



Public Health  
England

# **PHE guidance on use of antiviral agents for the treatment and prophylaxis of influenza**

**Version 4: Reviewed December 2013**

## About Public Health England

Public Health England's mission is to protect and improve the nation's health and to address inequalities through working with national and local government, the NHS, industry and the voluntary and community sector. PHE is an operationally autonomous executive agency of the Department of Health.

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## Foreword

This guidance summarises the current Public Health England (PHE) recommendations for the antiviral treatment and prophylaxis of influenza. It draws on guidance already issued by PHE, the National Institute for Health and Clinical Excellence, the Department of Health (DH) and the World Health Organization. In areas where adequate evidence is absent, the recommendations rely on expert consensus opinion.

This guidance should be used in secondary care for any patient where influenza is suspected or confirmed at any time; contractually, in primary care it should only be used once the DH issues notice that influenza is circulating and that antiviral agents can be used. It applies to the management of the currently circulating influenza viruses, influenza A (H1N1) pdm09 and H3N2 and influenza B.

This guidance covers common treatment and prophylaxis scenarios. A list of documents referred to in the guideline is provided in Appendix 2. This guidance does not cover infection control, which is an essential part of the response to a case of suspected or confirmed influenza. Please refer to the influenza infection control information available from the PHE website (1).

Influenza management is a complex and evolving area. Early specialist advice is recommended for the management of patients with complicated influenza. Specialist advice should be obtained from a local microbiologist or virologist in the first instance; further advice can be obtained from PHE Centre for Infectious Disease Surveillance and Control (CIDSC) if required.

**Please note that in some instances this guidance describes the unlicensed use of medications and use of some unlicensed medications for which there are limited safety and efficacy data. Specialist advice should always be obtained before using these products. This guidance represents the view of PHE only and not that of any manufacturer of medicines.**

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## Definitions

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

**2. 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

**3. Risk factors for complicated influenza:**

- a. Neurological, hepatic, renal, pulmonary and chronic cardiac disease.
- b. Diabetes mellitus.
- c. Immunosuppression.
- d. Age over 65 years.
- e. Pregnancy (including up to two weeks post partum)
- f. Morbid obesity (BMI  $\geq 40$ ).

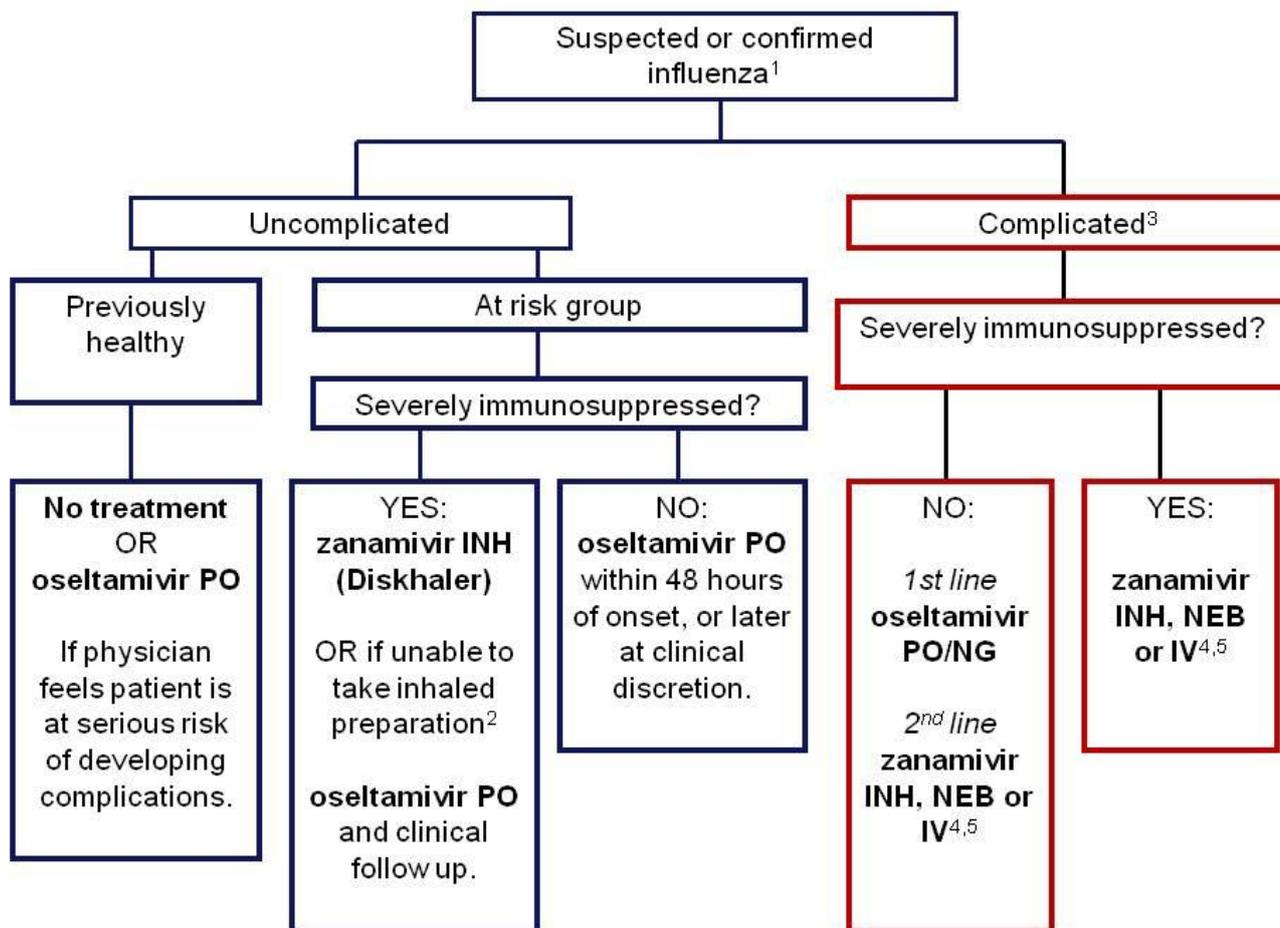
For further details refer to the Green Book (2). Morbid obesity is not described in the Green Book but there is independent evidence that it is a risk factor.

