for the purpose of clinical diagnosis and initial treatment decision. These case definitions are listed below:

2.1 Suspected case of pandemic (H1N1) 2009

A suspected case of pandemic (H1N1) 2009 virus infection is defined as an individual with acute respiratory illness and fever (reported or documented fever), and one of the followings; cough, sore throat, shortness of breath, difficulty in breathing or chest pains with onset:

- Within 7 days of close contact with a person who is probable or confirmed case of pandemic (H1N1) 2009 virus infection, **OR**
- Within 7 days of travel to a country/community where there has been one or more confirmed cases of pandemic (H1N1) 2009 virus infection; **OR**
- Resides in a community where there is one or more confirmed cases of pandemic (H1N1) 2009 virus infection.

2.2 Probable case of pandemic (H1N1) 2009

A probable case of pandemic (H1N1) 2009 virus infection is defined as an individual with an influenza-like illness who is positive for influenza A that is unsubtypeable by real-time PCR

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.

2.3 Confirmed Case of pandemic (H1N1) 2009

A confirmed case of pandemic (H1N1) 2009 virus infection is defined as an individual with an influenza-like illness with laboratory confirmed pandemic (H1N1) 2009 virus infection by one or more of the following test:

- Real-time RT-PCR
- Viral culture

2.4 Influenza-like illness (ILI)

A person with sudden onset of fever of $>38^{\circ}\text{C}$ and at-least one of the following two respiratory symptoms in the absence of other known causes:

- dry cough
- sore throat

2.5 Severe acute respiratory illness (SARI)

A person meeting the case definition of influenza-like illness (sudden onset of fever $> 38^{\circ}\text{C}$ with at-least one of the following two respiratory symptoms- dry cough, sore throat in the absence of other diagnosis)

AND shortness of breath **OR** difficulty in breathing requiring hospital admission

2.6 Acute Respiratory Infection (ARI)

For the purposes of this interim guidance, Acute Respiratory Infection (ARI) is defined as an acute respiratory tract illness that is caused by an infectious agent transmitted from person to person. The onset of symptoms is typically rapid, over a period of hours to several days.

Symptoms include fever, cough, and often sore throat, coryza, shortness of breath, wheezing, or difficulty breathing.

3. Clinical Presentation

Presentation of influenza caused by pandemic (H1N1) 2009 virus infection can vary from asymptomatic infection through to serious fatal illness that may include exacerbation of other underlying conditions and severe viral pneumonia with multi-organ failure. Since a clinical diagnosis of influenza caused by the pandemic (H1N1) 2009 virus infection early on is critical to guide treatment decisions and follow the subsequent case management pathways, three categories of clinical presentations with pandemic (H1N1) 2009 virus infection have been used in this interim guidance. These are- (i) mild or non-severe illness; (ii) signs and symptoms of progression to severe illness; and (iii) severe illness. These clinical presentations are listed below.

3.1 Mild illness (Non severe)

Patients with mild Influenza-like illness may present with some or all of the following symptoms:

- Fever ($\geq 38^{\circ}\text{C}$), dry cough, sore throat, rhinorrhea, headache, muscle pain, malaise, **but no shortness of breath or dyspnoea.**
- Gastrointestinal illness, such as diarrhoea and/or vomiting, especially in children, but without any evidence of dehydration.

The general condition of these patients will be good without any signs of hypotension or mental confusion.

3.2 Signs and symptoms of progression to severe illness

Patients presenting initially with mild influenza-like illness may rapidly progress to more severe illness in the course of the disease. The followings are some of the clinical signs and symptoms indicating rapid progression of a patient to severe illness, which would necessitate an urgent review of patient's clinical management:

- Symptoms and signs suggesting oxygen impairment or cardiopulmonary insufficiency:
 - Shortness of breath (with activity or at rest), difficulty in breathing, turning blue, bloody or coloured sputum, chest pain, low blood pressure;
 - Fast or laboured breathing in children less than 5 years of age;
 - Hypoxia as indicated by pulse oximetry, if available (Oxygen saturation $\leq 92\%$)
- Symptoms and signs suggesting CNS complications:

- Altered mental status, unconscious, drowsiness, or difficult to awaken; recurring or persistent convulsions (seizures), confusion, severe weakness or paralysis.

- Evidence of sustained virus replication or invasive secondary bacterial infection:
 - Based on laboratory testing or clinical signs (e.g. persistent or recurrent high fever and other symptoms beyond three days even when under treatment with analgesics or antipyretics).

- Severe dehydration:
 - Decreased activity, dizziness, decreased urine output, lethargy.

3.3 Severe illness

Patients may also present with severe influenza- like illnesses. Patients showing any of the following clinical signs and symptoms would be considered as suffering from severe illness due to influenza:

- Severe respiratory distress:
 - Severe breathlessness, e.g. unable to complete sentences in one breath. Use of accessory muscles, supra-clavicular recession, tracheal tug or feeling of suffocation (***For adult patients***)
 - Lower chest in-drawing, sternal recession or noisy breathing when calm (***For paediatric patients***)

- Increased respiratory rate measured over at least 30 seconds:
 - Over 30 breaths per minute (***For adult patients***)
 - ≥ 50 breaths per minute if under 1 year or ≥ 40 breaths per minute if ≥ 1 year (***For paediatric patients***)

- Oxygen saturation $\leq 92\%$ on pulse oximetry, breathing air or on oxygen:
 - Absence of cyanosis is a poor discriminator for severe illness.

