REVISED HEALTH WORKERS HANDBOOK

ON

PANDEMIC INFLUENZA A(H1N1) 2009
"SWINE FLU"

Version 3
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of the National Health Laboratory Service (NHLS),

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DEPARTMENT OF HEALTH
Republic of South Africa

NHLS

NICD

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Prefix and Disclaimer

This advice is based on available information concerning the new pandemic influenza A (H1N1) virus as well as data on the natural history pathogenesis and clinical characteristics of human infections caused by seasonal and avian viruses. It is intended to expand on advice for health workers on the clinical management of pandemic influenza A (H1N1), presented in the NICD document entitled Revised Health Workers Handbook on Pandemic Influenza A(H1N1) 2009 "Swine Flu" – 22nd July 2009.

This material is intended for use by healthcare professionals. While the greatest care has been taken in the development of the document, the National Dept of Health and the National Institute for Communicable Diseases do not accept responsibility for any errors or omissions. All healthcare professionals should exercise their own professional judgement in confirming and interpreting the findings presented in the guidelines.

1. Background on pandemic influenza A(H1N1) 2009

1.1 What is pandemic influenza A(H1N1) 2009 virus?

This is a new influenza A(H1N1) virus that has never before circulated among humans. This virus is not related to previous or current human seasonal influenza viruses. It has also been called “swine flu” and “novel flu”.

1.2 Transmission

The virus is spread from person-to-person. It is transmitted as easily as the normal seasonal flu and can be passed to other people by exposure to infected droplets expelled by coughing or sneezing that can be inhaled, or that can contaminate hands or surfaces. To prevent spread, people who are ill should cover their mouth and nose when coughing or sneezing, stay home when they are unwell, wash their hands regularly, and keep some distance from healthy people, as much as possible.

1.3 Typical signs and symptoms of infection

Signs of pandemic influenza A(H1N1) 2009 are flu-like, including: fever, cough, headache, muscle and joint pain, sore throat and runny nose, and sometimes vomiting and diarrhoea.

1.4 Public health concerns about the new virus

Seasonal influenza occurs every year and the viruses change each year - but many people have some immunity to the circulating virus which helps limit infections. South Africa also uses seasonal influenza vaccines to reduce illness and deaths. Pandemic influenza A(H1N1) 2009 is a new virus and one to which most people have little or no immunity. Therefore, this virus could cause more infections than are seen with seasonal flu.

The new pandemic influenza A(H1N1) 2009 virus appears to have a higher attack rate than seasonal influenza and is spreading fast, particularly among young people (from ages 10 to 45). The severity of disease ranges from very mild symptoms to severe illnesses that can result in death. The majority of people who contract the virus experience mild disease and recover without antiviral treatment or medical care. Of the more serious cases, more than half of hospitalized people had underlying health conditions or weak immune systems. Although the majority of persons affected experience mild, self-limiting illness, a characteristic of pandemic strains is the ability to cause severe disease and fatalities in otherwise healthy, young persons. Therefore it is vital that pandemic influenza A(H1N1) 2009 be considered in the differential diagnosis of all patients currently being admitted with severe acute respiratory illness. The overall severity of this influenza pandemic has been assessed to be moderate.

1.5 Recent changes in South Africa

It is now clear that the pandemic virus has been established throughout the country and that sustained community transmission is occuring. Moving forward, a strategy that concentrates on the detection, laboratory confirmation and investigation of all cases, including those with mild illness is extremely resource-intensive, leaving little capacity for the monitoring and management of severe cases. In addition, this diverts limited resources away from managing other diseases such as HIV and TB. In line with a World Health Organization (WHO) recommendation, it is therefore prudent to limit routine laboratory testing of all suspected cases of pandemic influenza A(H1N1) 2009 infection, to focus on persons at risk for complications, those with severe illness and to monitor virus characteristics.

2. Identification and progression of pandemic influenza A(H1N1) 2009

Influenza A (H1N1) 2009 must be considered in the differential clinical diagnosis of febrile patients. Clinical diagnosis (based on the acute onset of fever and cough) can be increasingly predictive of infection with the new pandemic influenza A (H1N1) infection as its incidence increases. The symptoms of pandemic influenza are non-specific and may be similar to seasonal influenza infections. A spectrum of disease ranging from non-febrile, mild upper respiratory tract illness to severe or fatal lower respiratory tract infection has been described. The most commonly reported symptoms have included cough, fever, sore throat, malaise and headache. Some cases have experienced gastrointestinal symptoms (nausea, vomiting and or diarrhoea).

The case definitions below will enable you to recognise a case that may be infected with pandemic influenza A(H1N1) 2009, and classify them into one of two categories:

2.1 ILI (Influenza Like Illness) – Mild Disease:

- An individual with recent onset of an influenza-like illness (ILI), which may include fever ≥38^{0}C PLUS ONE OR MORE of the following acute respiratory symptoms (sore throat, rhinorrhoea / nasal congestion, cough or other signs part of the respiratory complex, myalgia, diarrhoea) **PLUS absence of evidence of lower respiratory tract disease**.

2.2 SARI (Severe Acute Respiratory Infection) – Moderate to Severe Disease:

- **Persons 2 days to < 3 months old:**
    - Any child with diagnosis of suspected sepsis or physician diagnosed lower respiratory tract infection (LRTI) irrespective of signs and symptoms. Patient presenting within 7 days of the onset of illness.
- **≥ 3 months old to < 5 years old:**
    - Any child ≥ 3 months to < 5 years with physician-diagnosed acute lower respiratory infection (LRTI) including bronchiolitis, pneumonia, bronchitis and pleural effusion. Patient presenting within 7 days of the onset of illness.
- **≥ 5 years old:**
    - Any person presenting with: sudden onset of fever (>38ºC) AND cough or sore throat AND shortness of breath, or difficulty breathing with or without clinical or radiographic findings of pneumonia. Patient presenting within 7 days of the onset of illness.

