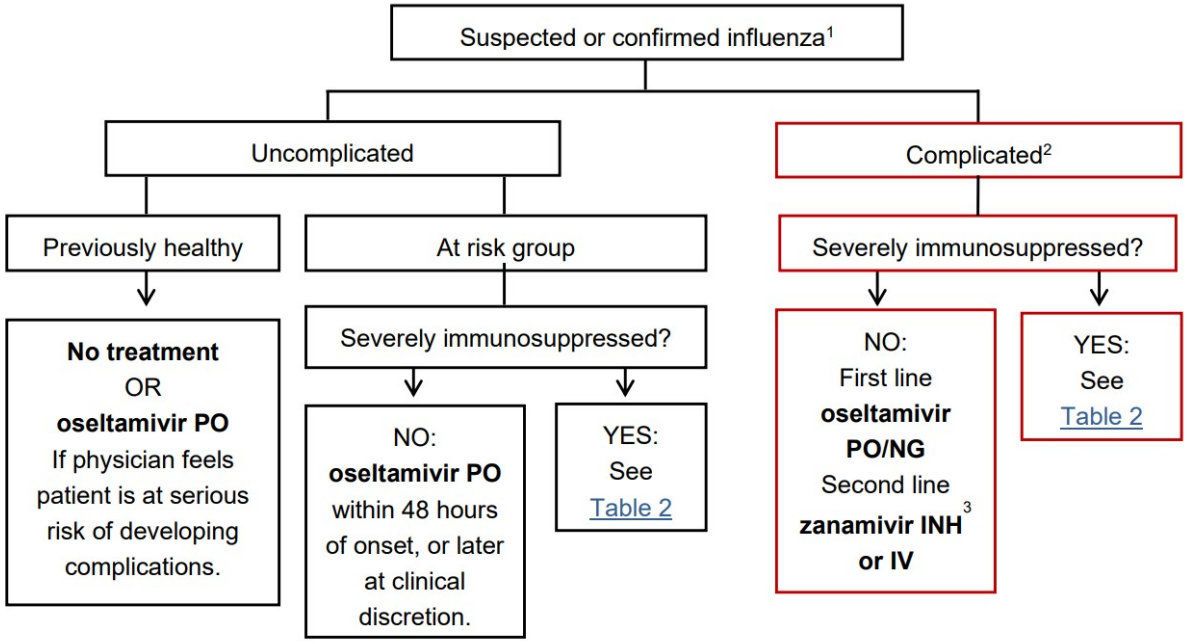
Figure 1. Algorithm for selection of antiviral therapy for treatment of influenza



Examples of severe immunosuppression relevant to this guidance:

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.

Table 3. Treatment dosage

Treatment	Premature (less than 36 weeks post conceptional age)	Infants under 12 months (36 weeks post conceptional age or greater)	Children 1 to 12 years: Dose according to weight below				Adults (13 years and over)[3]
			10 to 15kg	more than 15 to 23kg	more than 23 to 40kg	over 40kg	
Oseltamivir PO (treatment course: 5 days)[1]	1mg/ kg/dose twice a day (BD) Off-label[2]	3mg/kg/dose BD	30mg BD	45mg BD	60mg BD	75mg BD	75mg BD
Zanamivir INH (treatment course: 5 days)	Not licensed for children less than 5 years old. Children over 5 years: 10mg BD						10 mg BD

[1] Note recommendation from manufacturer regarding treatment length for immunosuppressed patients (section 2.1). Source: Summary of Product Characteristics updated April 2020.
[2] This is an off-label use of oseltamivir, and is based on evidence from the literature, and expert opinion 19, 20, 21.
[3] If a person in this age group weighs 40kg or less, it is suggested that the more than 23 to 40kg dose for those aged 1 to 12 years, is used.

Table 2. Selection of antivirals for severely immunosuppressed patients

	Dominant circulating strain has a **lower risk** of oseltamivir resistance, for example A(H3N2), influenza B*	Dominant circulating strain has a **higher risk** of oseltamivir resistance, for example A(H1N1)pdm09*
Uncomplicated influenza	oseltamivir PO and clinical follow up. Commence therapy within 48 hours of onset (or later at clinical discretion).	Zanamivir inhaler (INH) (Diskhaler®) Commence therapy within 48 hours of onset (36 for children) or later at clinical discretion OR if unable to take inhaled preparation use oseltamivir PO and clinical follow up. Commence therapy within 48 hours of onset (or later at clinical discretion).
Complicated influenza	First line: oseltamivir PO/NG Second line: zanamivir INH++ Consider switching to zanamivir if: • poor clinical response • evidence of gastrointestinal dysfunction • subtype testing confirms a strain with potential oseltamivir resistance, for example A(H1N1)pdm09 (see right)	zanamivir INH++ Commence therapy within 48 hours of onset (36 for children) or later at clinical discretion.