- Respiratory exhaustion
 - New abnormal breathing pattern, e.g. alternating fast and slow rate or long pauses between breaths (***For adult patients***)
 - Apnoea defined as a ≥ 20 second pause in breathing (***For paediatric patients***)

- Evidence of severe clinical dehydration or clinical shock

- Systolic blood pressure <90mmHg and/or diastolic blood pressure <60mmHg. Sternal capillary refill time >2 seconds, reduced skin turgor (**For adult patients**)
- Sternal capillary refill time >2 seconds, reduced skin turgor, sunken eyes or fontanelle (**For paediatric patients**)

- Altered conscious level
 - New confusion, striking agitation or seizures (**For adult patients**)
 - Strikingly agitated or irritable, seizures, or floppy infant (**For paediatric patients**)

- Causing other clinical concern to the clinician or to the specialist doctor
 - e.g. a rapidly progressive or an unusually prolonged illness.

3.4 Groups at high risk for complications

In order to guide treatment decisions, this interim guidance on clinical management considers the following categories of patients, listed below, as “*Groups at high risk for complications*” due to influenza leading to severe illness or fatal clinical outcome:

- Pregnant women
- Adults 65 years of age and older;
- Children younger than 5 years old (In particular less than 2 years);
- Persons with the following underlying conditions at any age:
 - Chronic Broncho-pulmonary disease (Including asthma),
 - Chronic cardiovascular disease (except hypertension)
 - Chronic neurologic disorder (Cerebral palsy, stroke, multiple sclerosis, muscular dystrophy, etc)
 - Immune suppressed patients
 - Haematological disorder
 - Chronic liver or renal failure (GFR <30 ml/min)
 - Metabolic disorder (specially Diabetes mellitus),
 - Morbid obesity
- Healthcare personnel in the hospital settings caring for patients infected with pandemic (H1N1) 2009 influenza virus;

3.5 Special considerations for pregnant women

Evidence from previous pandemics further supports the conclusion that pregnant women are at heightened risk of complications. While pregnant women are also at increased risk during epidemics of seasonal influenza, the risk takes on added importance in the current pandemic. In areas, therefore, where infection with the pandemic (H1N1) 2009 influenza virus is widespread, pregnant women and the clinicians, treating them, need to be alert of symptoms of influenza-like illness.

Pregnant women with pandemic (H1N1) 2009 virus infection would be expected to present with typical acute respiratory influenza-like illness (e.g., cough, sore throat, rhinorrhea) and fever. Other symptoms can include body aches, headache, fatigue, vomiting and diarrhoea. Many pregnant women will go on to have a typical course of mild illness. However, for some pregnant women, illness might progress rapidly, and might be complicated by secondary bacterial infections including pneumonia. Fetal distress associated with severe maternal illness can occur.

3.6 Special considerations for children

Aspirin or aspirin-containing products (e.g. bismuth subsalicylate – Pepto Bismol) should not be administered to any confirmed or suspected ill case of pandemic (H1N1) 2009 virus infection aged 18 years old and younger due to the risk of Reye syndrome. For relief of fever, other anti-pyretic medications such as acetaminophen or non-steroidal anti-inflammatory drugs are recommended.

Little is currently known about how this pandemic (H1N1) 2009 virus infection circulating in people may affect children. However, it is known that children, especially those younger than 5 years of age and those who have high risk medical conditions are at increased risk of influenza-related complications. Among children less than 5 years, the risk for severe complications from seasonal influenza is highest among children less than 2 years old.

Illnesses caused by influenza virus infection are difficult to distinguish from illnesses caused by other respiratory pathogens based on symptoms alone. Young children are less likely to have typical influenza symptoms (e.g., fever and cough) and infants may present to health centers with fever and lethargy, and may not have cough or other respiratory symptoms or signs.

The clinicians should, therefore, be aware that the risk of complications from seasonal influenza among children younger than 5 years old is highest among children younger than 2 years old.

4. Clinical Management

The clinical management of influenza-like illnesses caused by pandemic (H1N1) 2009 virus infection will follow a protocolized step in both the primary and secondary or tertiary level health care facilities.

4.1 At primary health care level

At primary health care level, the clinical management protocol for patients with suspected pandemic (H1N1) 2009 virus infection will start with screening and assessment of patients for suspected influenza like symptoms. The algorithm (flow chart) shown in annex-2 should be used to manage patients with suspected influenza caused by the pandemic (H1N1) 2009 virus infection at the primary health care level.

4.1.1 Assessment of patients

The clinical assessment should ideally begin in the triage area whenever a patient is suspected of ILI caused by pandemic (H1N1) 2009 virus infection. The triage area at the primary health care center should be pre-defined before hand. The assessment will lead to screening out of patients for treatment from those without having any visible signs or symptoms of ILI requiring no treatment. The assessment of patients should include, amongst others, the following clinical procedures as mentioned in box-1.

Box-1: Assessment of suspected cases with ILI at the primary health care level

- Assess general state;
- Assess hydration;
- Measure the body temperature (fever $\geq 38^{\circ} \text{C}$ / $> 100.4^{\circ} \text{F}$);
- Measure the respiratory rate;
- Observe sub-costal recession or nasal flaring;
- Observe the colour of the skin, nails and mucosa;
- Perform pulmonary auscultation to detect crepitations;

4.1.2 Home referral

Following assessment, those patients presenting mild influenza-like illness but without

- any visible signs of severe illness; and
- not in high-risk groups for complications

can be sent home for isolation and subsequently treated at home in accordance with the procedures mentioned in section 4.1.3.