**4. Severe immunosuppression:**

- 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 who received it within the last 12 months (longer with graft versus host disease).
- e. Patients currently receiving high dose systemic corticosteroids (equivalent to  $\geq 40$  mg prednisolone per day for  $\geq 1$  week in an adult or  $\geq 2$  mg/kg/day for  $\geq 1$  week in a child), and for at least three months after treatment has stopped.
- f. Patients currently or recently (within six months) on other types of immunosuppressive therapy.
- g. HIV infected patients with severe immunosuppression (CD4  $< 200/\mu\text{l}$  or  $< 15\%$  of total lymphocytes in an adult or child over five; CD4  $< 500/\mu\text{l}$  or  $< 15\%$  of total lymphocytes in a child aged one to five; expert clinical opinion in a child aged under one).

# Part 1: Treatment of suspected or confirmed influenza

## Algorithm: Selection of antiviral therapy for treatment of influenza



Please refer to the definitions provided on page 6 when using this algorithm.

<sup>1</sup>For treatment of suspected or confirmed oseltamivir resistant influenza, see **section 1.3**.

<sup>2</sup>Inhaled zanamivir via Diskhaler may not be an effective delivery route in some patients, including those unable to administer the Diskhaler and patients with severe underlying respiratory disease. It is not licensed for use in children under five years.

<sup>3</sup>For treatment of complicated influenza, see **section 1.2**. Use second line treatment if there is poor response to oseltamivir, or if there is poor gastrointestinal absorption.

<sup>4</sup>Zanamivir solution for IV or nebulised administration is an unlicensed medication and is available on a compassionate use basis for named patients in the UK, see **section 1.3**. Where possible, patients who have good respiratory function despite their illness and can use the

Diskhaler should receive inhaled zanamivir rather than nebulised or IV zanamivir. See **section 1.2**.

<sup>5</sup>Zanamivir is available for inhalation (Diskhaler device) or as unlicensed aqueous solution for nebulised or intravenous use. The powder preparation for the Diskhaler should NEVER be made into nebuliser solution or administered to a mechanically ventilated patient.