Notes to Table 2

* also applicable if this is the strain known to be infecting patient. However, treatment should not be delayed while waiting for test results.

++ Consider Zanamivir IV if patients:
- cannot use inhaled Zanamivir
- have severe complicated illness such as multi-organ failure

Table 4. Recommended oseltamivir treatment dosing in relation to renal function (adults and those aged 13 years or over)

Creatinine clearance (CrCL) (mL/min)	**Oseltamivir PO treatment for 5 Days**
Greater than 60mL/min*	75mg twice a day (BD)
31 to 60 mL/min*	30mg BD
11 to 30mL/min*	30mg OD
Less than or equal to 10mL/min++	30mg ONCE
Haemo-dialysis (HD)++	30mg ONCE and then 30mg after every HD session
Continuous Ambulatory Peritoneal Dialysis* (refer to Summary of Product Characteristics for advice in relation to automated peritoneal dialysis [APD] mode)	30mg ONCE
Haemo(dia)filtration++ 1 to 1.8L/hr exchange rate	30mg OD
Haemo(dia)filtration++ 1.9,3.6L/hr exchange rate	30mg BD
Haemo(dia)filtration++ Greater than 3.6L/hr exchange rate	75mg BD

Source: Summary of Product Characteristics updated April 2020 (*). The recommendations for haemo-dialysis, haemo(dia)filtration and established renal failure are based on expert opinion (++).

Table 5. Adult zanamivir IV dosing for adults and children (6 years and over with a body weight of ≥50kg) in relation to renal function

CrCl (mL/min)	Dose
Greater than or equal to 80mL/min OR haemo(dia)filtration greater than 4.7L/hour exchange rate	Initial dose: 600mg and 12 hours later, maintenance dose: 600mg BD
50 to 79 OR haemo(dia)filtration 3.0 to 4.7L/hour exchange rate	Initial dose: 600mg and 12 hours later, maintenance dose: 400mg BD
30 to 49 OR haemo(dia)filtration 1.8 to 2.9L/hour exchange rate	Initial dose: 600mg and 12 hours later, maintenance dose: 250mg BD
15 to 29 OR Haemo(dia)filtration 1 to 1.7L/hour exchange rate	Initial dose: 600mg and 24 hours later, maintenance dose: 150mg BD
less than 15	Initial dose: 600mg and 48 hours later, maintenance dose: 60mg BD

Source: Adapted from the SPC (24).

Nebulised administration

Zanamivir powder for inhalation should NOT be nebulised by dissolving the capsules in water. This practice has been linked to deaths in ICU believed to be due to blockage of ventilator tubes. Nebulisation of zanamivir aqueous solution is no longer recommended by UKHSA for any patient group, and the marketing authorisation of zanamivir aqueous solution in Europe is for IV administration only; if a patient requires zanamivir, but inhaled zanamivir via a Diskhaler is inappropriate (for example, the patient has critical illness and/or severe respiratory disease), IV zanamivir should be used.

Prophylaxis

Prophylaxis	Premature (less than 36 weeks post conceptional age)	Infants under 12 months (36 weeks post conceptional age or greater)	Children 1 to 12 years: Dose according to weight below				Adults (13 years and over)[2]
			less than or equal to 15kg	more than 15 to 23kg	more than 23 to 40kg	more than 40kg	
Oseltamivir PO (prophylaxis course: 10 days)	See below[1]	3mg/kg od	30mg od	45mg od	60mg od	75mg od	75mg od
Zanamivir INH (prophylaxis course: 10 days)	Not licensed for children under 5 years old. Adults and children equal or greater than 5 years old: 10mg od						10mg od

[1] Although it may be possible to provide half the treatment frequency, each day for 10 days, there is currently no publicly available dosing information for oseltamivir prophylaxis in pre-term infants, and so is outside the product licence (source: expert advice).
[2] If a person in this age group weighs 40kg or less, it is suggested that the greater than 23 to 40kg dose for those aged 1 to 12 years, is used.