4.1.3 Management of patients at home

Patients presenting only with mild illness but excluding those at-risk groups for complications and without any clinical signs of progression to severe illness can be treated at home. **These group of patients need not be treated with antiviral medication.**

The principles of treatment at home for these categories of patients include the followings:

- Using analgesics or antipyretics¹ (The drug of choice should be Acetaminophen). aspirin-containing products (e.g. bismuth subsalicylate – Pepto Bismol) should not be administered to patients aged 18 years old and younger due to the risk of Reye syndrome.
- Hydrating patients with abundant liquids in accordance with the need and patient's condition;
- Applying home isolation and advising rest till the patient becomes afebrile;
- Administering appropriate infection control measures at home (*Reference to special recommendations for home care -1, 2, 3 and 4*)
- Following-up clinical evolution of the patient by health care worker or by family members checking for signs and symptoms of progression to severe illness (Reference to Box-2 for worsening of clinical signs and symptoms indicating rapid progression of patients to severe illness)

Box-2: Worsening signs and symptoms signifying rapid progression to severe illness

- Shortness of breath (with activity or at rest), difficulty in breathing, turning blue, bloody or coloured sputum, chest pain, low blood pressure;
- Fast or laboured breathing in children less than 5 years of age;
- Altered mental status, unconscious, drowsiness, or difficult to awaken; recurring or persistent convulsions (seizures), confusion, severe weakness or paralysis.
- Persistent or recurrent high fever and other symptoms beyond three days).
- Decreased activity, dizziness, decreased urine output, lethargy.

(i) **Special recommendations for home-care-1: Placement of the sick person at home**

- Keeping the ill person from others in a separate room at home with proper ventilation until the symptoms subside or resolve. (*For example, a spare bedroom with its own bathroom, if that is possible.*)
- Keeping all the windows of the room open and ensure proper sunlight and good ventilation;
- Maintaining a distance of at-least 1.8m (6 feet) from the ill person, if protection barriers are unavailable at home;
- Having the sick person wear a facemask if they need to be in a common area of the house near other healthy persons.

¹ Acetylsalicylic acid should be avoided specially in children

- Unless necessary for medical care or other necessities, people who are sick with influenza-like-illness should stay home and keep away from others as much as possible, including avoiding travel, for at least 24 hours after resolution of fever².
- If the person with the influenza-like illness needs to go out (for example, for medical care), he/she should wear a facemask and cover the nose and mouth when coughing or sneezing;

(ii) Special recommendations for home-care-2: Protection of other persons at home

- The sick person should not have visitors other than the care-givers;
- Close contact (Less than about 6 feet) from the ill person should be avoided as much as possible;
- If possible, only one adult person should be identified at home to take care of the sick person. (*People in high-risk group for complication including the pregnant women should not be the designated caretaker, if possible*).
- People in high risk group for complications from influenza, should attempt to avoid close contact (within 6 feet) with household members who are sick with influenza. If close contact with a sick individual is unavoidable, wearing a facemask should be considered;
- The sick family members should not care for infants and other groups at high risk for complications of influenza.
- The sick persons should cover their coughs, and clean their hands with soap and water or an alcohol-based hand rub often, especially after coughing and/or sneezing;
- All persons in the household should clean their hands with soap and water or an alcohol-based hand rub frequently, including after every contact with the sick person or the person's room or bathroom and avoid sharing food;
- Paper towels should be used for drying hands and after hand washing or cloth towels should be dedicated to each person in the household.
- If possible, consideration should be given to maintaining good ventilation in shared household areas (e.g., keeping windows open in restrooms, kitchen, bathroom, etc.).

(iii) Special recommendations for home-care-3: Protection of care-giver

- A surgical mask should be used while providing care to the patient.
- When holding small children who are sick, their chin should be placed on the shoulder of the care-giver so that they will not cough in your face.
- Hands should be cleaned with soap and water or an alcohol-based hand rub after touching the sick person or handling used tissues, or laundries used by the sick person;
- The care-giver and the household members should monitor for flu-like symptoms and seek immediate medical care if symptoms occur.

(iv) Special recommendations for home-care-4: Household cleaning, laundry and waste disposal

² Children, especially younger children, might potentially be contagious for longer periods.

- Tissues and other disposable items used by the sick person should be thrown away in the trash. Hands should be washed after touching used tissues and similar waste.
- Household surfaces (especially bedside tables, surfaces in the bathroom, and toys for children) should be kept clean by wiping them down with a household disinfectant;
- Linens, eating utensils, and dishes belonging to those who are sick do not need to be cleaned separately, but importantly these items should not be shared without washing thoroughly first;
- Linens (such as bed sheets and towels) should be washed by using household laundry soap. Hands should be cleaned with soap and water or alcohol-based hand rub right after handling dirty laundry.
- Eating utensils should be washed either in a dishwasher or by hand with water and soap;
- The bathroom used by the sick person should be cleaned daily with household disinfectants.

4.1.4 Special treatment considerations for groups at high- risk for complication

Antiviral medication using Oseltamivir³ is strongly recommended without any delay in addition to home isolation and home management (as mentioned in section 4.1.3) of patients with mild influenza like illness and no visible signs of severe illness if the patients fall in either of the following risk categories (Groups at risk for complications also defined in section 3.4):

- Pregnant women
- Adults: 65 years of age and older;
- Children: younger than 5 years old (In particular less than 2 years);
- Persons with the following underlying conditions at any age:
 - Chronic Broncho-pulmonary disease (Including asthma),
 - Chronic cardiovascular disease (except hypertension)
 - Chronic neurologic disorder (Cerebral palsy, stroke, multiple sclerosis, muscular dystrophy, etc)
 - Immune suppressed patients
 - Haematological disorder
 - Chronic liver or renal failure (GFR <30 ml/min)
 - Metabolic disorder (specially Diabetes mellitus),
 - Morbid obesity

4.1.5 Referral of patients from primary health care level to higher centers

The following group of patients (also defined in section 3.2 and 3.3) with signs of either severe or progressive illness should be referred to higher health centers without any delay for appropriate management:

- Presence of prolonged fever $> 38^{\circ} \text{C} / > 100.4^{\circ} \text{F}$
- Dyspnoea or difficult breathing;

³ Zanamivir may be considered when oseltamivir is not available or in areas with proven evidence of resistance of pandemic (H1N1) 2009 virus infection to oseltamivir.

