

Trust Guideline for the Prophylaxis and Treatment of Influenza in Adults / Children for Seasonal Influenza

A clinical guideline recommended for use

For Use in:	All clinical areas
By:	Medical Staff
For:	Adults and paediatric patients with or at risk of influenza (During a pandemic see Pandemic Flu guideline, CA4009)
Division responsible for document:	Medical
Key words:	Influenza, prophylaxis, treatment, oseltamivir, zanamivir
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Description of changes:	Addition of flowchart for Oncology/Haematology patients with suspected Influenza
Compliance links:	NICE Technology Appraisal No 168 NICE Technology Appraisal No 158
If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	No deviation

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document.

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Contact numbers for Virology, Occupational Health and Medicines Information can be found on page 14

1. Objective of Guideline

The antiviral drugs, oseltamivir and zanamivir, are used for the treatment and prophylaxis of influenza. In the event of an influenza outbreak it is imperative that action is taken quickly in order to reduce transmission and to keep the number of cases to a minimum thereby reducing the burden on the hospital and staff in terms of sickness. Oseltamivir and zanamivir are effective in reducing symptoms, duration of symptoms and improving return to normal activity, reducing the requirement for antibiotics and hospitalisation and reducing the probability of dying.

This guideline applies to the management of the currently circulating influenza viruses which include:

- 1) Influenza A (H1N1) pdm09,
- 2) Influenza A (H3N2),
- 3) Influenza B (strains Yamagata and Victoria).

2. Rationale for the recommendations

In accordance with Department of Health and Trust guidance, immunisation is the most effective way to prevent and manage infection with influenza A and B. In 2008 and 2009, NICE guidance recommended that the neuraminidase inhibitors, zanamivir and oseltamivir, be used for treatment and prophylaxis of patients deemed to be at particular risk of developing complications following influenza infection. Therefore, neuraminidase inhibitors offer a second line of defence.

3. Definitions of cases of influenza

a) Uncomplicated influenza: Influenza presenting with fever, coryza, generalised symptoms (headache, malaise, myalgia, arthralgia) and sometimes GI symptoms, but without any features of complicated influenza.

b) Complicated influenza: Influenza requiring hospital admission and/or with symptoms and signs of lower respiratory tract infection (hypoxaemia, dyspnoea, lung infiltrate), central nervous system involvement and/or a significant exacerbation of an underlying medical condition

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People deemed to be at increased risk are those who have one or more of the following:

- Chronic respiratory disease (including asthma that requires continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospital admission OR patients with chronic obstructive pulmonary disease)
- Chronic heart disease
- Chronic renal disease
- Chronic liver disease
- Chronic neurological disease
- HIV infected patients with severe immunosuppression (CD4<200 or <15% of total lymphocytes in adults and children over five; and CD4<500 or <15% of total lymphocytes in a child aged one to five, expert clinical opinion in a child aged under 1)
- Compromised immune system: e.g. current or recent (within 6 months) chemotherapy or radiotherapy, solid organ transplant recipients on immunosuppressive therapy, bone marrow transplant recipients on immunosuppressive therapy or who received it within the last 12 months (longer with graft versus host disease), neutropenic patients, high dose systemic glucocorticosteroids ($\geq 40\text{mg/day}$ for ≥ 1 week in adults and $\geq 2\text{ mg/kg/day}$ for ≥ 1 week in children), and for at least three months after treatment has stopped
- Patients currently or recently (within six months) on other types of immunosuppressive therapy or malignancy
- Diabetes mellitus
- Morbid obesity $\text{BMI} \geq 40$
- Are aged over 65 years
- Pregnant women (including those 2/52 after delivery or miscarriage)
- Children under 6 months of age

The Chief Medical Officer recommends annual immunisation against influenza for individuals belonging to this group.

The purpose of this guideline is to make oseltamivir and zanamivir available within the Trust in defined circumstances when influenza A or B is circulating in the community (as confirmed by the Health Protection Agency) for:

- Treatment of at risk patients aged 1 year and older (see notes below re children under 1 year old)
- Prophylaxis of at risk patients who are not effectively protected by immunisation and who have been exposed to suspected or confirmed influenza case or ili.
- Prophylaxis of staff in the at risk group who are not effectively protected by immunisation and who have been exposed to suspected or confirmed case of influenza or ili.

