

Dear Colleague

SEASONAL INFLUENZA: USE OF ANTIVIRALS 2014-15

1. Recent surveillance information indicates that there is now a substantial likelihood that people presenting with an influenza-like illness are infected with an influenza virus. Accordingly, antiviral drugs can now be prescribed for the prevention or treatment of influenza in the community where clinically indicated/appropriate. Annex A to this letter summarises considerations for the use of antivirals this year.

2. For the avoidance of any doubt, this letter concerns the prescribing of antivirals in the community. Antivirals should be used in secondary care for any patient where influenza is suspected or confirmed at any time.

3. Recent media reporting has raised questions about the effectiveness about influenza antivirals following the 2014 Cochrane Review.^{1,2} However a more recently published analysis in *The Lancet, Respiratory Medicine* adds to a growing body of evidence that treatment with influenza antivirals can reduce the risk of death in patients hospitalized with influenza³. This letter provides further information on this important point in paragraphs 9 to 11.

Surveillance Update

4. Health Protection Scotland (HPS) uses information from a range of clinical and virological influenza surveillance schemes to identify when there is a substantial likelihood that people presenting with an influenza-like illness are likely to be infected with influenza virus each flu season.

5. In Scotland, clinical influenza activity is now increasing. Although activity is still at a low level, increases in a number of surveillance indicators including the number of outbreaks in closed settings (care homes/hospital wards), virological detections, and the number of severe cases of influenza, indicates community circulation of influenza is now occurring.

From the Chief Medical Officer
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Addresses

For action

Chief Executives, NHS Boards
Medical Directors, NHS Boards
Directors of Public Health, NHS Boards
Directors of Nursing & Midwifery, NHS Boards
Directors of Pharmacy
General Practitioners
Practice Managers
Practice Nurses
Health Visitors
Immunisation Co-ordinators
CPHMs
Scottish Prison Service
Scottish Ambulance Service
Maternity Services
Consultant Obstetricians
Occupational Health Leads

For information

Chairs, NHS Boards
Infectious Disease Consultants
Consultant Paediatricians
Consultant Physicians
Anaesthetists and ITU Physicians
Health Protection Scotland
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Further Enquiries

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Antivirals Usage in the Community

6. The use of antivirals for the treatment and prophylaxis of seasonal influenza in the community is covered by the National Institute of Health and Clinical Excellence (NICE) technology appraisal guidance, [endorsed for use in Scotland by NHS Healthcare Improvement Scotland \(NHS HIS\)](#). The terms of this guidance are that the use of antivirals in the community for prophylaxis and treatment of patients presenting with influenza-like symptoms are subject to certain controls. These controls limit the use of antivirals to circumstances in which there has been documented evidence that influenza virus is circulating in the community.

7. In light of the current surveillance picture reported above **the use of antiviral drugs for the prevention or treatment of influenza is now recommended in the community**. Oseltamivir (Tamiflu) continues to be recommended, along with Zanamivir (Relenza), for the prophylaxis and treatment of influenza. **Annex A** to this letter provides a two-page summary of information on the use of antivirals this flu season.

Further Information on the Use of Antivirals

8. Health Protection Scotland and Public Health England have provided a summary of issues to consider in using antiviral agents for the treatment and prophylaxis of influenza. This document has recently been refreshed and republished in December 2014:
<http://www.hps.scot.nhs.uk/resp/publicationsdetail.aspx?id=53562>

9. The latest PHE/HPS review includes previously unpublished data, and adds to the evidence base for the treatment of influenza in some settings. Recent media reporting around the **2014 Cochrane Review** suggested that antivirals are not effective for influenza. It must be noted that the Cochrane Reviews consider evidence only from randomised control trials, which by their nature are usually carried out in an otherwise healthy population in the community setting. The 2014 Cochrane Review did not consider the substantial volume of observational data which has been gathered on the use of antivirals in the hospitalised population, which demonstrates a significant reduction in mortality, particularly when antiviral treatment is commenced early.

10. The findings of the 2014 Cochrane Review^{1,2} were not substantially different to previous reviews, and there is no evidence to support a change to the existing guidance on the use of neuraminidase inhibitors. It is essential therefore that physicians treating severely unwell patients in any setting are not deterred from prescribing what may be lifesaving drugs as a result of confusion over efficacy in this situation; this is especially true for patients hospitalised with proven or suspected influenza.

11. A recent meta-analysis by researchers, 'Effectiveness of neuraminidase inhibitors [NAIs] in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data', compiled data from 78 observational studies across 38 countries on more than 29,000 patients who were hospitalized with 2009 H1N1 influenza virus infection during the 2009–10 pandemic³. Findings included:

- among patients aged >16 years, treatment with a NAI was associated with a 25% reduction in the likelihood of death compared with no antiviral treatment.
- early treatment with NAIs (ie within 48 hours of development of illness) halved the risk of death compared with no antiviral treatment.

12. This supports findings from previous observational studies in hospitalized influenza patients that the clinical benefit of NAI treatment is greatest when started within 2 days of onset of illness^{4,5,6}.

Conclusion

13. It should be noted that when HPS indicate that influenza levels have reduced we will recontact you to advise that the use of antivirals should cease.

