



Complete Summary

GUIDELINE TITLE

Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 37 p. (Technology appraisal guidance; no. 158).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Clinical Excellence (NICE). Guidance on the use of oseltamivir and amantadine for the prophylaxis of influenza. London (UK): National Institute for Clinical Excellence (NICE); 2003 Sep. 32 p. (Technology appraisal; no. 67).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [April 02, 2008, Relenza \(zanamivir\)](#): GlaxoSmithKline informed healthcare professionals of changes to the warnings and precautions sections of prescribing information for Relenza. There have been reports (mostly from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza.
- [March 4, 2008, Tamiflu \(oseltamivir phosphate\)](#): Roche and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of neuropsychiatric events associated with the use of Tamiflu, in patients with influenza. Roche has updated the PRECAUTIONS section of the package insert to include the new information and guidance under the Neuropsychiatric Events heading.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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SCOPE

DISEASE/CONDITION(S)

Influenza

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Prevention
Risk Assessment

CLINICAL SPECIALTY

Family Practice
Geriatrics
Infectious Diseases
Internal Medicine
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Health Plans
Managed Care Organizations
Nurses
Physician Assistants
Physicians
Public Health Departments
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the clinical and cost effectiveness of amantadine, oseltamivir and zanamivir for the prophylaxis of influenza

TARGET POPULATION

Healthy and at-risk* children, adults and the elderly

***Note:** See the "Major Recommendations" field for further definition of "at risk."

INTERVENTIONS AND PRACTICES CONSIDERED

1. Oseltamivir as post-exposure prophylaxis of influenza
2. Zanamivir as post-exposure prophylaxis of influenza

Note:

- Oseltamivir and zanamivir were considered but not recommended for seasonal prophylaxis of influenza
- Amantadine was considered but not recommended for prophylaxis of influenza

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
 - Cases prevented (measured in terms of symptomatic, laboratory-confirmed influenza or, in the absence of this outcome, clinical illness and/or infection)
 - Complications prevented
 - Adverse events
 - Health-related quality of life (HRQoL)
 - Mortality
 - Hospitalisations prevented
 - Length of influenza illness
 - Time to return to normal activities
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this appraisal was prepared by the School of Health and Related Research (SchARR), University of Sheffield (see the "Availability of Companion Documents" field).

Identification of Studies

Systematic searches were undertaken to identify studies relating to the clinical effectiveness of amantadine, oseltamivir and zanamivir in the prevention of influenza A and B. The search strategy comprised the following main elements:

- Searching of electronic databases listed below
- Contact with experts in the field
- Handsearching of bibliographies of retrieved papers
- Scanning of electronic archives of key journals for relevant evidence published within the preceding 12 months (searched October 2007)

Sources Searched

The electronic databases searched included MEDLINE; Medline in Process; EMBASE; Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, BIOSIS, CINAHL, Database of Abstracts of Reviews of Effectiveness (DARE), National Health Service Economic Evaluation Database (NHS EED) and Health Technology Assessment (HTA) databases; Office of Health Economics Health Economics Evaluation Database (OHE HEED), NRR (National Research Register); Science Citation Index; Current Controlled Trials; Clinical Trials.gov. Searches were undertaken in July 2007. Sponsor submissions to NICE were also handsearched.

Keyword Strategies

The search strategies included subject headings and free text terms, combined using Boolean logic, to identify all published and unpublished data relating to the prevention of influenza A and B. The Medline search strategy is presented in Appendix 1 of the Assessment Report (see the "Availability of Companion Documents" field).

Search Restrictions

Searches were restricted by publication type to controlled clinical trials, systematic reviews and economics or quality of life studies. Searches were not restricted by the date of publication or by language.

Inclusion and Exclusion Criteria

The following inclusion criteria were used to identify relevant studies for inclusion in the assessment.

Population

- Adults and children who have been exposed to a clinically diagnosed case of influenza (which may or may not be true influenza)
- Adults and children for whom seasonal prophylaxis would be appropriate in exceptional circumstances, such as in the event of mismatch between the circulating influenza virus and vaccine strains. For the purposes of this assessment, healthy and at-risk children, adults and the elderly were considered.

Interventions

The following medications used for influenza prophylaxis administered in line with current UK marketing authorisations:

- Amantadine
- Oseltamivir
- Zanamivir

Trials of these interventions in seasonal prophylaxis and post-exposure prophylaxis (both in prevention of the transmission of influenza within households and in outbreak control in settings where individuals live or work in close proximity) were included in the review. Trials in which interventions were used in prophylaxis against experimentally-induced influenza in line with licensed indications were also included. The results of these challenge studies should be interpreted with caution due to their limited external validity. These studies are presented to provide a comprehensive review of the effectiveness of prophylaxis; these studies were not used to inform the health economic model.

