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Procedural Guidelines for the Treatment and Prophylaxis of Suspected Influenza in In-Patient Units

1. Introduction

1.1 This Procedural Guideline reflects Public Health England (PHE) recommendations on Antiviral prophylaxis and treatment of influenza (PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza Version 7.0, October 2016 and the PHE Winter Flu Plan 2017-18) as well as NICE guidance on treatment and prophylaxis.

1.2 It is intended as a prescribing and administration guide for those clinicians who find themselves faced with the possibility of an influenza outbreak on an inpatient ward within the Trust. Clinicians may wish to seek specialist advice about the use of antiviral medicines from local infection specialists for an individual patient.

1.3 Antiviral medicines may be prescribed at any time on an inpatient ward for at risk patients with suspected seasonal influenza infection.

1.4 The Trust recognises that in following these Procedural Guidelines then staff prescribing and administering antiviral medicines may be acting outside of NICE guidance on antivirals and the Product Licences for these medicines.

2. Scope of this Procedural Document in Prophylaxis and Treatment

2.1 This Procedural Guideline is intended for use in Trust In-Patient units for the management of any at risk patient where influenza is suspected or confirmed at any time.
NB: Patients treated within the community setting should follow the advice of the CMO letter concerning circulating influenza.

2.2 Treatment of Complicated influenza usually requires acute hospital admission and is outside of the scope of this guideline.

2.3 The use of Zanamivir is outside of the scope of this guideline as inhaled zanamivir via Diskhaler may not be an effective delivery route in some patients, such as those with severe underlying respiratory disease. Patients for whom oseltamivir is contraindicated should be treated on an individual clinical basis with referral to acute hospital as required.

2.4 Refer to the PHE Guidance for further information on:

- Complicated influenza
- Patients with Severe immunosuppression
- suspected or confirmed Oseltamivir resistant influenza

3. Definitions

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

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

- **At-risk population**: those individuals with any of the following:
- Neurological, hepatic, renal, pulmonary and chronic cardiac disease.
- Diabetes mellitus.
- Severe Immunosuppression.
- Age over 65 years.
- Pregnancy (including up to two weeks postpartum)
- Children under 6 months of age
- Morbid obesity (BMI >=40).

Severe immunosuppression

Examples of severe immunosuppression relevant to this guidance are given below. Degrees of immunosuppression are difficult to quantify and individual variation exists, therefore this list is not comprehensive.

a. Severe primary immunodeficiency.
b. Current or recent (within six months) chemotherapy or radiotherapy for malignancy.
c. Solid organ transplant recipients on immunosuppressive therapy.
d. Bone marrow transplant recipients currently receiving immunosuppressive treatment, or within 12 months of receiving immunosuppression.
e. Patients with current graft-versus-host disease.
f. Patients currently receiving high dose systemic corticosteroids (equivalent to ≥40 mg prednisolone per day for >1 week in an adult, or ≥ 2mg/kg/day for ≥1 week in a child), and for at least three months after treatment has stopped.
g. HIV infected patients with severe immunosuppression (CD4<200/µl or <15% of total lymphocytes in an adult or child over five; CD4< 500/µl or <15% of total lymphocytes in a child aged one to five; expert clinical opinion in a child aged under one).
h. Patients currently or recently (within six months) on other types of highly immunosuppressive therapy or where the patient's specialist regards them as severely immunosuppressed.

Some influenza subtypes are associated with a greater risk of developing oseltamivir resistance. The risk of resistance is greatest in people who are severely immunosuppressed. The selection of first line antivirals in severely immunosuppressed individuals should take account of the subtype of influenza causing infection, or if not yet known, the dominant strain of influenza that is circulating during the current influenza season. **Therefore, patients with severe immunosuppression should be admitted to acute hospital care.**

4. Formulary

The following medicines may be held in stock in some In-patient units for Influenza treatment and prophylaxis (check if this is the case for your ward/unit):

- Oseltamivir 75mg and 30mg Capsules;
- Oseltamivir Oral suspension, 30mg in 5mL for infants under one year only.

- Where a patient has swallowing difficulties or an enteral tube in situ, capsules can be opened and the contents mixed with a small amount of sweetened food, such as sugar water or chocolate syrup, just before administration.