Important Note: Rapid progression from mild ILI to SARI has been a feature of Pandemic Influenza A(H1N1) 2009 infection in a subset of patients. Deterioration is due to viral pneumonia and/or secondary bacterial pneumonia commonly with *Streptococcus pneumoniae* or *Staphylococcus aureus*. In young persons without co-morbidity, ARDS is a particular feature of complicated disease. There are currently no clinical or laboratory predictors to identify which patients will progress to these complications. **High fever, persistent vomiting, and marked prostration with progressive / persistent symptoms may suggest ongoing viral replication and predict progression to more severe illness.**

2.3 Features of severe illness

The criteria for severe pneumonia according to the WHO integrated management of childhood illness (IMCI) guidelines are as follows:

- Any child age 2 months up to 5 years with:
    - Cough or difficult breathing, AND with
    - Any general danger signs (unable to drink or breast-feed, vomits everything, convulsions, lethargy or unconsciousness), OR
    - Chest indrawing or stridor in a calm child.

- Severity criteria in adults of any age group include: respiratory distress, dyspnoea, hypotension and / or evidence of hypoxia.

Although data on the spectrum of illness is limited with pandemic influenza A(H1N1) 2009, clinicians should expect complications to be similar to those seen with seasonal influenza which include:

- Exacerbation of underlying chronic medical conditions,
- Upper respiratory tract disease (sinusitis, otitis media, croup),
- Lower respiratory tract disease (primary viral pneumonitis progressing to ARDS, bronchiolitis, pulmonary emboli with hypercoagulable state (particularly noted in obese patients)),
- Cardiac disease (myocarditis, pericarditis, hypotension),
- Musculoskeletal disease (myositis, rhabdomyolysis),
- Neurologic disease (acute and post infectious encephalopathy - encephalitis and febrile seizures),
- Secondary bacterial pneumonia (particularly *Streptococcus pneumoniae* and *Staphylococcus aureus,* which may be severe, rapidly progressive and necrotizing),
- Rhabomyolisis with renal failure, and
- Complications seen in pregnancy, especially in the third trimester, include spontaneous abortion and premature rupture of membranes.

Global experience to date, suggests that patients who required hospitalization, including those who were previously healthy and those with chronic underlying medical conditions, have frequently experienced rapidly progressive, serious lower respiratory tract disease. In some cases, an initial typical influenza like illness (ILI) with high fever has been followed several days later by rapid deterioration and severe respiratory disease. Furthermore, disease has been complicated by a variety of nosocomial pathogens in patients who have required prolonged hospitalization. The clinical, clinico-pathological and radiological features of respiratory complications in pandemic influenza A(H1N1) 2009 are not specific and include ARDS, pneumonitis and bronchopneumonia. Leucopenia, lymphopenia and raised levels of creatine phosphopkinase have been documented in some severe cases.

3. Who should be tested?

As of 16 July 2009, the laboratory testing strategy has been modified to **only conduct testing if a clinical decision warrants these investigations**. Laboratory testing of mild illness (patients who fit the ILI case definition) is **NOT** recommended, as it provides very little advantage to the clinical management of individual patients. However, there is still an ongoing need to closely monitor unusual events in all countries, such as clusters of cases of severe or fatal influenza A(H1N1) infection, clusters of respiratory illness requiring hospitalization, and unexplained or unusual clinical patterns associated with serious or fatal cases. Molecular testing using PCR is the current standard test. The use of ' rapid' tests is not recommended due to low sensitivity

Important note: Since influenza-like illnesses due to seasonal influenza strains has decreased significantly and there is widespread community transmission of the current pandemic strain, patients presenting with influenza-like illness is now likely due to pandemic influenza A(H1N1) 2009. Hence, testing in all cases is not indicated. Furthermore, **laboratory confirmation of pandemic influenza A(H1N1) 2009 is NOT a pre-requisite for commencing specific anti-viral treatment**.

Thus, testing is only recommended for the following patients:

1. Patients who meet the SARI case definition (i.e. moderate or severe infections) where a laboratory diagnosis will assist in patient management, or patients hospitalised due to a lower-respiratory infection where no other explanation for illness is indicated and influenza forms part of the differential diagnosis.
2. Patients with co-morbid disease and at risk for serious complications (as per list under point 3.5) AND who are symptomatic with ILI / SARI should be considered for testing if it will guide clinical management.
3. Clusters of cases where a diagnosis of the cause of the outbreak is needed (first 2-3 cases to be tested, thereafter testing not needed).
4. An individual who has died where pandemic influenza A(H1N1) 2009 is suspected as the cause of death (section 4.8).

Note: These recommendations for laboratory testing do not apply to surveillance activities managed by the NICD (e.g. Viral-watch, SARI surveillance, etc., and testing should continue as guided by those individual surveillance programmes.

3.1 Laboratories conducting testing

Private sector laboratories are providing diagnostic services for patients seen at private sector health facilities whilst, testing of patients attended to by public sector healthcare facilities is being conducted by selected sites within the National Health Laboratory Service. NICD will continue to support both sectors as required until such time as these systems have been fully implemented. However, the NICD will focus on enhanced clinical and virological surveillance at specific sites around the country.

Private sector patients: Patients seen at private sector healthcare facilities should be tested at private sector laboratories, in accordance with these guidelines. Please discuss with your individual laboratory about the requirements and recommendations for testing, as well as the cost implications to the patient/medical aid.

