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# Antiviral prescribing when A(H1N1)pdm09 influenza virus is the dominant circulating strain

## Update letter, December 2018

**To:** All clinicians involved in prescribing influenza antivirals in England
**From:** Respiratory Virus Unit, National Infection Service, Public Health England, Colindale.
Tel: 020 8327 6017
**Date:** 31/12/2018

### Background

Resistance to neuraminidase inhibitors (oseltamivir, zanamivir) can occur in infections caused by any influenza A virus, but A(H1N1) viruses are at greater risk of becoming resistant than A(H3N2) viruses. The incidence of resistance in circulating influenza A (H1N1) viruses has been very low globally over the last eight years (<1%) and there are no indicators to suggest this has changed recently. However, severely immunosuppressed patients are at increased risk for developing resistant influenza A infections, particularly when receiving oseltamivir. This needs to be considered when prescribing oseltamivir for the treatment or prophylaxis of influenza, and also during monitoring of treatment in this patient group, when the likely or confirmed infecting virus is A (H1N1)pdm09.

Currently, influenza A(H1N1)pdm09 is the dominant virus nationally, as suggested by community and hospital surveillance schemes. The advice contained within existing guidance (see links, below), concerning when to use zanamivir in immunosuppressed patients, needs to be interpreted accordingly.

### Implications for those caring for severely immunosuppressed patients

PHE has issued guidance on the use of antivirals for the treatment and prophylaxis of seasonal influenza during the 2018-19 season (http://www.gov.uk/government/publications/influenza-treatment-and-prophylaxis-using-anti-viral-agents). As A(H1N1)pdm09 is known to be the dominant circulating virus this season, **it is recommended that zanamivir is prescribed as the first line antiviral for severely immunosuppressed patients**. This applies to all

indications for prescribing, including prophylaxis and empirical treatment while awaiting results of diagnostic testing. Examples of severe immunosuppression are provided in the guidance.

The different formulations of zanamivir (diskhaler, unlicensed intravenous solution, unlicensed aqueous solution for nebulisation), and when it might be reasonable to use oseltamivir as an alternative to zanamivir, are also explained in the PHE antivirals guidance. Diskhaler powder should never be made into nebuliser solution or administered to a mechanically ventilated patient.

## IV zanamivir (unlicensed) is preferred for complicated influenza in severely immunosuppressed patients

In severely immunosuppressed patients with *complicated* influenza, particularly those with critical illness, the systemically-active intravenous preparation of zanamivir is preferred over locally-acting inhaled or nebulised preparations. Information on how to access unlicensed intravenous zanamivir (and also unlicensed aqueous solution for nebulisation) on a named patient basis is provided in Appendix 4 of the PHE 2018/19 antiviral guidance. This is an established named-patient programme and zanamivir aqueous solution for IV administration and nebulisation can be issued rapidly by the manufacturer to requesting hospitals.

## Continuation of zanamivir in severely immunosuppressed patients when oseltamivir resistance has not been demonstrated

If it is revealed through subsequent testing that a severely immunosuppressed patient with confirmed A(H1N1)pdm09 infection has an *oseltamivir-sensitive* virus, it is recommended that the course of zanamivir is completed, rather than switching to oseltamivir, because of the increased risk of developing on-treatment resistance to oseltamivir in this patient population.

For severely immunosuppressed patients who have commenced treatment with zanamivir, but then subtyping tests reveal infection with influenza A(H3N2) virus, it is recommended that the course of zanamivir is completed, rather than switching to oseltamivir.

Zanamivir resistance is rare. If zanamivir resistance is suspected or detected, please seek advice about treatment from relevant specialists and contact the Respiratory Virus Unit at PHE Colindale.

## Treatment of severely immunosuppressed patients with confirmed influenza A infection when the subtype is unknown

If infection with influenza A virus is confirmed, but subtyping has not been performed, then assume the virus is A(H1N1)pdm09 and treat as per the relevant advice in PHE's 2018/19 antiviral guidance.

## Monitoring of treatment in severely immunosuppressed patients

Regardless of the antiviral being used, it is recommended that all severely immunosuppressed patients with influenza A infections are monitored during treatment, with a low threshold for requesting antiviral resistance testing. Antiviral resistance may be considered as an underlying explanation when there is an inadequate clinical response to antiviral treatment, or if the patient's condition deteriorates, of if serial virological monitoring (if performed) suggests failure to clear the virus. Serial virological monitoring using PCR can detect viral RNA during clinical

recovery, so local teams should consider serial testing in the context of the patient's clinical condition; further advice is provided in Appendix 3 of the 2018/19 antiviral guidance.

Some hospital laboratories can perform tests to detect the H275Y mutation, which is the most common oseltamivir resistance mutation seen in A(H1N1) viruses. Most regional PHE Public Health Laboratories (PHLs) also offer H275Y testing; please check with your nearest PHL. When required, the detection of other antiviral resistance mutations affecting A(H1N1)pdm09 and other influenza A and influenza B viruses can be performed at PHE Colindale; this should be discussed with the Respiratory Virus Unit (see contact details at end of this document).

## Antiviral prescribing in other patient groups

Currently, there is a low risk of oseltamivir resistance occurring in influenza A infections in non-immunosuppressed patients. The risk of resistance is greater for A(H1N1)pdm09 infections than A(H3N2) infections. However, clinicians should be aware of the possibility of antiviral-resistant infections in all populations and consider requesting resistance testing when a patient with complicated influenza fails to improve or deteriorates despite appropriate treatment, or if a patient with confirmed influenza is known to be a contact of an individual infected with a resistant virus.

When antiviral resistance is suspected, clinicians may wish to switch from oseltamivir to zanamivir before the results of antiviral resistance testing are known; this is a particularly important consideration when prescribing for contacts of individuals known to be infected with a resistant virus, and also when prescribing for critically-ill patients.

When there is confirmed resistance to an antiviral agent, the agent should be discontinued (this applies to all patients).

## Further updates

This advice is based on knowledge of currently circulating influenza viruses and antiviral resistance data from the UK. PHE will issue further updates for clinicians, as appropriate, based on changes in surveillance data.

## Additional information

Seasonal Influenza: guidance, data and analysis:
http://www.gov.uk/government/collections/seasonal-influenza-guidance-data-and-analysis
Influenza: treatment and prophylaxis using anti-viral agents:
http://www.gov.uk/government/publications/influenza-treatment-and-prophylaxis-using-anti-viral-agents
Influenza antiviral resistance and testing: http://www.gov.uk/government/collections/seasonal-influenza-guidance-data-and-analysis#antiviral-resistance
Weekly national flu reports:
https://www.gov.uk/government/statistics/weekly-national-flu-reports-2018-to-2019-season

## For further advice, please contact:

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