- Alteration of vital sign: Arterial hypotension, respiratory frequency increased, cardiac frequency increased, etc;
- Altered level of consciousness;
- Altered mental status: drowsiness, or difficult to awaken; recurring or persistent convulsions (seizures), confusion, severe weakness or paralysis.
- Evidence of severe dehydration and other signs of imminent shock;
- Patient that return for a second consultation with persisting and recurrent fever for 3 days even when under treatment with analgesics or antipyretics;
- Patient from geographically remote area
- Patients with social, personal or familial circumstances for whom the illness implies a high risk for them (example: patients who can not take care of themselves); and
- Causing other clinical concern to the clinician or to the specialist doctor

4.1.6 Special considerations for pregnant women and children

Pregnant women with pandemic (H1N1) 2009 virus infection would be expected to present with typical acute respiratory influenza-like illness (e.g., cough, sore throat, rhinorrhea) and fever. Other symptoms can include body aches, headache, fatigue, vomiting and diarrhoea. Many pregnant women will go on to have a typical course of uncomplicated influenza. However, for some pregnant women, illness might progress rapidly, and might be complicated by secondary bacterial infections including pneumonia. Fetal distress associated with severe maternal illness can occur.

Pregnant women with influenza-like illnesses should receive empiric antiviral treatment. Because of its systemic activity, the drug of choice for treatment of pregnant women is oseltamivir. Recommended dose and duration of treatment is 75 mg two times daily for five days. Treatment should not be delayed while waiting for the results of viral testing. As is recommended for other persons who are treated, antiviral treatment should be initiated as soon as possible after the onset of influenza symptoms, with benefits expected to be greatest if started within 48 hours of onset, based on data from studies of seasonal influenza.

Aspirin or aspirin-containing products (e.g. bismuth subsalicylate – Pepto Bismol) should not be administered to any confirmed or suspected ill case of pandemic (H1N1) 2009 virus infection aged 18 years old and younger due to the risk of Reye syndrome. For relief of fever, other anti-pyretic medications such as acetaminophen or non-steroidal anti-inflammatory drugs are recommended.

4.1.7 Treatment Flow Chart for primary level health care facilities

The algorithm shown in annex-2 is intended to guide the primary level health care workers in exercising their clinical discretion for management of patients with suspected, probable or confirmed pandemic (H1N1) 2009 influenza virus infection.

4.2. At secondary or tertiary level

At the secondary or tertiary level care, the clinical management protocol for patients with pandemic (H1N1) 2009 virus infection will start with a detailed clinical assessment of patients for suspected influenza like symptoms. The algorithm (flow chart) shown in section 4.2.8 should be used in combination with the detailed procedures set out below for management of patients with suspected influenza caused by the pandemic (H1N1) 2009 virus infection at the secondary or tertiary health care level.

4.2.1 Assessment of cases

All suspected patients with ILI whenever they present themselves either directly to the secondary or tertiary level health care facilities or referred from the primary level health care facilities need to be triaged through detailed clinical assessment in order to select those patients who meet the criteria for hospitalization. The triage area should be pre-defined before and while triaging patients, appropriate infection control measures and procedures should be followed by the health care workers.

Following clinical assessment of cases, decisions to hospitalize those patients with suspected ILI symptoms will be taken whenever the following clinical criteria (as detailed out in the box-3 below), is met.

Box-3 Criteria for hospitalization of patients

Signs of severe illness or signs of rapid progression of illness, such as

- Presence of fever $> 38^{\circ}\text{C}$ / $> 100.4^{\circ}$ associated with
- Dyspnoea or difficult breathing
- Hypoxia as indicated by pulse oximetry, if available(Oxygen saturation $\leq 92\%$ despite full oxygen saturation)
- Alteration of vital sign : Arterial hypotension (Systolic blood pressure < 90 mm HG and diastolic blood pressure < 60 mm Hg); Respiratory frequency increased (over 30 breaths per minute); Cardiac frequency increased (Heart rate > 120 bpm);
- Altered level of consciousness: New confusion, striking agitation or seizures;
- Severe Dehydration (Loss of more than 10 of body weight as evidenced by absent or low peripheral pulse, poor skin turgor, undetectable blood pressure and sunken eyes)
- Abnormal chest-x ray (Chest x-ray showing pulmonary infiltrates)
- Patient that return for a second consultation with recurrent or persistent fever (fever not subsiding beyond 3 days despite under treatment with analgesics)
- Patient from geographically remote area
- Patients with social, personal or familial circumstances for whom the illness implies a high risk for them (example: patients who can not take care of themselves)

4.2.2 General treatment consideration for hospitalized patients

The following general treatment guidelines should be followed for all hospitalized patients with either suspected, probable or laboratory confirmed pandemic (H1N1) 2009 influenza virus infection:

- Antiviral Treatment using oseltamivir is recommended for all hospitalized patients with confirmed, probable or suspected pandemic (H1N1) 2009 virus infection;
- Antiviral treatment using oseltamivir should be initiated empirically when the decision is made to treat patients in the hospitals who have illnesses that are clinically compatible with influenza. Treatment should not await laboratory confirmation;
- Antiviral treatment using oseltamivir should be initiated as early as possible because studies show that treatment initiated early (i.e., within 48 hours of illness onset) is more likely to provide benefit.
- Clinical judgment is an important factor in antiviral treatment decisions for all patients presenting for medical care who have illnesses consistent with influenza.