Public sector patients: The NICD and the Virology Department of the University of Stellenbosch at Tygerberg Hospital (for patients within Western Cape Province), will continue to provide diagnostic support for patients seen at public sector health facilities, until such time that this is available within the NHLS. Note, testing will be offered as a diagnostic service and will therefore be charged for at a standard rate. Costs associated with testing may vary between laboratories and over time, therefore please consult the laboratory prior sending the specimens.

3.2 Step-by-step guide for specimen collection, storage and transportation

1. Put on appropriate personal protective equipment including a surgical mask and surgical gloves. An N95 mask should be worn for procedures that may generate aerosols (e.g. bronchoscopy, etc.)
2. Swab each nostril with a single swab. Swab the throat using a second swab. (Use only Dacron or Rayon swabs. Wooden swabs are not suitable for testing).
3. Place both swabs together into a container of viral transport medium (VTM).
4. If dispatching specimens to NICD, the following applies: Wrap the container (containing VTM and swabs) in absorbent material (e.g. cotton wool).
5. Place in a secondary container (preferably sturdy plastic or stainless steel) with a well fitting lid.
6. Wrap again in absorbent material and place in a third container (e.g. a cooler box) containing ice (specimens and VTM must be transported at 4^0C).
7. Put the patient details on the OUTSIDE of this container including:
   - Patient Name,
   - Health facility (where appropriate),
   - Doctor and contact numbers,
   - Lab name, contact person, telephone and fax number for receipt of results,
   - Attach a copy of any investigation forms / specimen slips that have been completed, and
   - ***NB* Clinical features of patient should be clearly indicated on the specimen slip e.g. presence of pneumonia, myocaridtidis, etc. Due to the high number of specimens received specimens without clinical information indicating that the patient has moderate to severe disease will be rejected.**
8. Transport specimens directly to appropriate laboratory for patients seen at your health facility (see section 3.1).

Specimens to be tested at the NICD should be sent to the following address:

Dhamari Naidoo
National Influenza Unit, National Institute for Communicable Diseases (NICD)
1 Modderfontein Road
Sandringham, Johannesburg, 2131
South Africa

3.3 Additional information about specimen collection

- Specimens for virus isolation or for detection of viral nucleic acids or antigens should be taken preferably during the first three days after onset of clinical symptoms, but may be taken up to a week after onset or even later in severely ill or immunocompromised patients or children under 12 years of age.
- Specimens should preferably be taken prior to commencement of antivirals.
- Nasopharyngeal swabs may be collected instead of nose and throat swabs. Swabs pose a lower risk of infection for staff than do nasopharyngeal aspirates (NPA) or nasal washes, both of which may generate aerosols.

- In addition to swabs from the upper respiratory tract, invasive procedures such as bronchoalveolar lavage or lung biopsy can be performed for the diagnosis of virus infections of the lower respiratory tract where clinically indicated.
- Post mortem samples may also be submitted. These may include nasal, nasopharyngeal and throat swabs, lung biopsy or lung aspirate specimens.

3.4 Swabs and Viral transport medium (VTM)

- Wooden swabs are not suitable for respiratory virus PCR. Please use Dacron or Rayon swabs.
- All specimens must be transported in viral transport medium (VTM) as instructed above.
- The appropriate swabs and viral transport medium may be obtained from your usual local laboratory. Public sector health practitioners should contact their local NHLS laboratory. Private sector practitioners should contact their private laboratory.
- Laboratories should stock VTM and the appropriate swabs, which may be obtained through your supplier (see below).

Product	Hank's based Viral Transport medium Supplied in 4ml Sarstead tubes	Hank's based Viral Transport medium (RTS) Supplied in 4ml Sarstead tubes **This product is stable at room temp and need not be refrigerated**	Dacron / Rayon swabs	VIROCULT VTM (swab + VTM system)
Cat. #	206	VTM-RTS	-	-
Oracle # (for NHLS)	P01R0259	P02H0881	-	-
Supplier	Highveld Biological		Pro-Gen Diagnostics	
Contact details	Tel: 011-608-3508. Email: elke@hibi.co.za Web: www.highveldbiological.com		Tel: 011-467-7510. Email: info@pro-gensa.com Web: www.pro-gensa.com	

3.5 Individuals at high risk for serious complications of pandemic influenza A(H1N1) 2009

1. Persons (adults or children) with underlying medical conditions and who are receiving regular medical care for conditions such as chronic pulmonary disease (including asthma) and cardiac disease (excluding hypertension), chronic renal and hepatic diseases, diabetes mellitus and similar metabolic disorders.
2. Individuals who are immunosuppressed (including HIV-infected persons, and persons on immunosuppressive medications). Currently, there is no good data on the interaction between HIV and pandemic influenza A(H1N1) 2009; however, experience with seasonal influenza would suggest that HIV-infected persons may be at higher risk of complications.
3. Adults and children who have any condition (e.g. cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration.
4. Morbid obesity (BMI > 30) has been identified as a risk factor for complications of influenza as well as pulmonary embolic disease.
5. Children and adolescents who are receiving long-term aspirin therapy and who might be at risk for experiencing Reye's syndrome after influenza virus infection;
6. Residents of nursing homes and other chronic-care facilities
7. Pregnant women (see section 4.5)

4. Case Management & Infection Control

Important note: Laboratory confirmation of pandemic influenza A(H1N1) 2009 is NOT a pre-requisite for commencing specific anti-viral treatment. **Treatment should NOT be deferred if confirmation is pending.**

4.1 Mild cases

- **Mild cases do NOT require confirmatory laboratory testing and should NOT be admitted to hospital**. They should be advised to isolate themselves at home for 7 days after the onset of symptoms and be managed symptomatically.
- Supportive care at home is adequate for recovery. Provide the patient with advice which should include: resting, drinking plenty of fluids and keeping warm and dry. Use a pain reliever for head and muscle aches. Non-aspirin pain relievers should be used by children and young adults due to the risk of Reye's syndrome.
- Antiviral medication is NOT recommended for mild cases or contacts.
- The patient and their contacts should be given infection control guidance as follows:
    - Regular hand washing with soap and water
    - Cover nose and mouth with a tissue when coughing and sneezing (or use the upper part of your sleeve).
    - Dispose of used tissues in a dustbin, and then wash hands with soap and water.
- Contacts of cases should NOT be quarantined but should stay at home at the first sign of illness and follow guidelines as above. They should seek medical care only if required.