## 1.1 Adults and children in community / A&E with uncomplicated influenza

**All patients should be advised of the symptoms of complicated influenza and told to seek medical help should their condition worsen. The following dose recommendations are for adults. For paediatric dosing, see section 1.3.1.**

**Previously healthy people (excluding pregnant women):** No treatment, or oseltamivir (PO), only if physician feels patient is at serious risk of developing serious complications from influenza.

**At risk population, including pregnant women:** Oseltamivir 75mg bd for five days (PO). 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.

**Severely immunosuppressed patients:** Rapid emergence of oseltamivir resistance on treatment has been described in these patients. They should receive zanamivir (INH) 10 mg bd for five days.

**Suspected or confirmed oseltamivir resistant influenza in a patient who requires treatment:** Zanamivir (INH) 10 mg bd for up to ten days (off label duration).

**Management of patients who are severely immunosuppressed or have suspected or confirmed oseltamivir resistant influenza but are unable to administer inhaled zanamivir:** Some patients who would normally receive inhaled zanamivir are unable to use it, either due to underlying severe respiratory disease or inability to effectively administer the Diskhaler (including children under 5, for whom zanamivir is unlicensed). Patients who are severely immunosuppressed and cannot take inhaled zanamivir should receive oseltamivir PO. As they are at increased risk of developing oseltamivir resistant influenza, they should be reviewed clinically to assess response to therapy. Patients who have suspected or confirmed oseltamivir resistant infection and cannot take inhaled zanamivir should receive nebulised aqueous zanamivir. This is an unlicensed medication and the dose is provided on the manufacturer's guidance supplied with the drug (see Section 1.3.2 and Appendix 3)

## 1.2 Adults and children in hospital and/or with complicated influenza

**All patients with complicated influenza should receive treatment, usually in hospital. 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 five days of treatment.

The following recommendations include the use of IV antivirals and nebulised aqueous zanamivir, which are **unlicensed medications** (see Section 1.3.2 and Appendix 3).

**First line treatment:** Oseltamivir PO or NG (see exceptions below). There is evidence that PO/NG oseltamivir is adequately absorbed in critical illness at standard doses.

**Second line treatment:** If there is a poor clinical response to first line treatment or if there is poor gastrointestinal absorption, use zanamivir. Some patients who are considered to have good respiratory function despite their illness may be able to use inhaled zanamivir (Diskhaler). Those who cannot should receive nebulised aqueous zanamivir. The following patients should receive IV zanamivir: patients 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. IV oseltamivir is available as an alternative but there is very limited experience of its use in the UK.

***Exceptions:***

**Severely immunosuppressed patients:** Do not use oseltamivir. Some patients considered to have good respiratory function despite their illness may be able to use inhaled zanamivir (Diskhaler). Those who cannot should receive nebulised aqueous zanamivir (unlicensed). IV zanamivir (unlicensed) should be used for patients who are not responding to nebulised zanamivir, who have respiratory conditions affecting nebuliser delivery, or who have multi-organ involvement or are on intensive care.

**Suspected or confirmed oseltamivir resistance:** e.g. contact of known oseltamivir resistant case. Do not use oseltamivir. Some patients considered to have good respiratory function despite their illness may be able to use inhaled zanamivir (Diskhaler). Those who cannot should receive nebulised aqueous zanamivir (unlicensed). IV zanamivir (unlicensed) may be used for patients who are not responding to nebulised zanamivir, who have respiratory conditions affecting nebuliser delivery, or who have multi-organ involvement or are on intensive care.

### **1.3 Supplementary material: Treatment**

**Note for prescribers:** NICE guidance is relevant to all clinicians (primary and secondary care). The grey list, which is included within the Drug Tariff, restricts GPs to only prescribe antiviral medicines to specified people who are listed in the Drug Tariff (the clinical at risk groups). GPs have the discretion to prescribe antiviral medicines for people who may not be in the specified at-risk groups but who they believe would suffer serious complications if not treated with an antiviral medicine. However, clinicians in secondary care are not subject to the grey list restrictions, so can use their clinical judgement to prescribe antiviral medicines, including for those patients not in the 'at risk' groups.