4.2.3 Treatment protocol for antiviral treatment in hospitals using oseltamivir

The following dose regimen (shown in table-1) should be followed for antiviral treatment using oseltamivir for all hospitalized patients

Table-1: Dosage recommendations for antiviral treatment using oseltamivir

| Agent | Age Groups (yrs) | | | | | |
|------------------------------|------------------|---|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| | Duration | 1-4 | 5-9 | 10-12 | 13-64 | ≥ 65 |
| Oseltamivir | 5 days | Weight-adjusted doses ^c : - 30 mg twice daily for ≤ 15 kg - 45 mg twice daily for >15 to 23 kg - 60 mg twice daily for >23 to 40 kg - 75 mg twice daily for >40 kg | | | 75 mg twice daily ^c | 75 mg twice daily ^c |
| Zanamivir⁴ | 5 days | Not licensed for use | 10 mg (2 inhalations) twice daily | 10 mg (2 inhalations) twice daily | 10 mg (2 inhalations) twice daily | 10 mg (2 inhalations) twice daily |

c Reduction in dose of oseltamivir is recommended for persons with creatinine clearance <30 ml/min.

4.2.4 Use of antibiotics, corticosteroids and other supporting treatment for hospitalized patients

In addition to antiviral treatment using oseltamivir, the following supportive treatment should be considered for all hospitalized patients whenever warranted:

⁴ In situations where oseltamivir is not available or not possible to use, or if the virus is resistant to oseltamivir but known or likely to be susceptible to zanamivir, treatment with zanamivir should be considered instead of oseltamivir.

- i) Symptomatic and supportive measures
 - Supportive cares (antipyretics like acetaminophen for fever, adequate rehydration for correcting dehydration, etc) are sufficient in the majority of patients.
- ii) Oxygen Therapy
 - At presentation and routinely during subsequent care in hospitalized patients, oxygen saturation should be monitored by pulse oximetry whenever possible. Supplemental oxygen should be provided to correct hypoxemia depending on the severity (nasal cannula, facemask, facemask with reservoir, intubation and assisted ventilation).
- iii) Use of Corticosteroids
 - Corticosteroids should not be routinely used.
- iv) Use of Antibiotics
 - Antibiotic chemoprophylaxis should not be used. When secondary bacterial pneumonia is suspected, treatment with antibiotics should follow recommendations from national guidelines for community-acquired pneumonia;
 - The results of microbiological studies, wherever possible, should be used to guide antibiotic usage for suspected bacterial co-infection in patients with pandemic (H1N1) 2009 virus infection.

4.2.5 General laboratory investigations for hospitalized patients

If facilities are available, the following laboratory investigations could be considered with a view to monitoring the clinical condition of the hospitalized patients:

| For hospitalized patients | For patients admitted at the Intensive Care Unit |
|---|--|
| <ul style="list-style-type: none"> • Laboratory Test <ul style="list-style-type: none"> - Full blood count (CBC) - Serum electrolytes - Hepatic function (AST, ALT) - Renal function (BUN, creatinine) - CPK - LDH - Glucose - Urinalysis - Microbiological studies of respiratory secretions (*) and blood cultures if suspected bacterial infection - Arterial blood gases - Pulse oximetry - Chest x-ray (at admission and to follow up, as per health care facility protocols) Other investigations, according to established protocols of the health care facility, such as erythrocyte sedimentation rate, C-reactive protein (CRP), and ECG | <p>In addition to the hospitalization investigations:</p> <ul style="list-style-type: none"> • Coagulation profile • Procalcitonin (if available) • Serial arterial blood gases • Serial chest x-ray • Serial electrocardiogram |

4.2.6 Special treatment considerations for pregnant women and children

Case reports of adverse pregnancy outcomes and maternal deaths have been associated with severe illness due to ILI.

Ideally, pregnant women who have suspected pandemic (H1N1) 2009 virus infection should be tested for influenza. However, treatment should not be delayed pending results of testing and treatment should not be withheld in the absence of testing. Clinicians should be aware of circulation of pandemic (H1N1) 2009 influenza virus in their area and not wait for test results to initiate influenza treatment in women who have symptoms consistent with influenza illness

When considering antiviral treatment, pregnancy should not be considered as contraindication to oseltamivir use. The pregnant women should receive the same dose regimen as adults for antiviral treatment. Because of its systematic activity, oseltamivir is preferred for treatment of pregnant women.

Children younger than 1 year of age are at higher risk for influenza-related complications and have a higher rate of hospitalization compared to older children. Oseltamivir is not approved for use in children younger than 1 year of age. However, since infants experience high rates of morbidity and mortality from influenza, infants with pandemic (H1N1) 2009 influenza virus infections may benefit from treatment using oseltamivir. The following dose regimen (shown in table-2) should be followed when considering antiviral treatment for children less than 1 year of age using oseltamivir:

Table-2. Dose recommendations for antiviral treatment of children younger than 1 year using oseltamivir

| <i>Age</i> | <i>Recommended treatment dose for 5 days</i> |
|-----------------------|--|
| Younger than 3 months | 12 mg twice daily |
| 3-5 months | 20 mg twice daily |
| 6-11 months | 25 mg twice daily |

Salicylates (such as aspirin and aspirin-containing products) should not be used in children and young adults (<18 years) because of the risk of Reye’s Syndrome.

4.2.7 Hospital discharge criteria for patients with either confirmed, probable or suspected pandemic (H1N1) 2009 influenza virus infection

When the following discharge criteria (shown in box-4) are met as a proof of showing improvement of patient’s clinical condition and signs of responding to antiviral treatment, the hospitalized patient can be discharged.