An ILI is defined as an acute upper respiratory tract infection with fever with or without other symptoms which may include myalgia or cough.

The NICE guidance does not cover the circumstances of a pandemic, impending pandemic or a widespread epidemic of a new strain of influenza to which there is little or no community resistance.

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Consultant virologists are available to recommend whether oseltamivir or zanamivir should be used depending on the circulating strain of influenza, evidence of resistance to individual drugs, the patient's age, whether the patient is pregnant or breast feeding and any other considerations if necessary.

4. Broad recommendations

In the event of the Health Protection Agency declaring that influenza is circulating in the community then at risk groups of patients and staff, who are not immunised against the circulating strain, can be offered prophylaxis. Also under the same circumstances the same group of patients and staff presenting with influenza like illness (ILI) might be considered for treatment after discussion with consultants virologists.

Treatment Recommendations: Adults and Children in Community/A and E with uncomplicated influenza	
Previous healthy people <i>(excluding pregnancy)</i>	No treatment (or oseltamivir PO if physician feels patient is at serious risk of developing serious complications from influenzae- discuss with Consultant Virologist- approval required)
At risk population, including pregnant women	Oseltamivir PO (see below table for dose) <ul style="list-style-type: none"> • Do not wait for laboratory confirmation. Start treatment as soon as possible, ideally within 48 hours of onset. • Use clinical judgement for treatment after 48 hours of onset (discuss with Consultant Virologist). Oseltamivir use is off license in these patients.
Severely Immunocompromised patients	Discuss with Virology and start treatment as soon as possible Oseltamivir is first line unless the dominant circulating strain is influenza A (H1N1) which has a higher risk for developing oseltamivir resistance, in which case, use Zanamivir (INH).
Suspected or confirmed oseltamivir resistant influenza in a patient who requires treatment	Zanamivir INH (see below table for dose) for up to 5 days (liaise with Consultant Virologist)
Severely immunocompromised patients who are unable to administer inhaled zanamivir OR patients with suspected or confirmed oseltamivir resistant influenza but who are unable to administer inhaled zanamivir	Severely immunocompromised: Oseltamivir PO Review frequently to assess response to therapy as at increased risk of developing oseltamivir resistant influenza. Patient with suspected or confirmed oseltamivir resistant infection: Zanamivir nebulised <i>(this is unlicensed - liaise with Consultant Virologist).</i>

All patients with complicated influenza should receive treatment, usually in hospital. Rapid testing for respiratory viruses including influenza virus is recommended for all patients fulfilling the clinical criteria for complicated infection. Treatment should be started as early as possible but should always be given, no matter how long after onset of illness. Do not wait for laboratory confirmation.

Previous influenza immunisation does not exclude influenza.

Duration of therapy depends on clinical response. Test for antiviral resistance in patients who do not respond after 5 days.

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Unlicensed Preparations of Zanamivir:

The following recommendations include the use of IV zanamivir and nebulised aqueous zanamivir which are unlicensed medications and only available on a named patient basis.

They should only be prescribed after liaising with a Consultant Virologist.

Clinicians should therefore make a very careful judgement about the use of unlicensed zanamivir. The clinician prescribing zanamivir as an unlicensed medicine either for use as a nebulised treatment or intravenously, accepts clinical and professional responsibility for their prescribing decision. To obtain a supply the pharmacist or member of clinical team (e.g. doctor or nurse) should contact GSK to obtain the relevant paperwork. [GSK contact details: 0208 990 4855 Freephone: 00800 2468 3579, 24 hours per day, 365 days per year, however hours of dispatch, 8am to 7pm Monday to Friday or 8am -3pm Saturday/Sunday]