5. Treatment of Suspected or Confirmed Uncomplicated Influenza (except severely immunosuppressed patients)

For the at risk population, including pregnant women:

Patient Type	Weight (kg)	Dose	Frequency	Duration
Adults and children aged 13 years and over with normal renal function	Not applicable	75mg	Twice daily	5 days
Children aged 1 to 12 years	10 to 15 kg	30mg	Twice daily	5 days
	> 15 to 23kg	45mg	Twice daily	5 days
	> 23 to 40kg	60mg	Twice daily	5 days
	> 40kg	75mg	Twice daily	5 days
Infants aged 0 to 12 months	Not applicable	3mg/kg/dose	Twice daily	5 days

- **Note: Dose adjustment may be necessary for patients with impaired renal function – see Table 1, section 8.**
- Do not wait for laboratory confirmation.
- Start treatment as soon as possible, and within 48 hours of onset. (Or later at clinical discretion - there is limited evidence that treatment may reduce the risk of mortality up to five days after onset. Commencement of treatment more than 48 hours after onset is an unlicensed use of Oseltamivir and clinical judgement should be exercised).
- See Table 1, section 8 below for dosage adjustment in renal dysfunction
- Prescribe medication on *Influenza Outbreak Treatment Prescription & Administration Record Chart for In-Patient Units* or *Influenza Outbreak Prophylaxis (Prevention) Prescription & Administration Record Chart for In-Patient Units* as applicable. (see appendices 1 and 2)

6. Treatment of complicated influenza or severely immunosuppressed patient – admit to Acute Trust

7. Post-Exposure Prophylaxis of Suspected or confirmed Influenza Contact cases

For patients at risk of complicated influenza (but excluding severely immunosuppressed patients) NB: Therapy must be started within 48 hours of last contact

Patient Type	Weight (kg)	Dose	Frequency	Duration
Adults and children aged 13 years and over with normal renal function	Not applicable	75mg	Once daily	10 days

Children aged 1 to 12 years	10 to 15 kg	30mg	Once daily	10 days
	> 15 to 23kg	45mg	Once daily	10 days
	> 23 to 40kg	60mg	Once daily	10 days
	> 40kg	75mg	Once daily	10 days
Infants aged 0 to 12 months	Not applicable	3mg/kg/dose	Once daily	10 days

- **Note: Dose adjustment may be necessary for patients with impaired renal function – see Table 1, section 8.**
- Previous influenza immunisation does not preclude post exposure prophylaxis(1).
- Exposure to an influenza-like illness is defined as close contact with a person in the same household or residential setting who has had recent symptoms of influenza (3)
- Consider consulting the local Health Protection Team.
- See below for dosage adjustment in renal dysfunction

8. Dosage Adjustments in Renal Dysfunction

8.1 The choice of dose in renal failure is complicated by the different measures available to describe degree of renal impairment, as well as a lack of specific data in some circumstances. CrCl is used in this document as it is a more accurate measure upon which to make dosing recommendations and is congruent with the manufacturers prescribing information for oseltamivir. The limitations for using eGFR are described in the British National Formulary (Prescribing in renal impairment: BNF). CrCL can be estimated in adults by utilising the Cockcroft and Gault equation (See 8.2). Both eGFR and CrCL (using Cockcroft and Gault) assume the patient's renal function is stable. Clinical judgement will be required where renal function is unstable (i.e. in acute renal failure).
It is recognised that eGFR may be more readily available at the outset of therapy. If this is the only value available then do not delay therapy and prescribe a dose according to eGFR (substituting eGFR for the CrCL figure in the following tables).

Table 1

adults and adolescents aged 13 years and over	**Oseltamivir oral** ***Treatment - 5 Days***	**Oseltamivir oral** ***Prophylaxis – 10 Days***
Moderate impairment (CrCL 30-60 mL/min)	30mg BD	30mg OD
Severe impairment (CrCL 10-30mL/min)	30mg OD	30mg every 48 hours
Established renal failure (CrCL <10mL/min)	Not recommended	Not recommended
Haemodialysis	30 mg after each haemodialysis session	30 mg after every second haemodialysis session
Peritoneal dialysis	30mg once	30mg once weekly

For children aged 0-12 years with renal dysfunction, seek specialist advice.