Comparators

Interventions were compared against each other and no prophylaxis (in which subjects received any of the following: placebo, no treatment or expectant treatment following onset of symptomatic influenza).

Outcomes

- Cases prevented (measured in terms of symptomatic, laboratory-confirmed influenza or, in the absence of this outcome, clinical illness and/or infection)
- Complications prevented
- Adverse events
- Health-related quality of life (HRQoL)
- Mortality
- Hospitalisations prevented
- Length of influenza illness
- Time to return to normal activities
- Cost and cost-effectiveness

Study Types

- Randomised controlled trials (RCTs)

If evidence was not available from RCTs, other study types would have been considered according to the hierarchy of evidence. Systematic reviews were not included in the analysis, but were handsearched to identify randomised controlled trials meeting the inclusion criteria of this review and retained for discussion.

The following exclusion criteria were used:

- Intervention medications not used in accordance with their licensed indications

- Studies only published in languages other than English

Based on the above inclusion/exclusion criteria, study selection was undertaken by one reviewer, with involvement of a second reviewer when necessary to provide consensus on inclusion or exclusion of studies.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Total full papers accepted reporting randomised controlled trials (RCTs): n = 26 (relating to 22 RCTs); an additional unpublished report was identified from sponsor submissions, resulting in a total of 23 RCTs.

Cost-Effectiveness

- Number of studies included in review of cost-effectiveness (n=7).
- The manufacturer of oseltamivir and the Assessment Group presented their economic models.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this appraisal was prepared by the School of Health and Related Research (SchARR), University of Sheffield (see the "Availability of Companion Documents" field).

A systematic review of the clinical effectiveness of amantadine, oseltamivir and zanamivir for influenza prophylaxis was undertaken according to the general principles recommended in the QUOROM statement.

Data Abstraction Strategy

Data were extracted with no blinding to authors or journal. Data was extracted by one reviewer using a standardised form. Any studies giving rise to uncertainty were reviewed independently by a second reviewer, and discrepancies, for example where studies were not clearly reported, were resolved by discussion. All data abstraction was checked and confirmed by a second reviewer.

Critical Appraisal Strategy

The quality of included randomised controlled studies was assessed using quality criteria based on those developed by the NHS Centre for Reviews and Dissemination; these are presented in Appendix 2 of the Assessment Report (see the "Availability of Companion Documents" field). The purpose of such quality assessment was to provide a narrative account of trial quality for the reader. Quality assessment was confirmed by a second reviewer.

Methods of Data Synthesis

The pre-specified outcomes were presented within a narrative synthesis. Where quantitative synthesis was considered to be appropriate, statistical meta-analysis was undertaken using a random effect model using RevMan software (version 4.2.10) in order to calculate pooled estimates for relative risks for outcomes of interest. The presence of heterogeneity within the identified evidence and the lack of any head-to-head direct comparative RCTs of antiviral prophylaxis were considered to preclude the use of sensitivity analyses and mixed treatment comparisons.

Efficacy data are presented as relative risks (RR) and protective efficacy (PE = 1 minus RR, expressed as a percentage). Where the RR or PE values were not described in the study publication, or where the value differed (usually only by a small margin) from that calculated from the formula below, the RR was calculated by the Assessment Group using the following formula:

$$RR = (a/(a+c))/(b/(b+d))$$

Where a = event present for treatment group, b = event present for control group, c = event absent for treatment group, and d = event absent for control group.

Where publications have reported a 95% confidence interval (95% C.I.) around the RR or PE, these have been presented. Where no C.I. was published, it was calculated using the following formula:

$$SE [\ln(RR)] = \text{square root} [(1/a - 1/(a+c) + 1/b - 1/(b+d))].$$

$$\text{Lower 95\% confidence limit for RR} = \exp [\log RR - 1.96 \times SE [\ln(RR)]].$$

$$\text{Upper 95\% confidence limit for RR} = \exp [\log RR + 1.96 \times SE [\ln(RR)]].$$

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals,

patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Assessment Group identified seven cost-effectiveness studies that included oseltamivir, amantadine or zanamivir for the prophylaxis of influenza, one of which was a sponsor submission from the manufacturer of oseltamivir. No cost-effectiveness analyses were submitted by the manufacturers of amantadine and zanamivir.