### 1.3.1 Antiviral dosage and schedules:

TREATMENT	0-1 month	1-3 months	3-12 months	1-13 years: Dose according to weight below				Adults (13 years and over)
				<15kg	15-23kg	23-40kg	>40kg	
Oseltamivir PO (treatment course: 5 days)	2mg/kg/dose bd	2.5mg/kg/dose bd	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. Adults and children >5 years: 10mg bd							10 mg bd

Oseltamivir oral suspension should be used only for children under the age of one. It is available as Tamiflu® oral suspension (Roche, 6mg/ml powder for oral suspension). This preparation replaces the 12 mg in 1 ml suspension. The new pack includes an oral dispenser, which is marked in millilitres (mls), since prescriptions for Tamiflu® 6 mg in 1 ml powder for oral suspension should state the dose in millilitres. This is an off-label use of oseltamivir but is supported by the BNF for children. Children over one year of age and adults with swallowing difficulties, and those receiving nasogastric oseltamivir, should use capsules which are opened and mixed into an appropriate sugary liquid as oseltamivir has a very bitter taste. If the powder for suspension is used for children over one year of age and/or adults, there may not be adequate quantities of the powder for suspension to meet demand for the under 1 year age group. It is important that the powder for suspension is reserved for the under one year age group.

Aqueous zanamivir solution for nebulised or IV administration is an unlicensed medicine. Dosing information is supplied by the manufacturer on the physician's guidance document that accompanies the medicine when issued.

**For the use of oseltamivir and zanamivir in pregnancy, breastfeeding, or renal or hepatic dysfunction, see Appendix 1.**

### 1.3.2 Unlicensed treatments

**All of the following influenza treatments are unlicensed medicines. They can be issued for individual patient use. The prescription of unlicensed medicines is the clinical responsibility of the prescribing physician. It is part of the prescribing responsibility of the physician to return the case data requested to the manufacturer, as this is an**

**important source of safety monitoring data. Always seek specialist advice before initiating an unlicensed treatment for influenza.**

**Zanamivir aqueous solution:** Zanamivir is available as a powder for inhalation (licensed) or in aqueous solution (unlicensed). Aqueous zanamivir may be administered through a nebuliser or intravenously. It is the only unlicensed treatment recommended by PHE in certain circumstances for first and second line therapy based on the significant experience of using it during the 2010/11 flu season. It is available on a compassionate use basis for named patients from GlaxoSmithKline. Details of how to obtain aqueous zanamivir are provided in Appendix 3. Recommendations for when to use nebulised or intravenous delivery are included in sections 1.1 and 1.2 above. Note that the powder preparation should **NOT** be used to make nebuliser solution.

**IV oseltamivir:** Intravenous oseltamivir is also available on a named patient basis but there is very limited experience of its use in the UK.

**Peramivir (IV) and laninamivir (INH)** are other antiviral agents licensed outside the UK. In the UK they are for use in approved research trials only.

**Ribavirin (IV)** is unlicensed for the treatment of influenza and may be used in combination only in the context of an approved research protocol. It should never be used for treatment or prophylaxis of influenza in pregnant women.

### *1.3.3 Treatment of oseltamivir resistant influenza*

The same criteria apply in deciding whom to treat. Previously healthy people with uncomplicated disease, or those who have recovered with or without oseltamivir, do not require treatment. Those who do require treatment should have zanamivir. Those with uncomplicated influenza should receive inhaled zanamivir (or nebulised aqueous zanamivir if the inhaled route is unsuitable); those with complicated influenza may receive inhaled, nebulised or intravenous zanamivir as is appropriate to their clinical condition (see section 1.2). In the event of changes in the epidemiology or clinical aspects of drug resistant influenza during the season, PHE will alert clinicians and provide updated advice.

### *1.3.4 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. The dose may be increased to 150 mg (this is an off label dosage) in critically ill patients in an attempt to maximise drug levels in the lungs, reduce shedding and prevent viral rebound. However as with complicated influenza, zanamivir should be used when there is suspected poor GI absorption or failure to respond to oseltamivir. **In intensive care, zanamivir should be given intravenously.**

Further guidance on management of influenza on intensive care is provided in the Practice Notes **Critical Care Management of adults with influenza including H1N1**, and **Critical Care Management of children with influenza H1N1 (3)**.

## Part 2: Post exposure prophylaxis

*Table: Prophylaxis*

Previous influenza immunisation does not preclude post exposure prophylaxis. For further information on which contacts of a case of influenza should receive prophylaxis, refer to guidance from NICE (4), and consider consulting the local health protection team.