8.2 Cockcroft and Gault Equation:

Renal Function expressed as Creatinine Clearance (CrCl) can be calculated using the Cockcroft and Gault Formulation:

$$\text{Estimated Creatinine Clearance in mL/min)} = \frac{(140\text{-Age}) \times \text{Weight} \times \text{Constant}}{\text{Serum Creatinine}}$$

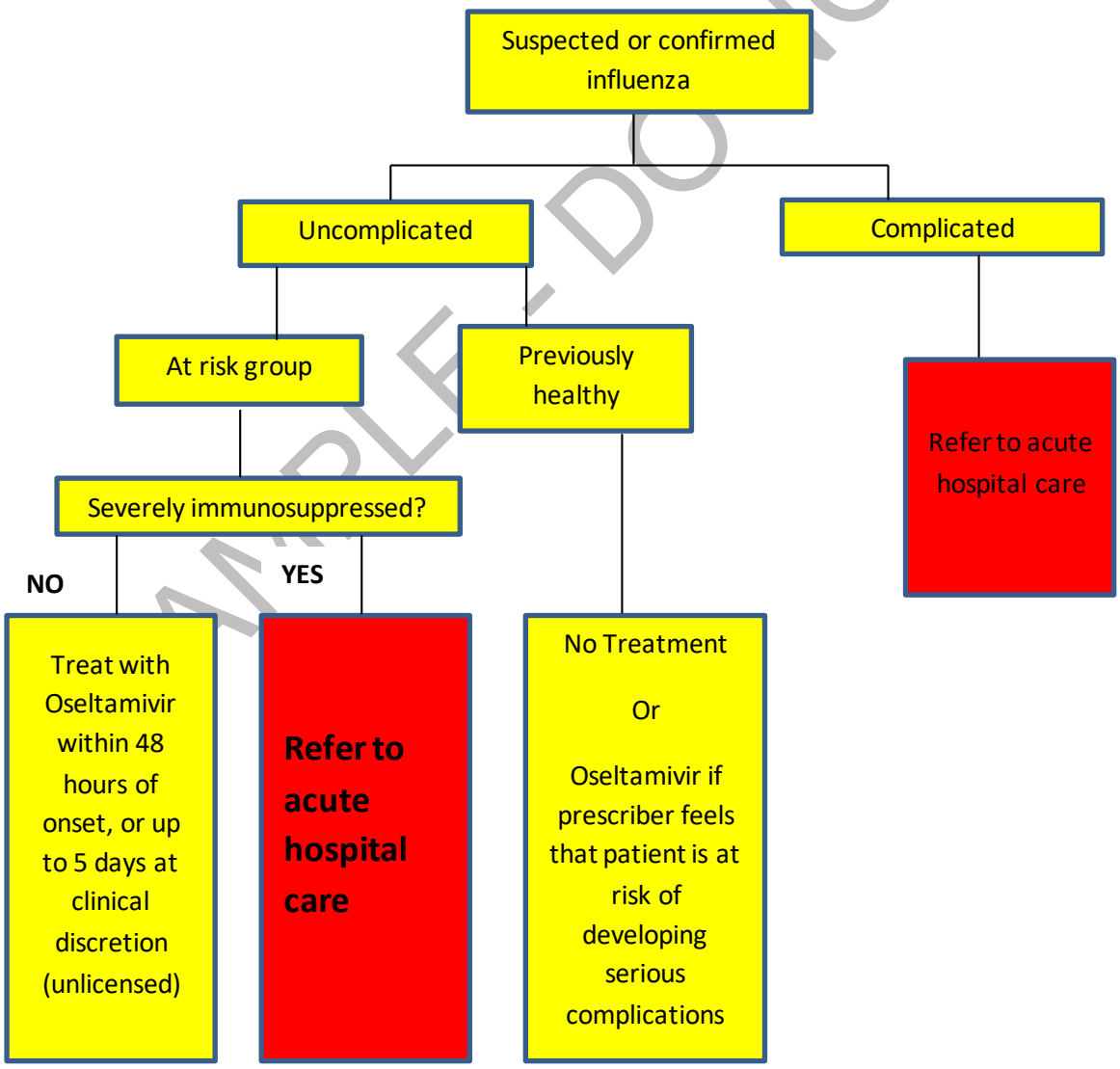
•Age in years

•Weight in kilograms; use ideal body-weight

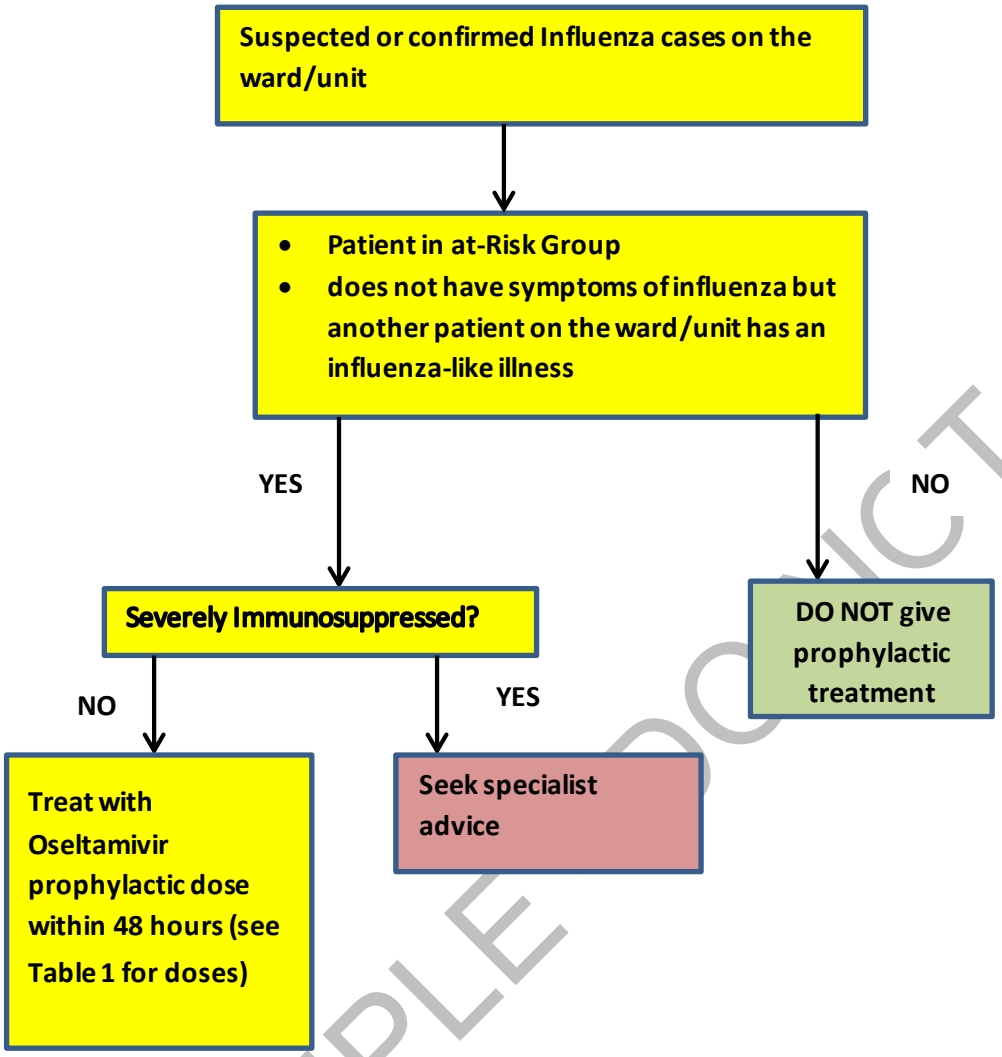
•Serum creatinine in micromol/litre

•Constant = 1.23 for men; 1.04 for women

8.3 Treatment of suspected or confirmed influenza in In-Patient Wards/Units



8.4 Prophylactic antiviral treatment following a suspected or confirmed influenza cases on an In-Patient Unit.



9. References

1. Public Health England. PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza Version 7.0, October 2016 Available at https://www.gov.uk/government/publications/influenza-treatment-and-prophylaxis-using-anti-viral-agents [Accessed 5.5.17]
2. Public Health England. Flu Plan Winter 2017-18. PHE publications gateway number: 2016697 March 2017. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/600532/annual_flu_plan_2017to2018.pdf [Accessed 6.5.17]

3. NICE technology appraisal guidance 168: Amantadine, Oseltamivir and Zanamivir for the treatment of influenza. Issued: February 2009. Viewed 30 July 2014 http://www.nice.org.uk/guidance/ta168/resources/guidance-amantadine-oseltamivir-and-zanamivir-for-the-treatment-of-influenza-pdf

