1. Introduction

This guideline provides information on the recommended antiviral treatment and post exposure prophylaxis regimens for confirmed influenza. During the COVID-19 pandemic, it is anticipated that patients presenting with flu like symptoms are more likely to have COVID-19 than influenza therefore routinely prescribing empirical treatment prior to confirmation of influenza is not currently recommended.

2. Scope

This guideline is intended for use by all clinical staff who care for adult patients and applies to all patients that have confirmed infection with influenza. It also covers adult patients who have been exposed to influenza whilst an inpatient.

3. Recommendations, Standards and Procedural Statements

3.1 Definitions for use in the management of influenza

- **Uncomplicated influenza**: Influenza presenting with fever, coryza, generalised symptoms (headache, malaise, myalgia, arthralgia) and sometimes GI 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 UHL, influenza is considered complicated in paediatric patients if there is risk factors for complicated influenza, the patient requires HDU level care or has CNS involvement

- **Risk factors for complicated influenza in adults**: This list is not exhaustive and prescribers may wish to refer to *the Green Book* [2] for further information:
    - Pregnancy (including up to two weeks post-partum).
    - Age over 65 years
    - Chronic cardiac, pulmonary, renal, hepatic or neurological disease.
    - Diabetes mellitus
    - Morbid obesity (BMI ≥40)
    - Severe immunosuppression (see below)

- **Severe immunosuppression**: Prescribers should apply clinical judgement to take into account the risk of influenza exacerbating any underlying disease that a patient may have, as well as the risk of serious illness from influenza itself. Examples of severe immunosuppression relevant to this guidance are:
    - Severe primary immunodeficiency.
    - Current or recent (within six months) chemotherapy or radiotherapy for malignancy.
    - Solid organ transplant recipients on immunosuppressive therapy.

- Bone marrow transplant recipients currently receiving immunosuppressive treatment, or who received it within the last 12 months
- Patients with graft-versus-host-disease
- Patients currently receiving high dose systemic corticosteroids (equivalent to ≥40mg prednisolone per day for ≥1 week in an adult) and for at least three months after treatment has stopped.
- Patients currently or recently (within six months) on other types of immunosuppressive therapy where the patient's specialist regards them as severely immunosuppressed.
- HIV infected patients with severe immunosuppression (CD4 <200/µl or <15% of total lymphocytes in adult.

3.2 Choice of antivirals for TREATMENT of confirmed influenza

Consider prescribing the antiviral treatment for patients with confirmed influenza.
If confirmed COVID-19 negative and influenza is suspected consider empirical treatment in patients with complicated disease or who are in an at risk group.

Severity of disease	Patient factors	Severely immunosuppressed?	Recommended Treatment
Uncomplicated	Previously Healthy and not in an at risk group	n/a	**No treatment** Or enteral oseltamivir BD for 5 days if patient at serious risk of developing complications. In children, discuss with consultant and consider treatment if lower respiratory tract involvement.
	At risk group	No	**Enteral oseltamivir BD for 5 days** if therapy can be started within 48 hours of symptom onset; or after 48 h on specialist advice only
	At risk group and non-H1N1 subtype confirmed	Yes	**Enteral oseltamivir BD for 5 days** Consider switching to second line zanamivir 10mg inhaled** BD for 5 days if there is poor clinical response, poor gastrointestinal absorption.
	At risk group and H1N1 subtype confirmed	Yes	**Zanamivir 10mg inhaled** BD for 5 days**
Complicated Refer to section 3.1 for definition Includes all adult patients hospitalised for treatment of Influenza	All patients	Yes or No	**Enteral oseltamivir BD for 5 days** Consider switching to second line zanamivir 10mg inhaled** BD for 5 days if there is poor clinical response, poor gastrointestinal absorption, or if subtype testing confirms H1N1.

Prescribing notes:

- Where doses are not stated follow the usual dose recommended in BNF or BNFC. Note - dose adjustment of oseltamivir may be needed in patients with renal impairment
- Zanamivir dry powder for inhalation (Relenza® Diskhaler®) must never be made into a nebuliser solution or administered to a mechanically ventilated patient.
- Patients given zanamivir for confirmed influenza should complete the zanamivir course regardless of whether a non-H1N1 strain is identified, or the strain in shown to be oseltamivir sensitive.
- Higher doses are not recommended in critical care patients with influenza A due to a lack of evidence that it is any more effective. Virology advice should be sought for dosing in critically ill patients with influenza B.
- Influenza treatment can be used in pregnancy and breast feeding. Speak to your pharmacist for more information.
- If the patient is not responding to treatment: Discuss the case with virology for advice regarding on-going management. In complicated influenza, treatment may still be beneficial if started beyond 48 hours and if continued for up to 10 day.