Treatment of ILI - mild disease

1. ILI (mild disease) WITHOUT significant co-morbidity: Antivirals are generally **NOT** recommended, but may be prescribed at the discretion of the treating physician.

2. ILI (mild disease) WITH significant co-morbidity:

(i) Any patient with one of the following co-morbidities presenting **within 48 hours** should receive antiviral therapy: HIV, Immunosuppression other than HIV (Steroids, Methotrexate, Chemotherapy, transplant recipients, etc.), Dialysis patients, Pregnancy, Chronic Lung Disease, Chronic Heart Disease (excluding hypertension), Chronic Liver Disease, Chronic Renal Disease, Diabetes, Morbid obesity (see section 3.5 for high risk individuals).

(ii) Patients with specific features of severe immunosuppression should be considered for oseltamivir **AFTER 48 hours** at the discretion of the attending physician. Although not exhaustive, these include:

- HIV: CD4 < 200 OR WHO Stage 4 (AIDS) OR HIV plus Active TB on treatment or other pulmonary infection
- Immunosuppression other than HIV: Transplant recipients, steroids >20mg once daily for >2 months, Chemotherapy or other long-term immunosuppressants
- Pregnancy: Pregnant women within third trimester or multiple pregnancies
- Chronic Lung Disease: Brittle or poorly controlled asthmatics, poorly controlled COPD
- Diabetes: All brittle or poorly controlled diabetics

4.2 Moderate and severe illness

- Cases with moderate to severe illness (based on a clinical assessment) that require hospital admission should be managed as follows:
    - Where possible these cases should be isolated in their own room with the door closed for the duration of hospital stay. If discharged prior to day 7 of onset of illness, they can complete home isolation as outlined above.
    - Droplet and contact precautions should be instituted.
    - Health workers should wear a surgical mask on entry into the patient's room, a properly fitting N95 mask should be used for aerosol-generating procedures
    - The patient should wear a standard surgical mask whenever he/she is required to leave the isolation room.
    - Where separate isolation rooms are not available, suspected cases should be cohorted in a designated ward and the above precautions instituted.
    - Oseltamivir or zanamivir should be used for treatment of moderate to severe cases (see section 4.3)

Treatment of SARI - moderate to severe disease

Given the widespread current outbreak, infection with pandemic influenza A (H1N1) 2009 must be considered as part of the differential diagnosis in all patients presenting with community acquired pneumonia, Acute Respiratory Distress Syndrome (ARDS), any severe acute respiratory infection (SARI) and myocarditis. Strong consideration must be given to urgent empiric treatment with a neurominadase inhibitor such as oseltamivir or zanamivir without waiting for laboratory confirmation.

4.3 Treatment

Pandemic influenza A(H1N1) 2009 virus is currently sensitive (susceptible) to the neuraminidase inhibitor antiviral medications, zanamivir and oseltamivir. It is resistant to the adamantane antiviral medications, amantadine and rimantadine. There are sporadic reports of oseltamivir-resistant isolates and recommendations for use of antivirals may change as data on antiviral susceptibilities become available. Oseltamivir (Tamiflu®) and zanamivir (Relenza®) are neuraminidase inhibitor (NI) antivirals registered for use in South Africa and active against influenza A and B viruses. Oseltamivir (Tamiflu®) is orally administered and is registered for use in individuals aged ≥1 year of age. Zanamivir (Relenza®) is administered through an inhaler and is registered for use in individuals aged ≥ 12 year of age.

Antiviral treatment with oseltamivir or zanamivir should be initiated as soon as possible after the onset of symptoms. Although benefit is likely to be greatest when therapy is initiated within 48 hours, some benefit may still be obtained in patients whose therapy is started later in the course of illness. The use of antivirals should be guided by the clinical condition of the patient and the clinical judgement of the treating physician**,** at whose discretion the decision to treat ultimately rests with**.**

Recommended duration of treatment is five days, but there is limited data on the optimal dosage and duration for persons with severe illness from pandemic influenza A(H1N1) 2009. Antiviral doses recommended for treatment of pandemic influenza A(H1N1) 2009 virus infection in adults or children 1 year of age or older are similar to those for seasonal influenza and are described in Table 1.

Table 1: Recommended dosage of antiviral agents for treatment of pandemic influenza A(H1N1) 2009 cases*

Age Group	Weight	Oseltamivir dosage*	Zanamivir dosage*
Adults		75 mg twice per day	Two 5 mg inhalations (10 mg total) twice per day
Children	15 kg or less	30 mg twice per day	Two 5 mg inhalations (10 mg total) twice per day (only in children aged 12 years or older)
	15–23 kg	45 mg twice per day	
	24–40 kg	60 mg twice per day	
	>40 kg	75 mg twice per day	

*Recommended duration of treatment is 5 days. Oseltamivir is not currently licensed for use in <1 year old and zanamivir is only registered for children ≥ 12 years of age.

In addition to antiviral medications, other therapeutics to treat complications should be utilized where indicated (e.g. antibiotics for bacterial complication such as pneumonia). Supportive care is also advised depending on the clinical severity of disease (oxygen therapy, mechanical ventilation, etc.).