4. NICE technology appraisal guidance 158: Oseltamivir, amantadine (review) and Zanamivir for the prophylaxis of influenza: Issued: September 2008. Viewed 30 July 2014 http://www.nice.org.uk/guidance/ta158/resources/guidance-oseltamivir-amantadine-review-and-zanamivir-for-the-prophylaxis-of-influenza-pdf

5. Summary of Product Characteristics: Tamiflu® 30 mg and 45 mg Hard Capsules Roche Products Ltd. Updated 18.1.2017. Available at: http://www.medicines.org.uk/emc/medicine/20294 and Tamiflu® 6 mg/ml Powder for Oral Suspension. Roche Products Ltd. Updated 18.1.2017 http://www.medicines.org.uk/emc/medicine/26927 [Accessed 6.5.17]

6. Joint Formulary Committee. British National Formulary. April 2017. Available at: https://www.medicinescomplete.com/mc/bnf/current/PHP3896-oseltamivir.htm?q=Oseltamivir&t=search&ss=text&tot=10&p=1#_hit [Accessed 6.5.17]

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Appendix 1

Influenza Outbreak Treatment Prescription & Administration Record Chart For In-Patient Units

This chart is intended for **treatment of influenza** in this patient if both criteria 1 and 2 apply.

	☑
1. Those who have **one or more** of the following:	
• chronic respiratory disease (including asthma and chronic obstructive pulmonary disease	☐
• chronic heart disease	☐
• chronic renal disease	☐
• chronic liver disease	☐
• chronic neurological conditions	☐
• diabetes mellitus	☐
• aged 65 years or older	☐
• immunosuppressed (not severely)	☐
• pregnancy	☐
• obesity (BMI ≥ 40)	☐
• children under 6 months of age	☐
2. The patient presents with an influenza-like illness and can start treatment ideally **within 48 hours, or up to 5 days (unlicenced), of the onset of symptoms**	☐

Drug Allergies a Sensitivities

None known

Signed ..... Date .....

yes

Signed ..... Date .....

This Section Must be Completed

Drug / Allergen:	Description of Reaction:

NHS no: _____

Surname: _____

First name: _____

Address: _____

_____

Date of birth: _____

Height (m)	Weight (kgs)

Addressograph

Prescription & Direction				**Administration Records**						
Oseltamivir	capsules ☐ oral suspension ☐	Time to administer		Day	1	2	3	4	5	Stop
Dosage as per protocol / BNF	**……mg Twice daily**			Date						
Duration 5 days – **Do not start** treatment if more than 5 days after onset of symptoms				Signature						
Prescriber's signature				Signature						
Date to start										

- **Antimicrobial Stewardship note: Do not omit any administration of doses**

Attach this chart to the principal medicines Prescription & Administration Record chart

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Appendix 2
Influenza Outbreak Prophylaxis (Prevention) Prescription & Administration Record Chart For In-Patient Units

This chart is intended for **prophylaxis (prevention) of influenza** in this patient if **all** the following circumstances apply: Tick the circumstances that apply:

	☑
Those who have **one or more** of the following: • chronic respiratory disease (including asthma and chronic obstructive pulmonary disease • chronic heart disease • chronic renal disease • chronic liver disease • chronic neurological conditions • diabetes mellitus • aged 65 years or older • immunosuppressed (not severely) • pregnancy • obesity (BMI ≥ 40) • children under 6 months of age	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
• The patient presents with an influenza-like illness and can start treatment **within 48 hours of contact with the index case, or after 48 hours on specialist advice only**	☐

Drug Allergies a Sensitivities

None known
Signed ..... Date .....

yes
Signed ..... Date .....

Drug / Allergen:	Description of Reaction:

This Section Must be Completed

NHS no: _____
Surname: _____
First name: _____
Address: _____
_____
Date of birth: _____

Height (m)	Weight (kgs)

Addressograph

Prescription & Direction		
Oseltamivir	capsules ☐ oral suspension ☐	
Dosage as per protocol / BNF	**……mg Once daily**	Time to administer
Duration 10 days		
Prescriber's signature		
Date to start		

Administration Records											
Day	1	2	3	4	5	6	7	8	9	10	Stop
Date											
Signature											

- **Do not start** treatment if more than if more than 48 hours after contact with infected person, unless on specialist advice
- **Antimicrobial Stewardship note: Do not omit any administration of doses**

Attach this chart to the principal medicines Prescription & Administration Record chart