The submission from the manufacturer of oseltamivir reported a model to estimate the cost effectiveness of oseltamivir for seasonal and post-exposure prophylaxis of influenza, comparing it with amantadine, zanamivir and no prophylaxis for adults and children older than 12 years who were healthy or at risk, and for children aged 1–12 years and 1–5 years. A cost-effectiveness analysis was undertaken for the comparison of oseltamivir with amantadine or usual care. For the comparison of oseltamivir with zanamivir, it was assumed that both drugs are equally effective and a cost-minimisation analysis was undertaken. The Assessment Group reanalysed the results from the manufacturer's model for oseltamivir to generate full incremental cost-effectiveness estimates (the manufacturer's submission presented pair-wise comparisons rather than a full incremental analysis). Oseltamivir for post-exposure prophylaxis gave incremental cost-effectiveness ratios (ICERs) below 8,000 pounds sterling per quality-adjusted life year (QALY) gained for both groups of children, less than 2,000 pounds sterling for at-risk adults, and about 27,000 pounds sterling for healthy adults. For children in both age groups oseltamivir as seasonal prophylaxis gave ICERs above 46,000 pounds sterling per QALY gained. For healthy or at-risk adults and children (older than 12 years) oseltamivir was dominated by zanamivir (it was less effective and more costly), and for the at-risk group the ICERs for amantadine and zanamivir were less than 16,000 pounds sterling per QALY gained. The model was sensitive to the changes in assumptions for attack rates and the number of general practitioner (GP) visits per household.

The Assessment Group conducted an independent economic assessment. The three drugs were compared with each other and with no prophylaxis for three age groups: 'children' (aged 1–14 years), 'adults' (aged 15–64 years) and 'older people' (older than 65 years). Each age group was subdivided into healthy and at risk, and each of these six subgroups was further divided on the basis of vaccination status.

The Assessment Group model gave the following results for seasonal prophylaxis. In healthy children, oseltamivir economically dominated amantadine and zanamivir. That is, treatment with oseltamivir was expected to cost less and result in more QALYs gained. For unvaccinated children the ICER was 44,007 pounds sterling per QALY gained and for vaccinated children it was 129,357 pounds sterling per QALY gained. For at-risk children oseltamivir dominated the other drugs, with an ICER of 16,630 pounds sterling per QALY gained for unvaccinated

children and 51,069 pounds sterling per QALY gained for vaccinated children. In healthy adults oseltamivir dominated the other drugs, with ICERs of 147,505 pounds sterling per QALY gained in unvaccinated adults and 427,184 pounds sterling per QALY gained in vaccinated adults. For at-risk adults oseltamivir again dominated the other drugs, with ICERs of 63,552 pounds sterling per QALY gained in unvaccinated people and 186,651 pounds sterling per QALY gained in vaccinated people. For healthy older people oseltamivir dominated the other drugs, with ICERs of 49,742 pounds sterling per QALY gained in unvaccinated people and 121,728 pounds sterling per QALY gained in vaccinated people. In at-risk older people oseltamivir dominated the other drugs, with ICERs of 38,098 pounds sterling per QALY gained for unvaccinated people and 93,763 pounds sterling per QALY gained for vaccinated people.

For post-exposure prophylaxis in healthy children zanamivir economically dominated oseltamivir and amantadine, with ICERs of 23,225 pounds sterling per QALY gained in unvaccinated children and 71,648 pounds sterling per QALY gained in vaccinated children. For post-exposure prophylaxis in at-risk children zanamivir dominated the other drugs, with ICERs of 8,233 pounds sterling for unvaccinated children and 27,684 pounds sterling for vaccinated children. For post-exposure prophylaxis in healthy adults oseltamivir dominated zanamivir and amantadine, with ICERs of 34,181 pounds sterling for unvaccinated adults and 103,706 pounds sterling for vaccinated adults. For post-exposure prophylaxis in at-risk adults oseltamivir dominated the other drugs, with ICERs of 13,459 pounds sterling per QALY gained for unvaccinated adults and 43,970 pounds sterling for vaccinated adults. In healthy older people oseltamivir dominated zanamivir and amantadine, with an ICER of 10,716 pounds sterling per QALY gained for unvaccinated people and 28,473 pounds sterling for vaccinated people. For post-exposure prophylaxis in at-risk older people oseltamivir again dominated, with ICERs of 7,866 pounds sterling for unvaccinated people and 21,608 pounds sterling for vaccinated people.