Box-4: Discharge criteria for hospitalized patients

Patient showing clinical signs of improvement and proof of responding to antiviral treatment as evidenced by the followings:

- Patient becomes afebrile;
- Absence of dyspnoea;
- Satisfactory oral fluid tolerance;
- No signs of dehydration;
- Respiratory rate ≤ 30 bpm;
- Oxygen saturation $\geq 92\%$
- Underlying chronic health conditions not exacerbated in patients in high-risk group for complication.

Patients should be discharged after receiving the full five day course of oseltamivir or 24 hours after becoming afebrile, whichever is earlier.

4.2.8 Criteria for admission in the Intensive Care Unit

When the patient's clinical condition do not show any signs of improvement or remain non-responsive to antiviral treatment as shown below (In box-5), the specialists doctors should be consulted for admission of the patients at the ICU

Box-5: Admission criteria for consideration of patients' admission at the ICU

Patient showing no signs of improvement and remain non-responsive to antiviral treatment using oseltamivir as evidenced by the followings:

- Signs of progressive infiltrates on chest x-ray
- Persistent hypoxia ($SpO_2 < 92\%$) or respiratory exhaustion despite maximum oxygen saturation;
- Progressive hypercapnoea;
- Presence of compromised haemodynamics;
- Signs of sepsis and imminent shock

4.2.9 Antiviral Treatment using oseltamivir for patients admitted at the Intensive Care Unit

A higher dose regimen of Oseltamivir (150 mg twice daily for upto 10 days) may be considered in adult patients admitted in the Intensive Care Unit⁵, although there is no clinical trial evidence to show benefit.

A higher dose regimen (double the normal dose regimen) may be considered in severely ill children as well. However particularly for children aged less than 1 year there is a lack of data on safety and dosing for treatment and chemoprophylaxis; therefore infants needs to be monitored for adverse events when oseltamivir is used.

4.2.10 Treatment flow chart for secondary or tertiary level health care facilities

The algorithm presented in annex-3 is intended as guidance to the clinicians at the secondary or tertiary level health care facilities in exercising their clinical discretion and judgement for treatment of patients with either suspected, probable or confirmed pandemic (H1N1) 2009 influenza virus infection.

⁵ Patients admitted at the ICU and also in patients with severe or progressive illness not responding to normal antiviral treatment regimen, higher doses of oseltamivir and longer duration of treatment may be appropriate, although there is no clinical trial evidence to show benefit. An adult dose of 150 mg bd for upto 10 days is being used in some situations.

5. Chemoprophylaxis

Antiviral chemoprophylaxis for patients with suspected influenza-like illness caused by pandemic (H1N1) 2009 virus infection should be considered when benefits of providing short-term protection from illness and possibly infection are high. The following recommendations will act as guidance to clinicians in prioritizing use of antiviral medications for chemoprophylaxis as well as help them in exercising their clinical judgement for antiviral chemoprophylaxis.

5.1 General recommendations for chemoprophylaxis

The following general recommendations for chemoprophylaxis are targeted for health care settings only:

- Antiviral agents should not be used for post-exposure chemoprophylaxis in healthy children or adults;
- Post-exposure antiviral chemoprophylaxis with oseltamivir⁶ can be considered for the following group of people:
 - Persons who are at higher risk for complications of influenza and are a close contact of a person with confirmed, probable, or suspected pandemic (H1N1) 2009 virus infection during that person's infectious period.
 - Persons who can not take care of themselves and are exposed to a person with confirmed, probable, or suspected pandemic (H1N1) 2009 virus infection during that person's infectious period.
 - Health care personnel who have had a recognized, unprotected close contact exposure to a person with confirmed, probable, or suspected pandemic (H1N1) 2009 during that person's infectious period.
- Chemoprophylaxis is not indicated when contact occurred before or after, but not during, the ill person's infectious period as defined above.
- Chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last contact with an infectious person.
- Patients receiving chemoprophylaxis should be encouraged to seek medical evaluation as soon as they develop a febrile illness or other acute respiratory symptoms that might indicate influenza.

⁶ In situations where oseltamivir is not available or not possible to use, or if the virus is resistant to oseltamivir but known or likely to be susceptible to zanamivir, chemoprophylaxis with zanamivir should be considered instead of oseltamivir.

- Duration of post-exposure chemoprophylaxis is 10 days after the last known exposure to pandemic (H1N1) 2009 virus infection.

5.2 Specific recommendations for use of Oseltamivir as chemoprophylaxis

When considering antiviral chemoprophylaxis with oseltamivir, the following dose regimen (table-3) should be followed for 10 days:

Table 3: Antiviral dosage recommendations for chemoprophylaxis of pandemic (H1N1)2009 virus infection with oseltamivir⁷

| <i>Group</i> | | <i>Recommended prophylaxis dose (For 10 days)</i> |
|-----------------------------|---------------|---|
| Adults | | 75-mg capsule once per day for 10 days |
| Children ≥ 12 months | 15 kg or less | 30 mg once per day for 10 days |
| | 16-23 kg | 45 mg once per day for 10 days |
| | 24-40 kg | 60 mg once per day for 10 days |
| | >40 kg | 75 mg once per day for 10 days |

5.3 Use of antiviral chemoprophylaxis of antivirals in specific groups (pregnant women and children younger than 1 year)

When considering antiviral chemoprophylaxis, pregnancy should not be considered as contraindication to oseltamivir use. The pregnant women should receive the same dose regimen as adults for antiviral chemoprophylaxis. Oseltamivir can be used although the drug of choice for chemoprophylaxis is not clear, In some situations, however, Zanamivir may be preferable because of its limited systemic absorption. However, the clinical judgement would be the key to decide on the use of Zanamivir since respiratory complications associated with Zanamivir (because of its inhaled route of administration) may weigh against its use specially in pregnant women at risk for respiratory problems.