Treatment Recommendations: Adults and children in hospital and/or with complicated influenza	
First Line Treatment	<p>Oseltamivir PO or NG (for NG route open capsules, do not use liquid as reserved for pts under 1 year old)</p> <p>There is evidence that PO/NG oseltamivir is adequately absorbed in critical illness at standard doses</p>
Second Line Treatment	<p>Zanamivir <i>If poor response to first line treatment or if poor absorption</i></p> <p>Inhaler: If good respiratory function Nebulised aqueous zanamivir (unlicensed): If poor respiratory function IV Zanamivir (unlicensed): In the following patients</p> <ul style="list-style-type: none"> • Pts who have already failed to respond to nebulised zanamivir • Patients who have developed respiratory conditions affecting nebuliser delivery (e.g. airways disease, pulmonary oedema) • Patients who have multi-organ involvement or are on intensive care
Severely Immunocompromised Patients	<p>1st line treatment: Oseltamivir (PO or NG) unless the dominant circulating strain is influenza A (H1N1). Discuss with a Virologist Start treatment as soon as possible. Arrange influenza A subtype testing and monitor clinical condition closely. If poor clinical response, consider switching to zanamivir and test for oseltamivir resistance If dominant circulating strain is influenza A (H1N1) – use Zanamivir (INH or NEB) Inhaler: If good respiratory function Nebulised aqueous zanamivir (unlicensed): If poor respiratory function IV Zanamivir (unlicensed): In the following patients</p> <ul style="list-style-type: none"> • Pts who have already failed to respond to nebulised zanamivir • Patients who have developed respiratory conditions affecting nebuliser delivery (e.g. airways disease, pulmonary oedema) • Patients who have multi-organ involvement or are on intensive care
Suspected or confirmed oseltamivir resistance e.g. contact of known oseltamivir resistant case	<p>Zanamivir (do not use oseltamivir) Inhaler: If good respiratory function Nebulised aqueous zanamivir (unlicensed): If poor respiratory function IV Zanamivir (unlicensed): In the following patients</p> <ul style="list-style-type: none"> • Pts who have already failed to respond to nebulised zanamivir • Patients who have developed respiratory conditions affecting nebuliser delivery (e.g. airways disease, pulmonary oedema) • Patients who have multi-organ involvement or are on intensive care

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Treatment	Premature (less than 36 weeks post conceptual age)	0-12 months (36 weeks post conceptual age or greater)	>1-12 years : Dose according to weight below				Adults (13 years and over)*
			≤15kg	>15-23kg	>23-40kg	>40kg	
Oseltamivir PO (treatment course: 5 days)	1mg/kg/dose BD (unlicensed)	3mg/kg/dose BD	30mg BD	45mg BD	60mg BD	75mg BD	75mg BD
Zanamivir INH (treatment course: 5 days)	Not licensed for children <5 years old Children >5 years: 10mg BD						10mg BD

*If a person in this age group weighs 40kg or less, it is suggested that the >23-40kg dose for those aged >1-12 years is used.

Children <1 year old

Oseltamivir oral suspension (6mg/ml) should be used for *children under the age of one ONLY*. This is an off label use of oseltamivir but is supported by the BNF for children. Discuss with a Consultant Virologist before initiating.

Children >1 year old, adults with swallowing difficulties, patients with a NG tube

Open capsules and mix into small amount (1 teaspoon max) of strong flavoured sweetened food (i.e. yoghurt, chocolate sauce, honey, sugar)

The oral suspension should not be used for these patients as if it is, there may be insufficient quantities for children under 1 year old.

Special Patient Groups

Pregnancy

- Treatment - Oseltamivir is the first line option for the vast majority of pregnant women with influenza, including during seasons dominated by influenza A (H1N1). For pregnant women who meet additional criteria for requiring zanamivir first line, further assessment (i.e. rapid diagnostics) and antiviral treatment should be discussed with a Consultant Virologist

Do not wait for laboratory confirmation. Treatment should be started as soon as possible, ideally within 48 hours of onset. There is evidence that treatment may reduce the risk of severe illness up to five days after onset. Treatment after 48 hours is an off-label use of oseltamivir and clinical judgement should be exercised

Breastfeeding

- For Oseltamivir PO and Zanamivir (via any route) the overall consensus is that treatment with either drug is not a reason to discontinue, or put limitations on, breastfeeding full-term or pre-term infants. Due to the very small amounts transferred into breast milk, and the limited oral bioavailability of either drug, the benefits of breastfeeding are considered to outweigh any, albeit unidentified, risks.

