

NJDHSS Summary of WHO Rapid Advice Guidelines for pharmacological management of sporadic human infection with avian influenza A (H5N1) virus

CHEMOPROPHYLAXIS (See last page for a description of risk stratification):

In high-risk exposure groups oseltamivir or zanamivir **should** be administered as chemoprophylaxis continuing for 7–10 days after the last known exposure (strong recommendation, very low quality evidence).

In moderate-risk exposure groups oseltamivir or zanamivir **might be** administered as chemoprophylaxis, continuing for 7–10 days after the last known exposure (weak recommendation, very low quality evidence).

In low-risk exposure groups oseltamivir and zanamivir **should probably not** be administered for chemoprophylaxis (weak recommendation, very low quality of evidence). Pregnant women in the low exposure risk groups **should not** receive oseltamivir or zanamivir for chemoprophylaxis (strong recommendation, very low quality of evidence).

If the virus is known or likely to be an M2 inhibitor resistant H5N1 virus, neither amantadine nor rimantadine should be administered as chemoprophylaxis against human infection with avian influenza A (H5N1) virus (strong recommendation, very low quality evidence).

If neuraminidase inhibitors are not available and especially if the virus is known or likely to be susceptible, amantadine or rimantadine might be administered as chemoprophylaxis against human infection with avian influenza A (H5N1) virus in high or moderate-risk exposure groups, but should probably not be administered in low-risk exposure groups (weak recommendation, very low quality evidence).

In pregnant women, the elderly, people with impaired renal function, and individuals receiving neuropsychiatric medication or with neuropsychiatric or seizure disorders amantadine should not be administered as chemoprophylaxis against human infection with avian influenza A (H5N1) virus (strong recommendation, very low quality of evidence).

In pregnant women rimantadine should not be administered for chemoprophylaxis of human infection with avian influenza A (H5N1) virus (strong recommendation, very low quality of evidence).

TREATMENT

In patients with confirmed or strongly suspected H5N1 infection, clinicians should administer oseltamivir, treatment as soon as possible (strong recommendation, very low quality evidence).

Clinical Guidelines – Appendix 4a

In patients with confirmed or strongly suspected infection with avian influenza A (H5N1) virus, clinicians might administer zanamivir (weak recommendation, very low quality evidence).

If neuraminidase inhibitors are available, clinicians should not administer amantadine or rimantadine alone as a first-line treatment to patients with confirmed or strongly suspected human infection with avian influenza H5N1 (strong recommendation, very low quality evidence).

If neuraminidase inhibitors are not available and especially if the virus is known or likely to be susceptible, clinicians might administer amantadine or rimantadine as a first-line treatment to patients with confirmed or strongly suspected infection with avian influenza A (H5N1) virus (weak recommendation, very low quality evidence).

If neuraminidase inhibitors are available and especially if the virus is known or likely to be susceptible, clinicians might administer a combination of neuraminidase inhibitor and M2 inhibitor to patients with confirmed or strongly suspected infection with avian influenza A (H5N1) virus. *However, this should only be done in the context of prospective data collection* (weak recommendation, very low quality evidence).

The recommended dose and duration of treatment and chemoprophylaxis are shown in the table (from Lancet Infect Dis 2007; 7:23).