Table 1: Summary of clinical management of pandemic influenza A(H1N1) 2009 virus infection

Modalities	Strategies
Antibiotics	In case of pneumonia, empiric treatment for community acquired pneumonia (CAP) per published guidelines must include antibiotics to treat *Staphylococcus aureus* and *Streptococcus pneumoniae*, pending microbiologic results and tailored therapy thereafter if pathogen(s) identified.
Antiviral therapy	Only indicated for individuals with moderate to severe disease, and individuals at risk for development of severe disease. The pandemic influenza A(H1N1) 2009 virus is currently resistant to amantadine and rimantadine.
Corticosteroids	Moderate to high dose steroids are NOT recommended. They are of unproven benefit and potentially harmful.
Infection control	Standard plus Droplet Precautions. For aerosol-generating procedures use particulate respirator (N95, FFP2 or equivalent), eye protection, gowns, gloves,.
NSAIDS, antipyretics	Paracetamol can be administered for fever. Avoid administration of salicylates (aspirin and aspirin containing products) in children and young adults (< 18 years old) due to risk of Reye's syndrome.
Oxygen therapy	Monitor oxygen saturation and maintain SaO2 over 90% (95% for pregnant women) with nasal cannulae or face mask.

4.4 Prophylaxis

Antiviral post-exposure prophylaxis should NOT be offered routinely to contacts. It may be considered at the discretion of the treating physician to high-risk close contacts of suspected or confirmed cases of infection due to pandemic influenza A(H1N1) 2009 (see section 3.5). Dosage of agents for antiviral prophylaxis is described in Table 2. Duration of antiviral chemoprophylaxis post-exposure is 10 days after the last known exposure to an ill confirmed case.

Table 3: Recommended dosage of antiviral agents for prophylaxis of high risk contacts of confirmed, probable or suspected pandemic influenza A(H1N1) 2009 cases*

Age Group	Weight	Oseltamivir dosage*	Zanamivir dosage*
Adults		75 mg once per day	Two 5 mg inhalations (10 mg total) once per day
Children	15 kg or less	30 mg once per day	Two 5 mg inhalations (10 mg total) once per day (only in children aged 12 years or older)
	15–23 kg	45 mg once per day	
	24–40 kg	60 mg once per day	
	>40 kg	75 mg once per day	

*Recommended duration of prophylaxis is 10 days. Oseltamivir is not currently licensed for use in <1 year old and zanamivir is only registered for children ≥ 12 years of age.

4.5 Pregnant Women

Pregnant women, particularly in the third trimester of pregnancy, have been shown to be at significant risk of maternal complications of Pandemic Influenza A(H1N1) 2009 with ARDS, viral and secondary bacterial pneumonia as well as pulmonary emboli. Foetal loss has also been reported. No clinical studies have been conducted to adequately assess the safety of these antivirals for pregnant women. However, no adverse effects have been reported among women who received oseltamivir or zanamivir during pregnancy or among infants born to women who have received oseltamivir or zanamivir. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use and oseltamivir or zanamivir should be used during pregnancy if the potential benefit justifies the potential risk to the embryo or fetus; the manufacturers' package inserts should be consulted. Because zanamivir is an inhaled medication and has less systemic absorption, some experts prefer zanamivir over oseltamivir for use in pregnant women when feasible.

4.6 Children

An oral solution of oseltamivir may be prepared for children ≤40kg, younger than 8 years, or those unable to swallow a capsule. Empty contest of the capsule into 5ml of clean (not hot) water in a syringe. Mix for at least 1 minute, and use the mixture immediately according to weight specifications (see table below). Discard remainder. Add a small amount of flavored food or liquid (e.g. sugar, honey, or syrup) if necessary to mask the bitter taste (avoid fruit juice, carbonated drinks, and dairy products).

Weight	Oseltamivir dosage*	Required volume of mixture
15 kg or less	30 mg once per day	2ml
15–23 kg	45 mg once per day	3ml
24–40 kg	60 mg once per day	4ml
>40 kg and adults	75 mg once per day	5ml

*Recommended duration of prophylaxis is 10 days. Oseltamivir is not currently licensed for use in <1 year old.

Oseltamavir is not registered for use in children less than 1 year of age in South Africa. However, there is no alternative agent for treatment of Pandemic Influenza A(H1N1) 2009. Furthermore, as no significant adverse effects have been reported among children less than 1 year of age who received oseltamivir, the use oseltamivir or zanamivir should be undertaken if there is high suspicion or confirmation of infection with Pandemic Influenza A(H1N1) 2009 in a child with SARI, as potential benefit justifies any potential risk.

4.7 People living with HIV and AIDS

There is currently no information on the effect of pandemic influenza A(H1N1) 2009 in HIV co-infected persons. Evidence that influenza can be more severe for HIV-infected adults and adolescents comes from US studies of HIV-infected persons who had seasonal influenza; these data are limited. However, several studies have reported higher hospitalization rates, prolonged illness and increased mortality, especially among persons with AIDS. Hospitalizations for influenza and pneumonia have reduced in the HAART era.

4.8 Port-mortem management

Please notify the NICD of all deaths where pandemic influenza A(H1N1 2009) is suspected by contacting one of the NICD hotlines provided in section 5.

It is important to confirm pandemic influenza A(H1N1) 2009 in all deaths where it is clinically suspected. If a specimen has not been collected prior to death, suitable specimens should be collected as soon as possible following death. A nose and throat swab in VTM may be collected (see section 3) if carried out within a few hours of death; however, the sensitivity of such specimens has not been proven and the ability to detect virus decreases rapidly over time. A lung biopsy in VTM is the preferred post-mortem specimen for histology and PCR (in VTM). If you are unable to obtain a lung biopsy, a lung aspirate in VTM may also be submitted.

Contact and aerosol precautions (incl. a fitted N95 mask) is recommended during specimen collection and when handling of the corpse. Precautions should be taken to avoid unnecessary contact with the body by family and friends.