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- The breastfed infant should be monitored for vomiting and diarrhoea. If an infant being breastfed by the mother receiving oseltamivir or zanamivir needs direct treatment or chemoprophylaxis, the recommended dose of oseltamivir or zanamivir for infants should be given.

Dosing for extremes of weight

Oseltamivir: No dose adjustment is needed in obese patients

Inhaled or nebulised zanamivir: No dose adjustment is needed in obese patients

IV zanamivir: for adult patients (and adolescents with actual body weight 50kg or greater) the dose is not weight adjusted (in adolescents with actual body weight less than 50kg and in children, the dose is weight adjusted – refer to the physicians guide provided with the medication)

Patients with renal dysfunction

Recommended oseltamivir treatment dosing in relation to renal function (adults and those aged 13 years and over)

CrCl (mL/min)	Oseltamivir PO Treatment for 5 days
>60mL/min	75mg BD
31-60mL/min	30mg BD
11-30mL/min	30mg OD
≤10mL/min	30mg ONCE
Haemodialysis (HD)	30mg ONCE and then 30mg after every HD session
Peritoneal dialysis	30mg ONCE
Haemo(dia)filtration 1—1.8L/hr exchange rate	30mg OD
Haemo(dia)filtration 1.9-3.6L/hr exchange rate	30mg BD
Haemo(dia)filtration >3.6L/hr exchange rate	75mg BD

Adult zanamivir IV dosing in relation to renal function

CrCl (mL/min)	Dose
≥ 80mL/min OR Haemo(dia)filtration >4.7L/hr exchange rate	Initial dose: 600mg And 12 hours later, maintenance dose:600mg BD
50-79 OR Haemo(dia)filtration 3.0-4.7L/hr exchange rate	Initial dose: 600mg And 12 hours later, maintenance dose:400mg BD
30-49 OR Haemo(dia)filtration 1.8-2.9L/hr exchange rate	Initial dose: 600mg And 12 hours later, maintenance dose:250mg BD
15-29 OR Haemo(dia)filtration 1-1.7L/hr exchange rate	Initial dose: 600mg And 24 hours later, maintenance dose: 150mg BD
<15	Initial dose: 600mg And 48 hours later, maintenance dose: 60mg BD

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The required dose of IV zanamivir should be diluted in a convenient volume of 0.9% sodium chloride solution and administered over approximately 30 minutes.