The Committee considered the cost effectiveness of the use of seasonal prophylaxis. In doing so it was aware that clinical specialist opinion did not favour the use of drug prophylaxis in this manner. The Committee also noted that because seasonal prophylaxis would be considered only in exceptional situations such as a mismatch between vaccine and circulating virus, the efficacy of vaccination assumed should be intermediate between the extremes of the values used for unvaccinated and vaccinated relative risks in the model. The Committee concluded that the ICERs for the various subgroups examined in the modelling suggested that overall seasonal prophylaxis was not a cost-effective use of NHS resources.

The Committee considered the results of the economic evaluation for the use of the drugs for post-exposure prophylaxis. The Committee was aware that prophylaxis would not normally be considered in clinical practice for healthy people given the self-limiting nature of influenza and the potential for adverse effects with medication. The Committee noted that the ICERs for the various subgroups indicated that the use of post-exposure prophylaxis was cost effective in at-risk groups only who had either not been vaccinated or not been effectively protected by vaccination. The ICERs in these subgroups ranged from 7,866 pounds sterling per QALY gained for unvaccinated at-risk older people, to 8,233 pounds sterling per QALY gained for unvaccinated at-risk children, to 13,459

pounds sterling per QALY gained for unvaccinated at-risk adults. The Committee also noted that the contact with the index case would need to be of a sufficiently intense degree, such as that experienced by living together in the same residential setting, normally the same household. The Committee concluded that post-exposure prophylaxis was a cost-effective use of resources for at-risk persons who were not adequately protected by vaccination, but only when it has been established that influenza is circulating in the community.

See Sections 4.2 and 4.3 in of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

NOTE: This guidance replaces 'National Institute of Health and Clinical Excellence (NICE) technology appraisal guidance 67' issued in September 2003.

NICE reviews each piece of guidance it issues.

The review and re-appraisal of the use of amantadine and oseltamivir for the prophylaxis of influenza has resulted in inclusion of zanamivir in the guidance.

Guidance

This guidance has been prepared with the expectation that vaccination against influenza is undertaken in accordance with national guidelines. Vaccination has been established as the first-line intervention to prevent influenza and its complications, and the use of drugs as recommended in this guidance should not detract from efforts to ensure that all eligible people receive vaccination.

This guidance does not cover the circumstances of a pandemic, an impending pandemic, or a widespread epidemic of a new strain of influenza to which there is little or no community resistance.

Oseltamivir and zanamivir are recommended, within their marketing authorisations, for the post-exposure prophylaxis of influenza if **all** of the following circumstances apply.

- National surveillance schemes have indicated that influenza virus is circulating.

Note: The Health Protection Agency in England (and the equivalent bodies in Wales and Northern Ireland) uses information from a range of clinical, virological and epidemiological influenza surveillance schemes to identify periods when there is a substantial likelihood that people presenting with an influenza-like illness are infected with influenza virus.

- The person is in an at-risk group (as defined below).
- The person has been exposed (see below) to an influenza-like illness and is able to begin prophylaxis within the timescale specified in the marketing authorisations of the individual drugs (within 36 hours of contact with an index case for zanamivir and within 48 hours of contact with an index case for oseltamivir).
- The person has not been effectively protected by vaccination (as defined below).

The choice of either oseltamivir or zanamivir in the circumstances described above should be determined by the healthcare professional in consultation with patients and carers. The decision should take into account preferences regarding the delivery of the drug and potential adverse effects and contraindications. If all other considerations are equal, the drug with the lower acquisition cost should be used.

For the purpose of this guidance, people at risk are defined as those who fall into one or more of the clinical risk groups defined, and updated, each year by the Chief Medical Officer. The current list includes people with:

- Chronic respiratory disease (including asthma that requires continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospital admission)
- Chronic heart disease
- Chronic renal disease
- Chronic liver disease
- Chronic neurological disease
- Immunosuppression
- Diabetes mellitus

People who are aged 65 years or older are also defined as at-risk for the purpose of this guidance.

Exposure to an influenza-like illness is defined as close contact with a person in the same household or residential setting who has had recent symptoms of influenza.

People who are not effectively protected by vaccination include:

- Those who have not been vaccinated since the previous influenza season
- Those for whom vaccination is contraindicated, or in whom it has yet to take effect
- Those who have been vaccinated with a vaccine that is not well matched (according to information from the Health Protection Agency) to the circulating strain of influenza virus

During localised outbreaks of influenza-like illness (outside the periods when national surveillance indicates that influenza virus is circulating generally in the community), oseltamivir and zanamivir may be used for post-exposure prophylaxis in at-risk people living in long-term residential or nursing homes, whether or not they are vaccinated. However, this should be done 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 infection with influenza in the index case or cases.