4.9 Adverse events and contraindications

Clinicians should consult manufacturers' package inserts for further information on adverse events and contraindications for these agents.

5. Who to contact details if you have questions?

Answers to most questions are available on the following websites:

- NICD Website: www.nicd.ac.za
- Department of Health Website: www.doh.gov.za/swineflu/swineflu-f.html
- World Health Organisation Website: www.who.int/csr/disease/swineflu/en/
- Centers for Disease Control and Prevention (CDC, Atlanta): www.cdc.gov/h1n1flu/

Further questions from health professionals can be address to:

- Daytime NICD Influenza Hotline (8am to 5pm Monday to Friday) - 082 477 8026 ***for use by health professionals only***
- After-hours, weekends and public holidays – NICD Hotline - 082 883 9920 ***for use by health professionals only***
- For additional information on VTM and swabs contact the National Influenza Centre (Amelia Buys/Cardia Fourie, 011 386 6373). ***for use by health professionals only***

Further questions from general public and all other queries can be directed to:

- The Department of Health Communicable Disease Control hotline: 0861-DOH-CDC (0861-364-232)

Appendix 1: Home Care Guidance: Doctors/Nurses directions to Patients/Parents

Home Care Guidance: Doctors/Nurses directions to Patients/Parents

1. You will probably be sick for several days with fever and respiratory symptoms.

2. Take Medications as Prescribed:

- Take all of the antiviral medication as directed (where applicable).
- Continue to cover your cough and wash your hands often (even when taking antiviral medications), to prevent spreading influenza to others.
- Call the clinic/GP if you (or your child) experience any side effects; i.e. nausea, vomiting, rash, or unusual behaviour.
- Take medications for symptom relief as needed for fever and pain such as paraectamol or ibuprofen. These medicines do not need to be taken regularly if your symptoms improve.
- Do not give aspirin (acetylsalicylic acid) or products that contain aspirin to children or teenagers 18 years old or younger.
- Children younger than 4 years of age should not be given over-the-counter cold medications without first speaking with a health care provider.

3. Seek Emergency Care:

If your child experiences any of the following:

- Fast breathing or trouble breathing
- Bluish or grey skin colour
- Not drinking enough fluids
- Severe or persistent vomiting
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms improve but then return with fever and worse cough

In adults, emergency warning signs that need urgent medical attention include:

- Difficulty breathing or shortness of breath
- Pain or pressure in the chest or abdomen
- Sudden dizziness
- Confusion
- Severe or persistent vomiting
- Flu-like symptoms improve but then return with fever and worse cough

4. Follow These Home Care Recommendations:

- Stay home for 7 days after your symptoms begin or until you have been symptom-free for 24 hours, whichever is longer.
- Drink clear fluids (such as water, broth, sports drinks, electrolyte beverages for infants) to keep from being dehydrated.
- Dishes can be done with hot soapy water.
- Throw away tissues and other disposable items used by the sick person in the trash. Wash your hands after touching used tissues and similar waste.
- Have everyone in the household wash hands often with soap and water, especially after coughing or sneezing. Alcohol-based hand cleaners are also effective.
- Avoid touching your eyes, nose and mouth. Germs spread this way.
- Continue with medication for chronic diseases as prescribed (e.g. ART).

Appendix 2: Summary table on management of adult patients & children >5 years with suspected or proven pandemic influenza A(H1N1) 2009 infection

Category	Clinical Definition	Treatment	Diagnostic Tests
MILD Influenza-like illness (MILD-ILI)	Recent onset of temperature ≥38°C **PLUS** 1 or more of: Sore throat, Rhinorrhoea, Nasal congestion, Dry cough, Myalgia, Diarrhoea, Vomiting.	**NO CO-MORBIDITY PRESENT** Symptomatic treatment with paracetamol ± alternative analgesia. Avoid aspirin in children and adolescents who are at increase risk of Reye's Syndrome **CO-MORBIDITY* PRESENT** Oseltamivir 75mg orally twice per day for 5 days‡	NOT for routine diagnostic testing
Progressive Influenza-like illness (PROGRESSIVE-ILI)	Patient previously fulfils clinical criteria for MILD-ILI, **PLUS** evidence of clinical deterioration with 1or more of: Difficulty breathing, Chest pain, Productive cough, Altered mental state, Any new neurological symptom or sign, Hypotension, Persistance of T ≥38°C for > 3 days, Persistent vomiting with dehydration	Oseltamivir 75mg orally twice per day for 5 days for patients not already on treatment **Treatment should start as soon as any of the clinical criteria are met**. **URGENT EARLY REFERRAL to hospital for supportive care and assessment for respiratory, ventilatory support and antibiotics to cover *Strep. pneumoniae* & *Staph. aureus* such as co-amoxiclav (Augmentin) or ceftriaxone**	Send nasopharyngeal and throat swabs for H1N1 testing†
Severe Acute Respiratory Infection (SARI)	Sudden onset of T ≥38°C. **PLUS:** Cough or sore throat **PLUS:** Impaired breathing. **WITH OR WITHOUT:** Clinical or X-ray evidence of pneumonia.	Oseltamivir 75mg orally twice per day for 5 days. Antibiotics – to cover *Staph. aureus* & *Strep. pneumoniae* Early oxygen supplementation and close monitoring of oxygen saturation. Ensure adequate hydration and monitor renal function.	Send nasopharyngeal and throat swabs for H1N1 testing†

***** Co-morbid conditions: pregnancy, HIV, patients with other causes of immunosuppression (chemotherapy, immunosuppressant drugs, transplant recipients) chronic lung disease (e.g. asthma, COPD), diabetes, severe obesity (BMI>30), chronic liver, kidney and heart (excluding hypertension) disease.