Patients with hepatic dysfunction

Oseltamivir – standard dosing

Zanamivir INH (Diskhaler®) – standard dosing

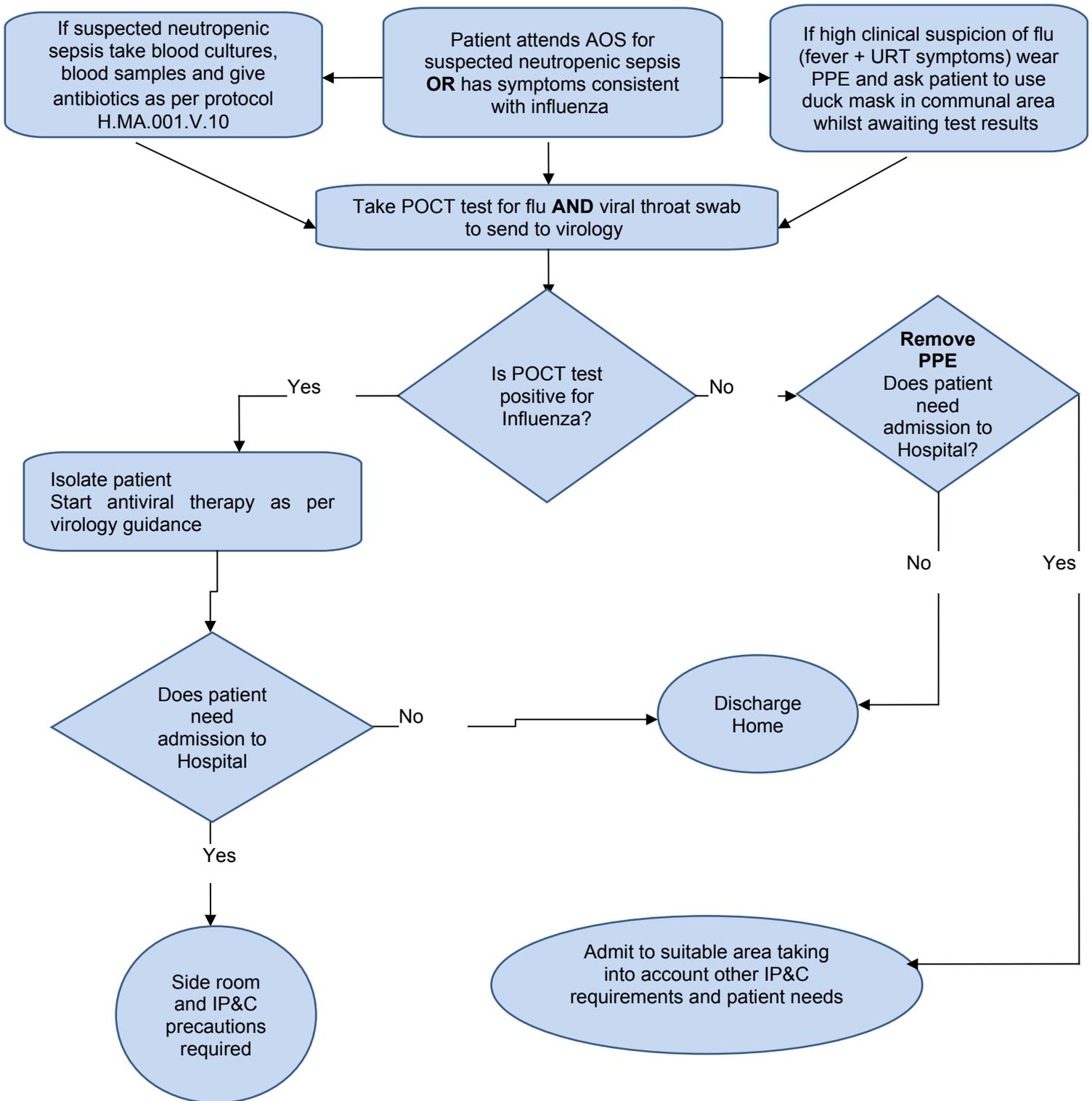
Zanamivir solution IV/NEB – refer to the physicians guidance document supplied by the manufacturer with the medication

Management of influenza in Critical Care

The principles are the same as for complicated influenza. The first line therapy remains PO/NG oseltamivir and there is evidence that standard dose oseltamivir PO or NG is adequately absorbed even in critical illness. Increasing the dosage is no longer recommended in patients who are severely ill with influenza A due to a lack of evidence that it is any more effective. Specialist advice should be sought for dosage of patients critically ill with influenza B. Zanamivir should be used when there is suspected poor gastrointestinal absorption or failure to respond to oseltamivir. In intensive care, zanamivir should be given intravenously for situations such as multi-organ failure. A consultant Virologist should be involved in the care of these patients.

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Oncology/Haematology patients with suspected Influenza



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Post Exposure Prophylaxis

Prophylaxis should be issued if the contact is not adequately protected by the vaccine, that is

- The vaccination is not well matched to the circulating strain, or
- There has been less than 14 days between vaccination and date of first contact with influenza.
- The individual has been exposed as part of a localised outbreak (such as in a care home), antiviral prophylaxis may be given regardless of vaccination status.

Prophylaxis is normally not considered in at risk groups who have been vaccinated against seasonal influenza at least 14 days before exposure with the above exceptions. Clinicians may reconsider this in extenuating circumstances such as for older persons in a season dominated by influenza A (H3N2) or in the immunosuppressed, as seasonal influenza vaccination may be less effective in these situations. However such use is outside NICE recommendations and would be a matter of individual clinical judgement.