Yours sincerely

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Bill Scott

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2. Jefferson T, Jones M, Doshi P, Spencer E, Onakpoya I, Heneghan C. Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. BMJ 2014;348:g2545
3. Muthuri S, Venkatesan S, Myles P, Leonardi-Bee J, Tarig S, Al Mamun A, Anovadiya A. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. The Lancet Respiratory Medicine. 2014; 2 (5): 395-404,
4. Hsu J, Santesso N, Mustafa R, Brozek J, Chen Y, Hopkins J et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. Ann Intern Med. 2012; 156: 512–524
5. Adisasmito W, Chan PK, Lee N, Oner AF, Gasimov V, Aghayev F. Effectiveness of antiviral treatment in human influenza A(H5N1) infections: analysis of a global patient registry. J Infect Dis. 2010; 202: 1154–1160
6. Chan PK, Lee N, Zaman M, Adasimato W, Coker R, Hanshaoworakul W. Determinants of antiviral effectiveness in influenza virus A subtype H5N1. J Infect Dis. 2012;206(9):1359

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Prophylaxis Advice

- Patients in the **general population** should not require prophylactic antivirals unless there are exceptional circumstances.
- Generally, **at-risk** patients who have been vaccinated should not require prophylactic antivirals. However the use of antivirals can be considered in vaccinated patients who present with symptoms.

Treatment Advice for At Risk Individuals

- Antivirals should now be considered when:
 - A person with an influenza-like illness is in an 'at-risk' group (including those over the age of 65) and they can start treatment within 48 hours (or within 36 hours for *zanamivir* treatment in children) of the onset of symptoms, as per licensed indications and;
 - The national surveillance schemes indicate that influenza virus A or B is circulating (as the first part of the letter confirms¹).
- Antivirals should be prescribed in accordance with NICE guidance. The full NICE guidance on the use of antivirals can be accessed at <http://www.nice.org.uk/guidance/ta168> for treatment and <http://www.nice.org.uk/guidance/ta158> for prophylaxis.
- Antiviral drugs are not in any way a substitute for vaccination, which remains the most effective way of preventing illness from influenza.
- For clinicians treating hospitalised patients with suspected influenza, rapid laboratory confirmation with subtype identification is advised to support patient management.

Treatment Advice for the General Population

- In November 2010, legislation was amended such that prescribers were able to rely on their clinical judgement to prescribe antivirals to any individual and not only those with risk conditions, where clinical judgement would suggest that this would reduce the severity of the course of serious infection.
- The relevant directions under NHS Circular PCA(M)(2010)22 remain in force (available at: [http://www.sehd.scot.nhs.uk/pcal/PCA2010\(M\)22.pdf](http://www.sehd.scot.nhs.uk/pcal/PCA2010(M)22.pdf)) and this means clinicians are still able to prescribe antivirals for any individuals, including those not in recognised risk groups and children under one year of age.

¹ During localised outbreaks of influenza-like illness (outside the periods when national surveillance indicates that influenza virus is circulating in the community), *Oseltamivir* and *Zanamivir* may be offered for the treatment of influenza in 'at-risk' people who live in long-term residential or nursing homes. However, these treatments should be offered only if there is a high level of certainty that the causative agent in a localised outbreak is influenza (usually based on virological evidence of influenza infection in the initial case) and the decision should be made in consultation with local Public Health colleagues.

- However, it is expected that the use of antivirals for the general population would only be in exceptional circumstances. Patients in the general population presenting with mild to moderate flu-like symptoms should be advised to take paracetamol and fluids and to seek further assistance should their condition deteriorate. Only those who have severe symptoms should be assessed and considered for antiviral treatment.

Prescribing for Children over the Age of One Year

- Wherever possible, for children over the age of one year and for adults who are not able to swallow capsules, the appropriate strength of capsules should be prescribed. The contents of the capsules can be emptied and added to a suitable sugary diluent. As far as possible, the liquid preparation should be restricted for children under one year of age. This will support the continuity of the limited supply of the liquid form of Oseltamivir for this vulnerable age group.

Prescribing for Children under One Year of Age

- Oseltamivir (Tamiflu) is not licensed for use in children under one year of age for seasonal influenza. Prescribing of Oseltamivir for this age group for seasonal influenza, should follow the usual process for the use of medicines outwith the terms of marketing authorisation (product license) and be based on the judgement of the clinician, after considering the risks and benefits of treatment.

Prescriptions – Advice for Prescribers for Endorsing Prescriptions

- Prescribers are reminded to endorse all prescriptions for antivirals with the reference “SLS”. Pharmacists can only dispense antivirals at NHS expense if this endorsement is made by the prescriber.

Access to Antivirals

- The normal route for prescribing antiviral medication will be through GP10. Community Pharmacies are advised to review their stock levels of antivirals via their wholesalers in response to local demand. Directors of Pharmacy should make sufficient supplies of antivirals available to local Out of Hours services.
- In the event of any national shortages of antiviral medicines further advice regarding the use of the national stockpile will be used.

Further Information

Health Protection Scotland/Public Health England summary of issues to consider:
<http://www.documents.hps.scot.nhs.uk/respiratory/seasonal-influenza/antiviral-guidance-season-14-15-v1.pdf>