Oseltamivir and zanamivir are not recommended for seasonal prophylaxis of influenza.

Amantadine is not recommended for the prophylaxis of influenza.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate and effective use of oseltamivir and zanamivir for post-exposure prophylaxis of influenza
- Reduced rates of influenza

POTENTIAL HARMS

- Adverse effects associated with *oseltamivir* include gastrointestinal symptoms, bronchitis and cough, dizziness and fatigue and neurological symptoms such as headache, insomnia and vertigo. Skin rashes and allergic reactions and, rarely, hepatobiliary system disorders have been reported. Convulsions and psychiatric events, mainly in children and adolescents, have also been reported but a causal link has not been established.
- Oseltamivir should be administered with caution to patients who:

- Have renal impairment
- Are pregnant or breast-feeding
- Have conditions of such severity or instability that imminent hospitalisation may be required
- Are immunocompromised
- Have chronic cardiac and/or respiratory disease
- Adverse effects associated with *zanamivir* are rare. They include bronchospasm and allergic phenomena.
- Zanamivir should be administered with caution to patients who:
 - Have asthma and chronic pulmonary disease
 - Have uncontrolled chronic illness
 - Are immunocompromised
 - Are pregnant

For full details of adverse effects and contraindications, see the summary of product characteristics (SPC).

CONTRAINDICATIONS

CONTRAINDICATIONS

- Oseltamivir is contraindicated in patients who have hypersensitivity to oseltamivir or any of the excipients.
- Zanamivir is contraindicated in patients who are pregnant or breast-feeding or are hypersensitive to any ingredient of the preparation.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance has been prepared in the expectation that vaccination against influenza is undertaken in accordance with national guidelines. Vaccination has been established as the first-line intervention to prevent influenza and its complications, and the use of drugs as recommended in this guidance should not detract from effort to ensure that all eligible people receive vaccination. This guidance does not cover the circumstances of a pandemic, impending pandemic, or a widespread epidemic of a new strain of influenza to which there is little or no community resistance.
- This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgment. This guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by the National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare Standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (www.nice.org.uk//TA158) [see also the "Availability of Companion Documents" field].
 - Costing report and costing template to estimate the saving and costs associated with implementation
 - Audit support for monitoring local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

Patient Resources

Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 37 p. (Technology appraisal guidance; no. 158).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Sep (revised 2008 Sep)

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor AE Ades, Professor of Public Health Science, Department of Community Based Medicine, University of Bristol; Dr Amanda Adler, Consultant Physician, Cambridge University Hospitals Trust; Dr Tom Aslan, General Practitioner, Stockwell, London; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Mrs Elizabeth Brain, Lay member; Professor Karl Claxton, Health Economist, University of York; Simon Dixon, Reader in Health Economics, University of Sheffield; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Mr John Goulston, Director of Finance, Barts and the London NHS Trust; Mr Adrian Griffin, Health Outcomes Manager, Johnson & Johnson Medical; Professor Philip Home (*Vice Chair*) Professor of Diabetes Medicine, Newcastle University; Dr Vincent Kirkbride, Consultant Neonatologist, Regional Neonatal Intensive Care Unit, Sheffield; Dr Simon Maxwell, Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Queens Medical Research

Institute, University of Edinburgh; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Dr Ann Richardson, Lay Member; Mrs Angela Schofield, Chairman, Bournemouth and Poole Teaching PCT; Mr Mike Spencer, General Manager, Facilities and Clinical Support Services, Cardiff and Vale NHS Trust; Dr Simon Thomas, Consultant Physician and Reader in Therapeutics, Newcastle Hospitals NHS Foundation Trust and Newcastle University; Mr David Thomson, Lay member; Dr Norman Vetter, Reader, Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Clinical Excellence (NICE). Guidance on the use of oseltamivir and amantadine for the prophylaxis of influenza. London (UK): National Institute for Clinical Excellence (NICE); 2003 Sep. 32 p. (Technology appraisal; no. 67).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 2 p. (Technology appraisal 158). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. Various p. (Technology appraisal 158). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 7 p. (Technology appraisal 158). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza. Evidence review group report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb 12. 312 p. (Technology appraisal 158). Available in Portable Document Format (PDF) from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1690. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Oseltamivir, amantadine and zanamivir to prevent influenza. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 4 p. (Technology appraisal 158).

Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N1691. 11 Strand, London, WC2N 5HR.

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