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	If identified strain in index case or dominant circulating strain is lower risk for oseltamivir resistance e.g. influenza A (H3N2), influenza B	If identified strain in index case or dominant circulating strain is known to higher risk for oseltamivir resistance e.g. influenza A (H1N1)	Exposed to suspected or confirmed oseltamivir resistant influenza
Previously healthy (excluding pregnant women)	No prophylaxis	No prophylaxis	No prophylaxis
At risk of complicated influenza (including pregnant women but excluding severely immunocompromised patients and children under 5 years)	Oseltamivir PO od 10 days If therapy can be started within 48 hours of last contact. After 48 hours on advice of Consultant Virologist Only	Oseltamivir PO od 10 days If therapy can be started within 48 hours of last contact. After 48 hours on advice of Consultant Virologist Only	Zanamivir INH od 10 days If therapy can be started within 36 hours of last contact. After 36 hours on advice of Consultant Virologist Only
Severely immunosuppressed patients (excluding children under 5 years)	Oseltamivir PO od 10 days If therapy can be started within 48 hours of last contact. After 48 hours on advice of Consultant Virologist Only	Zanamivir INH od for 10 days if therapy can be started within 36 hours of last contact. After 36 hours on advice of Consultant Virologist Only If unable to administer Zanamivir INH Oseltamivir PO od 10 days If therapy can be started within 48 hours of last contact. After 48 hours on advice of Consultant Virologist Only	Zanamivir INH od 10 days if therapy can be started within 36 hours or last contact. After 36 hours on advice of Consultant Virologist Only If unable to administer zanamivir INH, discuss with Consultant Virologist and consider nebulised aqueous zanamivir (unlicensed) after individual risk assessment.
Children under 5 years in at risk groups including severely immunocompromised children	Oseltamivir PO od 10 days If therapy can be started within 48 hours of last contact. After 48 hours on advice of Consultant Virologist Only	Oseltamivir PO od 10 days If therapy can be started within 48 hours of last contact. After 48 hours on advice of Consultant Virologist Only	Discuss with Consultant Virologist Consider nebulised aqueous zanamivir (unlicensed) after individual risk assessment.

Prophylaxis	Premature (less than 36 weeks post conceptual age)	0-12 months (36 weeks post conceptual age or greater)	>1-12 years : Dose according to weight below				Adults (13 years and over)*
			≤15kg	>15-23kg	>23-40kg	>40kg	
Oseltamivir PO (prophylaxis course: 10 days)	See below [∞]	3mg/kg OD	30mg OD	45mg OD	60mg OD	75mg OD	75mg OD
Zanamivir INH prophylaxis course: 10 days	Not licensed for children <5 years old Children ≥5 years: 10mg OD						10mg OD

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Although it may be possible to provide half the treatment frequency each day for 10 days for premature infants, there is currently no publicly available dosing information for oseltamivir prophylaxis in pre-term infants and so is outside the product license.

*If a person in this age group weighs 40kg or less, it is suggested that the >23-40kg dose for those aged >1-12 years is used.

Children <1 year old

Oseltamivir oral suspension (6mg/ml) should be used for *children under the age of one ONLY*. This is an off label use of oseltamivir but is supported by the BNF for children. Discuss with a Consultant Virologist before initiating.

Children >1 year old, adults with swallowing difficulties, patients with a NG tube

Open capsules and mix into small amount (1 teaspoon max) of strong flavoured sweetened food (i.e. yoghurt, chocolate sauce, honey, sugar)

The oral suspension should not be used for these patients as if it is, there may be insufficient quantities for children under 1 year old.

Oseltamivir prophylaxis dosing in renal impairment

CrCl (mL/min)	Oseltamivir PO prophylaxis for 10 days
>60mL/min	75mg OD
31-60mL/min	30mg OD
11-30mL/min	30mg every 48 hours
≤10mL/min	30mg ONCE, repeated after 7 days
Haemodialysis (HD)	30mg ONCE and then 30mg after each HD session
Peritoneal dialysis	30mg ONCE, repeated after 7 days
Haemo(dia)filtration 1-1.8L/hr exchange rate	30mg every 48 hours
Haemo(dia)filtration 1.9-3.6L/hr exchange rate	30mg OD
Haemo(dia)filtration >3.6L/hr	75mg OD

No difference in prophylaxis dosing for high flu and low flux intermittent haemodialysis (HD) is recommended due to a lack of published clinical data on oseltamivir carboxylate levels in high-flux intermittent HD patients; this advice is expert opinion based on information on pore size, OC molecule size and likely length of HD sessions.