	<b>Exposed to circulating influenza H1N1 (2009), H3N2, or B</b>	<b>Exposed to suspected or confirmed oseltamivir resistant influenza</b>
<b>Previously healthy (excluding pregnant women)</b>	No prophylaxis	No prophylaxis
<b>At risk of complicated influenza (including pregnant women but excluding severely immunosuppressed patients and children under 5 years)</b>	<b>Oseltamivir PO 10 days once daily</b> if therapy can be started within 48 hrs of last contact; or after 48 hrs on specialist advice only	<b>Zanamivir INH 10 days once daily</b> if therapy can be started within 36 hrs of last contact; or after 36 hrs on specialist advice only.
<b>Severely immunosuppressed patients (excluding children under 5 years)</b>	<b>Zanamivir INH 10 days</b> if therapy can be started within 36 hrs of last contact; or after 36 hrs on specialist advice only. If unable to administer zanamivir INH, <b>oseltamivir PO 10 days</b> (if therapy can be started within 48 hrs of last contact; or after 48 hours on specialist advice only).	<b>Zanamivir INH 10 days</b> only if therapy can be started within 36 hrs of last contact; or after 36 hrs on specialist advice only. If unable to administer zanamivir INH, discuss with specialist and consider nebulised aqueous zanamivir (unlicensed) after individual risk assessment.
<b>Children under 5 years in at risk groups and severely immunocompromised children</b>	<b>Oseltamivir PO 10 days</b> if therapy can be started within 48 hrs of last contact; or after 48 hrs on specialist advice only	<b>Discuss with specialist.</b> Consider nebulised aqueous zanamivir (unlicensed) after individual risk assessment.

Inhaled zanamivir is not licensed for children under five years old, and is unlikely to be an effective delivery route in these patients. Some other patients, such as those with severe underlying respiratory disease, may also be unable to use the Diskhaler effectively. Severely immunosuppressed children under five years and all other severely immunosuppressed patients who cannot use the Diskhaler and require prophylaxis after exposure to currently

circulating strains of influenza should receive oral oseltamivir, with advice to seek immediate medical attention if unwell.

Severely immunocompromised patients who are unable to use the Diskhaler, including severely immunosuppressed children aged under five years, and who are exposed to suspected or confirmed oseltamivir resistant influenza should be discussed with a specialist. The use of unlicensed nebulised aqueous zanamivir may be considered based on an individual risk assessment (See section 1.3.2).

Specialist advice should be sought for prophylaxis in institutional or healthcare settings where repeated or ongoing exposure is suspected.

## 2.1 Supplementary information: Prophylaxis

### 2.1.2 Antiviral dosage and schedules

PROPHYLAXIS	0-1 month	1-3 months	3-12 months	1-13 years: Dose according to weight below				Adults (13 years and over)
				<15kg	15-23kg	23-40kg	>40kg	
<b>Oseltamivir PO (prophylaxis course: 10 days)</b>	<b>2mg/kg od</b>	<b>2.5mg/kg od</b>	<b>3mg/kg od</b>	<b>30mg od</b>	<b>45mg od</b>	<b>60mg od</b>	<b>75mg od</b>	<b>75mg od</b>
<b>Zanamivir INH (prophylaxis course: 10 days)</b>	<b>Not licensed for children &lt;5 years old. Adults and children 5 years: 10mg od</b>							<b>10mg od</b>

Oseltamivir oral suspension should be used only for children under the age of one. It is available as Tamiflu® oral suspension (Roche, 6mg/ml powder for oral suspension). This preparation replaces the 12 mg in 1 ml suspension. The new pack includes an oral dispenser, which is marked in millilitres (mls), since prescriptions for Tamiflu® 6 mg in 1 ml powder for oral suspension should state the dose in millilitres. This is an off-label use of oseltamivir but is supported by the BNF for children. Children over one and adults with swallowing difficulties, and those receiving nasogastric oseltamivir, should use capsules which are opened and mixed into an appropriate sugary liquid as oseltamivir has a very bitter taste. If the powder for suspension is used for children over one year of age and/or adults, there may not be adequate quantities of the powder for suspension to meet demand for the under 1 year age group. It is important that the powder for suspension is reserved for the under one year age group. Inhaled zanamivir is not licensed for children aged under the age of 5.