‡ All attempts should be made to start oseltamivir within the first 48 hours of symptoms. Giving oseltamivir after 48 hours for mild ILI is at the discretion of the attending physician. Particular attention should be paid to; HIV-infected patients with CD4 <200 cells/µL **OR** WHO stage 4 (AIDS) **OR** HIV-infection with active tuberculosis / other respiratory infection; pregnant women in the 3rd trimester or with multiple pregnancy; brittle or poorly controlled diabetics, asthmatics or persons with severe lung disease; patients immunosupressed from chemotherapy, and other immunosuppressive drugs.

† Testing for pandemic influenza A(H1N1) 2009 should NOT delay the start of oseltamivir when clinically indicated.

Appendix 3: WHO Patient Care Checklist

Patient Care Checklist

New influenza A (H1N1)

June 2009

Replaces: 15 May 2009
Expires: December 2009.

This checklist is intended for use by hospital staff treating anyone with a medically suspected or confirmed case of new influenza A (H1N1) per local definition. This checklist highlights areas of care critical for the management of new influenza A (H1N1).

It is not intended to replace routine care.

UPON ARRIVAL TO CLINICAL SETTING/TRIAGE

- ☐ Direct patient with flu-like symptoms to designated waiting area
- ☐ Provide instruction and materials to patient on respiratory hygiene/cough etiquette
- ☐ Put medical/surgical mask on patient if available and tolerable to patient

UPON INITIAL ASSESSMENT

- ☐ Record respiratory rate over one full minute and oxygen saturation if possible
- ☐ If respiratory rate is high or oxygen saturation is below 90% alert senior care staff for action#
- ☐ Record history, including flu-like symptoms, date of onset, travel, contact with people who have flu-like symptoms, co-morbidities
- ☐ Consider specialized diagnostic tests (e.g. RT-PCR)
- ☐ Use medical/surgical mask, eye protection, gloves when taking respiratory samples
- ☐ Label specimen correctly and send as per local regulations with biohazard precautions
- ☐ Consider alternative or additional diagnoses
- ☐ Report suspected case to local authority

INITIAL AND ONGOING PATIENT MANAGEMENT

Supportive therapy for new influenza A (H1N1) patient as for any influenza patient including:

- ☐ Give oxygen to maintain oxygen saturation above 90% or if respiratory rate is elevated (when oxygen saturation monitor not available)
- ☐ Give paracetamol/acetaminophen if considering an antipyretic for patients less than 18 years old
- ☐ Give appropriate antibiotic if evidence of secondary bacterial infection (e.g. pneumonia)
- ☐ Consider alternative or additional diagnoses
- ☐ Decide on need for antivirals* (oseltamivir or zanamivir), considering contra-indications and drug interactions

BEFORE PATIENT TRANSPORT/TRANSFER

- ☐ Put medical/surgical mask on patient if available and tolerable to patient

BEFORE EVERY PATIENT CONTACT

- ☐ Put on medical/surgical mask
- ☐ Clean hands
- ☐ Put on eye protection, gown and gloves if there is risk of exposure to body fluids/splashes
- ☐ Clean and disinfect personal/dedicated patient equipment between patients
- ☐ Change gloves (if applicable) and clean hands between patients

IF USING AEROSOL-GENERATING PROCEDURES ALSO (e.g. intubation, bronchoscopy, CPR, suction)

- ☐ Allow entry of essential staff only
- ☐ Put on gown
- ☐ Put on particulate respirator (e.g. EU FFP2, US NIOSH-certified N95) if available
- ☐ Put on eye protection, and then put on gloves
- ☐ Perform planned procedure in an adequately ventilated room

BEFORE PATIENT ENTRY TO DESIGNATED AREA (Isolation room or cohort)

- ☐ Post restricted entry and infection control signs
- ☐ Provide dedicated patient equipment if available
- ☐ Ensure at least 1 metre (3.3 feet) between patients in cohort area
- ☐ Ensure local protocol for frequent linen and surface cleaning in place

This checklist is not intended to be comprehensive.

Additions and modifications to fit local practice are encouraged.

BEFORE ENTERING DESIGNATED AREA (Isolation room or cohort)

- ☐ Put on medical/surgical mask
- ☐ Clean hands

The above applies to visitors also

BEFORE LEAVING DESIGNATED AREA (Isolation room or cohort)

- ☐ Remove any personal protective equipment (gloves, gown, mask, eye protection)
- ☐ Dispose of disposable items as per local protocol
- ☐ Clean hands
- ☐ Clean and disinfect dedicated patient equipment and personal equipment that has been in contact with patient
- ☐ Dispose of viral-contaminated waste as clinical waste

The above applies to visitors also

BEFORE DISCHARGE OF CONFIRMED OR SUSPECTED CASE

- ☐ Provide instruction and materials to patient/caregiver on respiratory hygiene/cough etiquette
- ☐ Provide advice on home isolation, infection control and limiting social contact
- ☐ Record patient address and telephone number

AFTER DISCHARGE

- ☐ Dispose of or clean and disinfect dedicated patient equipment as per local protocol
- ☐ Change and launder linen without shaking
- ☐ Clean surfaces as per local protocol
- ☐ Dispose of viral-contaminated waste as clinical waste

*# See instructions on the back side for additional information and references. Equipment on this checklist is recommended if available.

World Health Organization

ABOUT THIS CHECKLIST

The WHO *Patient Care Checklist: new influenza A (H1N1)* is intended for use by hospital staff treating a patient with a medically suspected or confirmed case of new influenza A (H1N1). This checklist combines two aspects of care: i) clinical management of the individual patient and ii) infection control measures to limit the spread of new influenza A (H1N1).