Duration		Age groups (years)				
		1-6	7-9	10-12	13-64	≥65
Oseltamivir						
Treatment	5 days	Weight adjusted doses: • 30 mg twice daily for ≤15 kg • 45 mg twice daily for >15-23 kg • 60 mg twice daily for >23-40 kg • 75 mg twice daily for >40 kg	Weight adjusted doses: • 30 mg twice daily for ≤15 kg • 45 mg twice daily for >15-23 kg • 60 mg twice daily for >23-40 kg • 75 mg twice daily for >40 kg	Weight adjusted doses: • 30 mg twice daily for ≤15 kg • 45 mg twice daily for >15-23 kg • 60 mg twice daily for >23-40 kg • 75 mg twice daily for >40 kg	75 mg twice daily	75 mg twice daily
Prophylaxis	Begin as soon as exposure identified and continue for 7-10 days after last known exposure	Dose varies by child's weight as for treatment but administered once daily	Dose varies by child's weight as for treatment but administered once daily	Dose varies by child's weight as for treatment but administered once daily	75 mg/day	75 mg/day
Zanamivir						
Treatment	5 days	Not licensed for use	10 mg (two inhalations) twice daily	10 mg (two inhalations) twice daily	10 mg (two inhalations) twice daily	10 mg (two inhalations) twice daily
Prophylaxis	Begin as soon as exposure identified and continue for 7-10 days after last known exposure	1-4 years: NA; 5-6 years: 10 mg (two inhalations) once daily	10 mg (two inhalations) once daily	10 mg (two inhalations) once daily	10 mg (two inhalations) once daily	10 mg (two inhalations) once daily
Amantadine						
Treatment	5 days	5 mg/kg per day up to 150 mg in two divided doses	5 mg/kg/day up to 150 mg in two divided doses	100 mg twice daily	100 mg twice daily	≤100 mg/day
Prophylaxis	Begin as soon as exposure identified and continue for 7-10 days after last known exposure	5 mg/kg per day up to 150 mg in two divided doses	5 mg/kg per day up to 150 mg in two divided doses	100 mg twice daily	100 mg twice daily	≤100 mg/day
Rimantadine						
Treatment	5 days	Not licensed for use	Not licensed for use	Not licensed for use	100 mg twice daily	100 mg/day
Prophylaxis	Begin as soon as exposure identified and continue for 7 days after last known exposure	5 mg/kg per day up to 150 mg in two divided doses	5 mg/kg per day up to 150 mg in two divided doses	100 mg twice daily	100 mg twice daily	100 mg/day
NA=not applicable.						
Table: The recommended dose and duration of treatment and chemoprophylaxis for management of human infection of avian influenza A (H5N1) virus						

Clinical Guidelines – Appendix 4a

Risk stratification for the provision of chemoprophylaxis of H5N1 virus infection

Antiviral chemoprophylaxis should generally be considered according to the risk stratification described below. It is based on observational data for reported cases of human infection with avian influenza A (H5N1) virus and on high quality data from studies of seasonal human influenza virus infection.

High-risk exposure groups are currently defined as:

- Household or close family contacts* of a strongly suspected or confirmed H5N1 patient, because of potential exposure to a common environmental or poultry source as well as exposure to the index case

Moderate-risk exposure groups are currently defined as:

- Individuals with unprotected and very close direct exposure† to sick or dead H5N1 infected animals or to particular poultry that have been implicated directly in human cases
- Persons involved in handling sick animals or decontaminating known infected animals or environments, if personal protective equipment might not have been used properly
- Health-care personnel in close contact with strongly suspected or confirmed H5N1 patients, for example during intubation or performing tracheal suctioning, or delivering nebulized drugs, or handling inadequately screened/sealed body fluids without any, or with insufficient, personal protective equipment. This also includes laboratory personnel who might have an unprotected exposure to virus-containing samples‡

Low-risk exposure groups are currently defined as:

- Health-care workers not in close contact (distance greater than 1 m or no direct contact with infectious material) with a strongly suspected or confirmed H5N1 patient
- Health-care workers who used appropriate personal protective equipment during exposure to H5N1 patients
- Personnel involved in culling non-infected or likely noninfected animal populations to prevent viral spread
- Personnel involved in handling sick animals or decontaminating known infected animals or environments, who used proper personal protective equipment In the absence of sustained human-to-human transmission, the general population is currently not considered at risk.

*A close contact may be defined as an individual sharing a household with, or remaining unprotected while within speaking distance (<1 m) of, or in the care of, a patient with confirmed or strongly suspected H5N1 infection.

†Examples of high-risk exposure based on confirmed transmission to humans include: unprotected exposure to infected animal products such as consumption of blood from H5N1 infected ducks, preparation of food from infected animals (eg, plucking feathers), or prolonged exposure to infected birds in a confined space, such as playing with pets.

‡This definition of moderate risk is based on very few cases recognized under these situations to date. Because circumstances could change rapidly, it would be reasonable to consider the moderate and high-risk groups together for prophylaxis decisions. If a particular patient has been implicated in possible human-to-human transmission, then these examples of exposures could be defined as high risk.