## Appendix 1: Use of antivirals in pregnancy, breastfeeding, hepatic or renal dysfunction

	Liver dysfunction	Renal dysfunction	Pregnancy	Breastfeeding
Oseltamivir PO	Standard dosing	<p><b>Adults<sup>1</sup></b>  <b>Haemodialysis:</b> 30mg after each HD session for treatment, every 2nd session for prophylaxis  <b>Peritoneal dialysis:</b> single 30mg dose for treatment, weekly 30mg dose for prophylaxis  <b>CrCl &lt; 10ml/min:</b> Avoid for treatment or prophylaxis  <b>CrCl 10-30 ml/min:</b> 30mg od for treatment; 30mg every 48 hours for prophylaxis.  <b>CrCl 30-60 ml/min:</b> 30mg: bd for treatment &amp; od for prophylaxis  <b>CrCl &gt;60 ml/min:</b> standard dosing</p>	Use only if benefit outweighs risk. FDA category C <sup>2</sup>	Amount probably too small to be harmful; use only if benefit outweighs risk
Zanamivir INH (Diskhaler)	Standard dosing	Standard dosing	Use only if benefit outweighs risk. FDA category C <sup>2</sup>	Amount probably too small to be harmful; use only if benefit outweighs risk
Zanamivir solution IV/NEB	Refer to the physician's guidance document supplied by the manufacturer with the medication			

<sup>1</sup>Dosing information in renal failure is derived from the Summary Product Characteristics for oseltamivir (revised 23/10/2013) for treatment of adults and adolescents (13-17 years of age) It represents the most recent information available and may be different from that provided in the BNF.

<sup>2</sup>FDA pregnancy category C: No malformation, maternal toxicity or embryotoxicity were observed in animal studies. No data available in humans.

For further information about paediatric dosing in renal dysfunction, consult the guidance from the Royal College of Paediatrics and Child Health (5).

### **Use of IV or nebulised zanamivir in renal dysfunction**

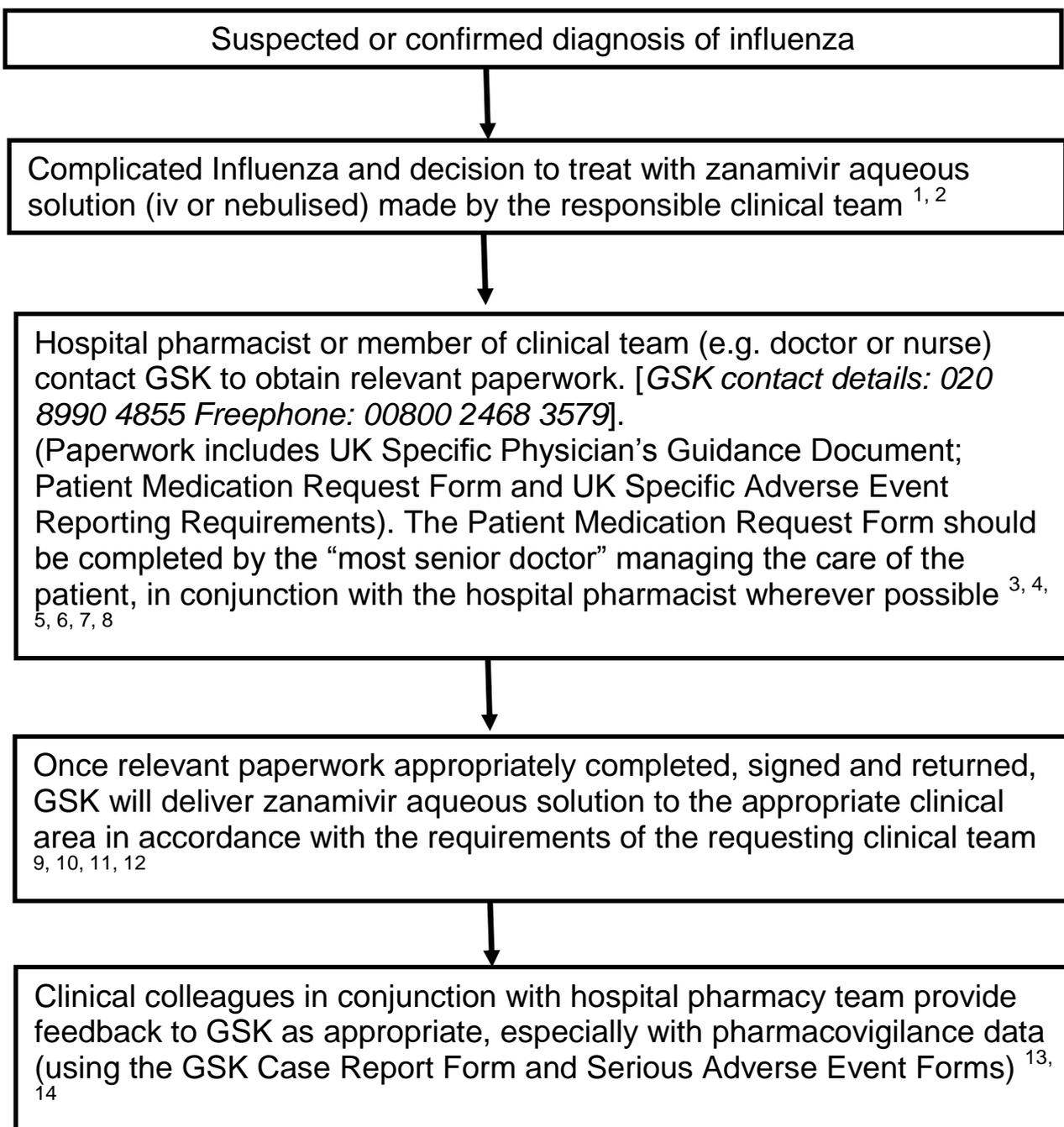
IV zanamivir is renally excreted and requires dose modification for patients with renal dysfunction including those on renal replacement therapy. Consult the manufacturer's physician guidance document that is supplied with the medication.