Because infants experience high rates of morbidity and mortality from influenza, infants with pandemic (H1N1) 2009 virus infections may benefit from antiviral chemoprophylaxis using oseltamivir. However particularly for children aged less than 1 year there is a lack of data on safety and dosing for treatment and chemoprophylaxis; therefore monitor infants for adverse events when oseltamivir is used.

The following dose regimen (Table-4) may be used for chemoprophylaxis of children younger than 1 year using oseltamivir:

Table- 4: Antiviral dosage recommendations for chemoprophylaxis of Children less than 1 year of age using oseltamivir

| <i>Age</i> | <i>Recommended prophylaxis dose (For 10 days)</i> |
|-----------------------|---|
| Younger than 3 months | Not recommended unless situation judged critical |
| 3-5 months | 20 mg once daily for 10 days |
| 6-11 months | 25 mg once daily for 10 days |

⁷ In case of Zanamivir, two 5-mg inhalations (10 mg total) once per day for 10 days may be considered while for children (age years or older), two 5-mg inhalations (10 mg total) once per day for 10 days may be considered.

LIST OF PARTICIPANTS WHO ATTENDED THE EXPERT CONSULTATIVE MEETING

1. Expert panel

Dr Adel Khattab

Professor and Head of Chest Department
Ain Shams University
Special Advisor to Minister of Health on H5N1
Egypt

Dr Amira Edris

Paediatrician
Professor of Pediatrics
Cairo University
Clinical Consultant at Ministry of Health
Egypt

Dr Jacques Mokhbat

Chairman, Department of Medicine
Lebanese University faculty of Medical Sciences
Add: Rafik Hariri Campus, Hadath
Lebanon

Dr Luis Septien Stute

Internal Medicine, Pulmonary Diseases and Bronchoscopy
PAHO Temporary Advisor
Hospital General de Mexico
Instituto Nacional de Nutrición y Ciencias Médicas "Salvador Zubiran"
México City, Mexico.

Dr Ali Al Barrak

Consultant Infectious Disease
Member of National H1N1 Committee
Riyadh, Kingdom of Saudi Arabia

Dr Sami Al Hajjar

Consultant Pediatric Infectious Disease
and Virology KFSHRC-R
Member of National H1N1 Committee
Riyadh, Kingdom of Saudi Arabia

Dr Jaisi Sinha

Consultant Microbiologist/Virologist
NPHS Microbiology Cardiff
(Velindre NHS Trust)
Welsh Specialist Virology Centre
University Hospital of Wales
Heath Park
Cardiff CF14 4XW
Wales, United Kingdom

Dr Andrew Williams

Consultant Intensivist in the adult ITU
University Hospital of Wales
Heath Park
Cardiff CF14 4XW
Wales, United Kingdom

2. WHO Secretariat

Dr Zuhair Hallaj, Adviser for Communicable Diseases, WHO/EMRO.

Dr Hassan El Bushra, Regional Adviser, Communicable Disease Surveillance, Forecasting and Response, WHO/EMRO.

Dr John Jabbour, Medical Officer, (Epidemiologist) International Health Regulations, Communicable Disease Surveillance, Forecasting and Response, WHO/EMRO.

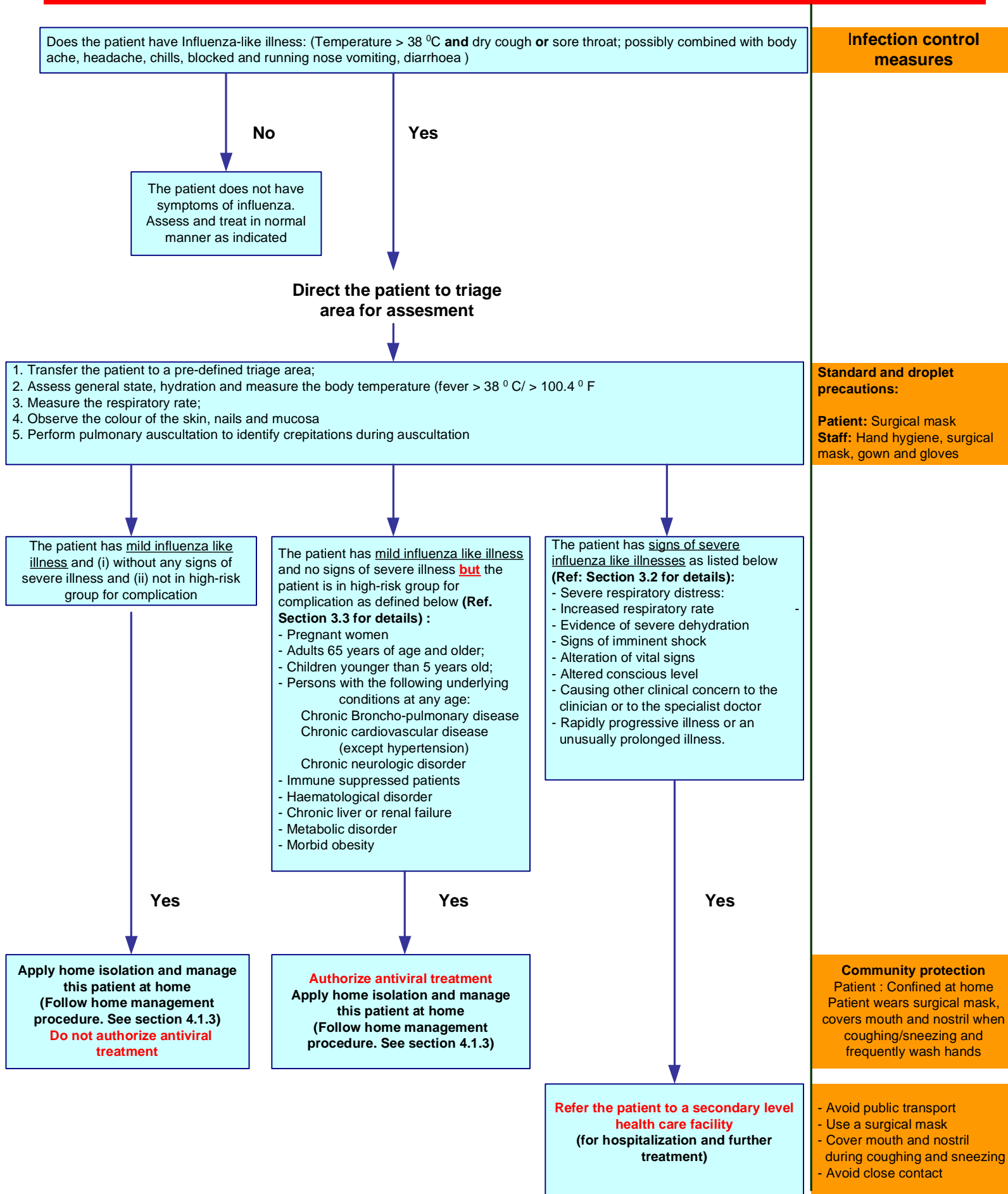
Dr Langoya Opoka, Epidemiologist, Communicable Disease Surveillance, Forecasting and Response, WHO/EMRO.