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5. Clinical Audit Standards derived from guideline

Audit standards can be derived from the NICE technology appraisal documents on which this guideline is based.

Treatment standards: -

Oseltamivir should be prescribed first line for at-risk “patients” with ILI and therapy should start within 48 hours of symptom onset.

Zanamivir should be prescribed second line, however in severely immunocompromised it is the preferred option as well as for those at-risk patients with ILI where oseltamivir is contraindicated. Therapy should start within 36 hours of symptom onset (children) and 48 hours of onset (adults).

Oseltamivir or zanamivir are not to be used in patients who are not at risk. Patients with risk factors for severe infection who are not improving may benefit from treatment even if the onset >48 hours. Such cases should be discussed with a virologist.

Prophylaxis standards: -

Oseltamivir offered to all at risk patients aged 1 year and over within 48 hours of exposure OR zanamivir is offered to all at-risk patients aged 5 and over within 36 hours of exposure.

Oseltamivir or Zanamivir is offered to staff who are in the at risk category, who have not been immunised with influenza vaccine if they come into direct contact with patients with ILI, as advised by a consultant virologist

6. Summary of development and consultation process undertaken before registration and dissemination

The authors listed above on behalf of the Antibiotic subgroup of the Drugs & Therapeutics Committee, which has agreed the final content, drafted the guideline in support of a formulary application for oseltamivir. During its development and the formulary application they have been circulated for comment to: Virology Department, Pharmacy Department, Microbiology Department, Infection control Committee, Occupational Health, Paediatric Department and the Drugs & Therapeutics Committee.

This version is endorsed by the Virology Department and the Drugs & Therapeutics Committee.

7. Distribution list/ dissemination method

All medical staff via NNUH intranet
All pharmacists via Caroline Hallam
All virology and microbiology staff via Samir Dervisevic

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8. References/ source documents

- PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza, October 2018
- HPA guidance on use of antiviral agents for the treatment and prophylaxis of influenza 12 December 2011 Version 3 Reviewed October 2012
http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317131466016
- NICE technology Appraisal No 168 (February 2009) –Amantadine, oseltamivir and zanamivir for the treatment of influenza.
- Influenza Season 2010/11-Use of Antivirals, DOH, Gateway reference:15274, 10 December 2010
- NICE Technology Appraisal No 158 (September 2008) – Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza.
- DOH guidance (June 2009) Pandemic Influenza, Recommendations on the use of antiviral medicines for pregnant women, women who are breastfeeding and children under the age of one year.
- Updated Interim Recommendations on the use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 season. Centers for Disease Control and Prevention
- Summary of Product Characteristics. Relenza 5mg/dose inhalation powder last updated 21/10/2009, accessed via Electronic Medicines Compendium 5/1/10
- H1N1 winter flu: Urgent advice for providers of maternity services. 17th December 2010. Department of Health, Royal College of Obstetricians and Gynaecologists

9. Key Contact Numbers

Virology Department: 01603 288587. Out of hours a consultant virologist can be contacted via switchboard.

Occupational Health: Extn 3035

Infection Control: Extn 5847

Medicines Information: Bleep 0500

10. Version Information

Version No	Updated By	Updated On	Description of Changes
JCG0328v1	THCGAP	01/10/2014	Change of header and footer to joint hospital version. On JPUH version changes to contact details.
JCG0328v2	Author	15/12/2016	Reviewed, minor amendments
JCG0328v3	Author	01/11/2017	Updated in line with PHE guidance on use of Antiviral agents for the treatment and prophylaxis of seasonal influenza version 8.0 September 2017
JCG0328v3.1	Author	15/01/2018	Reviewed, minor updates
JCG0328v3.2	Author	22/01/2018	Addition of flowchart