## Appendix 2: Sources of information

- (1) Public Health England. **Seasonal Influenza: Information for Health Professionals.**  
<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/SeasonalInfluenza/InformationForHealthProfessionals/>
- (2) Department of Health. **Immunisation against Infectious Disease** (The Green Book), 2013  
<https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book>
- (3) Public Health England. **Critical Care Management of adults with influenza including H1N1 and Critical Care Management of children with influenza H1N1** 2009  
<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/SeasonalInfluenza/InformationForHealthProfessionals/>
- (4) National Institute for Clinical Excellence **Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza** 2008 <http://guidance.nice.org.uk/TA158>
- (5) Royal College of Paediatrics and Child Health, British Association for Paediatric Nephrology and Department of Health **Antivirals and advice for children with renal failure** 2009  
[http://www.rcpch.ac.uk/sites/default/files/asset\\_library/Research/Clinical%20Effectiveness/Practice%20Statements/Antivirals%20and%20advice%20for%20children%20with%20renal%20failure%20v14%20final%20draft%20271109%20\\_3\\_.pdf](http://www.rcpch.ac.uk/sites/default/files/asset_library/Research/Clinical%20Effectiveness/Practice%20Statements/Antivirals%20and%20advice%20for%20children%20with%20renal%20failure%20v14%20final%20draft%20271109%20_3_.pdf)

## Appendix 3: Supply of zanamivir aqueous solution on a named patient basis from GlaxoSmithKline

(Note: The use of nebulised or intravenous aqueous zanamivir is unlicensed. Clinicians should make a very careful judgement about the use of unlicensed zanamivir – see Guidance Notes<sup>1, 2</sup>)