3.3 Choice of antivirals for POST-EXPOSURE PROPHYLAXIS

Inpatients that have been exposed to influenza should be assessed for their need for post-exposure prophylaxis.

Outbreaks within hospital settings warrant consideration of post-exposure prophylaxis, regardless of patient vaccination status.

Where continuous or repeated exposure to influenza is likely occur discuss with virology/microbiology.

Patient factors	Index case is known to be lower risk for oseltamivir resistance (eg influenza A (H3N2) or influenza B)	Index case is influenza H1N1	Index case is confirmed or suspected to be oseltamivir resistant
Previously Healthy	No prophylaxis	No prophylaxis	No prophylaxis
At risk of complicated influenza	**Oseltamivir orally once daily for 10 days** if therapy can be started within 48 h of last contact; or after 48 h on specialist advice only	**Oseltamivir orally once daily for 10 days** if therapy can be started within 48 h of last contact; or after 48 h on specialist advice only	**Zanamivir 5 mg dry powder inhaler, TWO puffs (10 mg) inhaled ONCE DAILY for 10 days** if therapy can be started within 36 h of last contact; or after 36 h on specialist advice only
Severely Immunosuppres-sed patients	**Oseltamivir orally once daily for 10 days** if therapy can be started within 48 h of last contact; or after 48 h on specialist advice only	**Zanamivir 5 mg dry powder inhaler, TWO puffs (10 mg) inhaled ONCE DAILY for 10 days** if therapy can be started within 36 h of last contact; or after 36 h on specialist advice only. If unable to administer zanamivir inhaler, **Oseltamivir orally once daily for 10 days** if therapy can be started within 48 h of last contact; or after 48 h on specialist advice only	**Zanamivir 5 mg dry powder inhaler, TWO puffs (10 mg) inhaled ONCE DAILY for 10 days** if therapy can be started within 36 h of last contact; or after 48 h on specialist advice only If unable to administer zanamivir inhaler, monitor closely contact virologist promptly if influenza like symptoms develop

Prescribing notes:

- Zanamivir dry powder for inhalation (Relenza® Diskhaler®) should never be made into a nebuliser solution or administered to a mechanically ventilated patient (see section 2.3.1).
- Where doses are not stated follow the usual dose recommended in BNF or BNFC. Note - dose adjustment of oseltamivir may be needed in patients with renal impairment
- Dose adjustment of oseltamivir may be needed in patients with renal impairment
- Influenza medicines can be used in pregnancy and breast feeding. Speak to your pharmacist for more information.

3.4 Zanamivir hydrate solution for intravenous infusion

Zanamivir hydrate solution for intravenous infusion (Dectova®) is indicated for the treatment of complicated and potentially life-threatening influenza A or B virus infection in adult and paediatric patients (aged ≥6 months) when:

- The patient's influenza virus is known or suspected to be resistant to anti-influenza medicinal products other than zanamivir,

and/or

- Other anti-viral medicinal products for treatment of influenza (including inhaled zanamivir, and oseltamivir administered via a nasogastric tube) are not suitable for the individual patient.

Zanamivir hydrate solution for intravenous infusion is a category 1 restricted antimicrobial; a code issued by an approved infection specialist is required to prescribe it. All patients who may require intravenous zanamivir should be discussed with virology (or microbiology out of hours).

4. Education and Training

No additional skills are required to implement the guideline

5. Monitoring Compliance

Key Performance Indicator	Method of Assessment	Frequency	Lead
Antivirals prescribed in line with guideline recommendations	Trustwide antimicrobial audit	Annual	Lead Antimicrobial Pharmacist

6. Supporting Documents and Key References

1. PHE (2021), PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza, Guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza (publishing.service.gov.uk) [accessed 25/10/22]
2. Public Health England (2019) The Green Book, Chapter 19: Influenza. [Accessed 25/10/22]

3. Seasonal Influenza and Viral Respiratory Tract Illness Guidelines Adults and Children' guideline Trust Ref: B35/2017

NICE (2009), Amantadine, oseltamivir and zanamivir for the treatment of influenza, https://www.nice.org.uk/guidance/ta168 [accessed 1/11/19]

6. Key Words

Influenza, flu, Tamiflu, oseltamivir, zanamivir, Relenza, Dectova, treatment

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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Reviewed by:	Corrine Ashton – Lead Antimicrobial Pharmacist	
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5/11/19	2	Corrine Ashton	• Treatment choice amended to non-H1N1 predominant strain choices • Prophylaxis choice clarified for severely immunosuppressed patients • IV zanamivir section updated to reflect new licensed product
9/9/2020	3	Corrine Ashton	• Guidance updated to remove routine empirical treatment during COVID-19 pandemic • Assessment section removed • Paediatric information added
25/10/2022	4	Corrine Ashton	• Paediatric recommendations removed as now included in specific paediatric document

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