WHO Patient Safety Checklists are practical and easy-to-use tools that highlight critical actions to be taken at vulnerable moments of care. They are produced in a format that can be referred to readily and repeatedly by staff to help ensure that all essential actions are performed. WHO Patient Safety Checklists are not comprehensive protocols and are not intended to replace routine care.

How to use the checklist

Staff can use this checklist in a variety of ways - ticking the boxes is optional. The objective is to ensure that no critical patient care items are missed during or immediately following care.

The checklist can be:

- used as part of the patient's clinical record;
- reproduced as wall posters for hospitals or clinics; or
- printed up as cards for staff members to carry around with them.

Parts of the checklist can also be extracted for use in any of these formats.

This checklist does not replace clinical guidance or clinical judgment. Its users should also familiarize themselves with the relevant WHO guidance documents referenced below, which were used in the development of the checklist.

Local modification

The WHO *Patient Care Checklist: new influenza A (H1N1)* may be reformatted or revised to accommodate local practice. Facilities and individuals are cautioned, however, against making the checklist too complex.

Related guidance

Guidance relating to infection control:

Infection prevention and control in health care in providing care for confirmed or suspected A (H1N1) swine influenza patients Interim guidance (Publication date: 29 April 2009) http://www.who.int/csr/resources/publications/Infection_control/en/index.html

Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care. WHO Interim Guidelines (Publication date: June 2007) http://www.who.int/csr/resources/publications/WHO_CDS_EPR_2007_6/en/

Guidance relating to clinical management:

Clinical management of human infection with new influenza A (H1N1) virus (Publication date: 21 May 2009) http://www.who.int/entity/csr/resources/publications/swineflu/clinical_managementH1N1_21_May_2009.pdf

*Currently there are a lack of data on the clinical effectiveness of antivirals for this disease. Antiviral drugs are to be used according to national pandemic influenza preparedness plans. If antivirals are prescribed, oseltamivir or zanamivir should be used for influenza A (H1N1) patients because of increased risk of the resistance with other antivirals. Where antiviral drugs are available for treatment, clinicians should make decisions based on assessment of the individual patient's risk. Risks versus benefits should also be evaluated on a case-by-case basis.

Such guidance may be updated as the situation evolves. For the most up-to-date guidance on the checklist and other documents, refer to the WHO web site (www.who.int) or contact your WHO country office.

GLOSSARY OF SELECTED CHECKLIST TERMS

Clean hands: Hands can be cleaned either by handwashing with soap and water or by handrubbing with an alcohol-based handrub formulation. The preferred technique while caring for suspected or confirmed cases of new influenza A (H1N1) is handrubbing, unless hands are visibly soiled. Hands must be cleaned at five key moments: 1) before touching a patient; 2) before clean/aseptic procedure; 3) after body fluid exposure risk; 4) after touching a patient; and 5) after touching patient surroundings.

Designated area (isolation room / cohort): The placing of patients either colonized or infected with the same pathogen in one designated area. It is specifically used when single or isolation rooms are not available. It allows for identified health-care workers to provide care to these specific patients with the aim of trying to prevent spread of infection to others. Patients with confirmed infection should ideally be in a separate cohort to those with suspected infection.

Cough etiquette: Health-care workers, patients and family members should cover mouth and nose (e.g. with a tissue) when coughing or sneezing. If a tissue is used, discard it in a bin with a lid and then clean hands. Cough etiquette should be communicated to patients through posters and leaflets.

Separate waiting area: Waiting area for symptomatic persons should be separate from general waiting area. This can be a separate part of the general waiting area as long as there is at least one metre (3.3 feet) distance between the designated area and the regular waiting area. Maintain at least one metre between symptomatic patients within this designated area.

Eye protection: This can either be an eye visor, goggles, or a face shield. Conventional eye glasses are not designed to protect against splashes to eye mucosa and should not be used as eye protection.

Flu-like symptoms: Fever, cough, headache, muscle and joint pain, sore throat, runny nose, and sometimes vomiting and diarrhoea.

Gown: A clean, non-sterile long-sleeved gown.

Infection control guidance to patient/caregiver on discharge: If patient still symptomatic or if patient less than one year old (Patients less than one year old may continue to be infectious for three weeks after cessation of symptoms):

- Patient quarantined: the sick person should be placed in a separate room and should have limited social contact.
- Instruction on cough etiquette.
- All persons in the household should perform hand hygiene frequently and after every contact with the sick person.
- The caregiver should wear the best available protection to prevent exposure to respiratory secretions, and avoid contact with body fluids or contaminated items; minimize close (less than 1 metre) and face-to-face contact with the patient; perform hand hygiene when indicated.

Medical/surgical masks: Procedure or surgical masks to protect the wearer's nose and mouth from inadvertent exposures (e.g. splashes).

Particulate respirator: A special type of fit-tested mask with the capacity to filter particles to protect against inhaling infectious aerosols (e.g. EU FFP2 and US NIOSH-certified N95).

Respiratory hygiene: See cough etiquette

#RESPIRATORY RATE

(reference for high values):

AGE	RESPIRATORY RATE
<2 months	≥60/minute
2–11 months	≥50/minute
1–5 years	≥40/minute
>5–12 years	≥30/minute
≥13 years	≥20/minute

CHECKLIST DEVELOPMENT PROCESS

In response to the pandemic threat by a new influenza A (H1N1) strain, the checklist development process began on 30 April 2009. The checklist development group in the WHO Patient Safety Programme collaborated with technical experts in WHO Health Security and Environment. They consulted experts in three areas: i) infection control, ii) clinical management of pandemic-prone influenza, and iii) health care checklists. The design and content of the checklist were developed iteratively through successive rounds of consultation. Clinical teams in a number of settings tested its clarity and usability. Its use in clinical practice will be the subject of ongoing evaluation.