## Guidance Notes

### *General*

1. Zanamivir aqueous solution is a globally unlicensed medicine, only available on a named patient supply basis. 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.**
2. NHS Trusts should also follow their own Unlicensed Medicines Policies and MHRA Guidance Note 14 “*The Supply of Relevant Medicinal Products for Individual Patients*” in conjunction with this guidance. For example (but not limited to) Trusts should ensure the recording of batch number and expiry dates of zanamivir aqueous solution received and supplied.
3. Wherever possible, ordering of zanamivir aqueous solution should follow “normal” medicines processes in Trusts, i.e. the hospital pharmacy should, if possible, order zanamivir aqueous solution.
4. GSK hours of despatch for zanamivir aqueous solution are [**See additionally, points 10 and 11 below**]:
  - a. Monday – Friday: 8am to 7pm
  - b. Saturday & Sunday: 8am to 3pm
  - c. Over the Christmas and New Year period, hours of dispatch are as follows:
    - Tuesday 24 December 2013: 8am – 5pm
    - Wednesday 25 December 2013: 8am – 3pm – Christmas Day (Bank Holiday)
    - Thursday 26 December 2013: 8am – 3pm – Boxing Day (Bank Holiday)
    - Friday 27 December 2013 : 8am – 3pm
    - Saturday 28 December 2013: 8am - 3pm
    - Sunday 29 December 2013: 8am - 3pm
    - Monday 30 December 2013: 8am - 3pm
    - Tuesday 31 December 2013: 8am – 3pm
    - Wednesday 1 January 2014: 8am – 3pm - New Years Day (Bank Holiday)
    - Thursday 2 January 2014: 8am – 5pm

### *Requesting a Named Patient Supply*

5. When a decision to prescribe zanamivir aqueous solution is confirmed, contact should be made with **GSK on 020 8990 4855 or Freephone: 0800 2468 3579**, or by email: [GSKClinicalSupportHD@gsk.com](mailto:GSKClinicalSupportHD@gsk.com). The hospital pharmacy team can make this initial contact with GSK, or GSK will also accept an initial request from a member of the clinical team looking

after the patient (i.e. senior nurse or doctor) [**See additionally, points 10 and 11 below**].

[**Note:** Any out of hours requests for zanamivir aqueous solution should be notified to the hospital pharmacy team through the usual pharmacy on call / residency arrangements as soon as possible and by close of play the next working day at the latest].

6. Whilst GSK can be contacted 24 hours a day to discuss medical emergencies, GSK will not despatch outside of the hours 8am-7pm Monday-Friday or 8am-3pm Saturday/Sunday; therefore consideration should be given by the clinical team whether GSK should be contacted after 7pm Monday-Friday /3pm Saturday/Sunday and before 7am in the morning.

7. GSK will email the relevant paperwork (i.e. UK Specific Physicians Guidance Document; Patient Medication Request Form; UK Specific Adverse Event Reporting Requirements) to the requestor and to the “most senior doctor”.

8. This paperwork **MUST** be completed and signed by the “most senior doctor” managing the care of the patient. [**Note:** The “most senior doctor” may be the consultant physician (or surgeon), consultant anaesthetist / intensivist managing the care of the patient or could be a senior trainee (ST grade doctor) or specialty doctor].

9. The completed paperwork must be faxed back to GSK with a follow up telephone call, to confirm request.

10. To guarantee same day despatch, hospitals are asked to allow up to 2 hours for processing of their request prior to close of despatch i.e. to send in their requests to GSK by

a. 5pm Monday – Friday or by

b. 1pm Saturday and Sunday

11. For requests received by GSK between 5pm-7pm, GSK will make every effort to process the request and despatch supplies, but depending on the time of receipt of the completed documentation, same day despatch **cannot** be guaranteed.

### *Despatch, Delivery and Receipt*

12. Once the relevant paperwork has been completed and confirmed, GSK will despatch via courier, zanamivir aqueous solution to the requesting hospital. a. Zanamivir aqueous solution should be delivered direct to the relevant clinical area. This is to ensure a simple and robust logistics solution recognising the variable opening hours of hospital pharmacy departments.

b. Care must be taken to ensure the delivery details are clear and unambiguous. Zanamivir aqueous solution should **NOT**, for example be delivered to a hospital reception desk.

c. The clinical area receiving zanamivir aqueous solution should sign for the receipt of the product, retain all paperwork, record the batch number and expiry date and inform the hospital pharmacy team of the delivery by close of play the next working day at the latest.

13. Once despatched, GSK will email the “most senior doctor” named on the patient medication request form and the pharmacy contact name, if provided, with details of the estimated arrival

time of the supplies, together with a case report form and serious adverse event forms for collection of outcomes and pharmacovigilance data.

*Pharmacovigilance Information*

14. Clinical colleagues in conjunction with the hospital pharmacy team **MUST** provide feedback to GSK to aid pharmacovigilance data collection. The case report form and serious adverse event forms provided in the email confirming the estimated time of arrival of the supplies, should be used for this purpose, as appropriate.