Dr Mamunur Rahman Malik, Epidemiologist, Communicable Disease Surveillance, Forecasting and Response, WHO/EMRO.

Dr Ali Mafi, Technical Officer, Communicable Disease Surveillance, Forecasting and Response, WHO/EMRO.

Ms Dalia Samhoury, Technical Officer, Communicable Disease Surveillance, Forecasting and Response, WHO/EMRO.

Algorithm for clinical management of patients at the primary health care level



Algorithm for management of patients at secondary or tertiary level care

Assessment of Patients

Signs of severe illness or signs of rapid progression of illness, such as

- Presence of fever $> 38^{\circ}\text{C}$ / $> 100.4^{\circ}\text{F}$ associated with
- Dyspnoea or difficult breathing
- Pulse oximeter saturation $\text{SpO}_2 < 90\%$ (if it is available)
- Alteration of vital sign : Arterial hypotension (Systolic blood pressure < 90 mm Hg and diastolic blood pressure < 60 mm Hg); Respiratory frequency increased (over 30 breaths per minute); cardiac frequency increased (Heart rate > 120 bpm);
- Hypoxia as indicated by pulse oximetry, if available (Oxygen saturation $\leq 92\%$ despite full oxygen saturation)
- Altered level of consciousness: New confusion, striking agitation or seizures;
- Severe dehydration (Loss of more than 10% of body weight as evidenced by absent or low peripheral pulse, poor skin turgor, undetectable blood pressure and sunken eyes)
- Abnormal chest-x ray (Chest x-ray showing pulmonary infiltrates)
- Patient returning for a second consultation with recurrent or persistent fever (Fever not subsiding beyond 3 days despite under treatment with analgesics);
- Patient from geographically remote area
- Patients with social, personal or familial circumstances for whom the illness implies a high risk for them (example: patients who can not take care of themselves)

No

Yes

Yes

Refer the case for home management

Management of case at home
(Follow the protocol for home care Ref: 4.1.3)

Hospitalize the Patients immediately for treatment and further care

Treat them with antiviral medication immediately along with other supporting treatment (Follow Protocol for Hospital Care- Ref: 4.2.3 and 4.2.4)

In addition to the above, the patient is also presenting with:

- Refractory hypoxaemia
- compromised haemodynamics
- signs of sepsis and imminent shock

Patient's conditions improving and responding to treatment as indicated by:

- Patient becoming afebrile
- Tolerating oral fluid;
- Absence of dyspnoea
- No evidence of dehydration
- Respiratory rate ≤ 30 bpm
- Oxygen saturation \geq than 92 %
- In patients at high-risk for complications : underlying chronic health conditions not exacerbated

Discharge criteria met
Discharge the patient with proper advice
(Patients should be discharged after receiving the full five day course of oseltamivir or 24 hours after becoming afebrile whichever is earlier)

Patient's conditions not improving and not responding to treatment as indicated by:

- Progressive pulmonary infiltrates
- Persistent hypoxia ($\text{SpO}_2 < 92\%$ despite maximum oxygen saturation);
- Progressive hypercapnoea;
- Presence of compromised haemodynamics
- Signs of sepsis and imminent shock

Consult specialists for advice and admission in the Intensive Care Unit (ICU)

Consider admission at the ICU upon advice from the specialists

Infection control measures

Standard and droplet precautions:

Patient: Surgical mask

Staff: Hand hygiene, surgical mask, apron and gloves

Standard and droplet precautions:

Patient: Surgical mask and strict isolation or cohorting. Isolation precaution may be discontinued when patient has had received 72 hours of antiviral treatment provided they have no fever for 24 hours in the absence of antipyretics

Staff: Hand hygiene, surgical mask, apron, gloves and eye protection if there is a risk of splash. *If aerosol generating procedure is undertaken, use gown, gloves, a correctly fitted facial particulate respirator-N 95 or FFP2 mask and eye protection.*