Complete Summary

GUIDELINE TITLE

Guidance on the use of oseltamivir and amantadine for the prophylaxis of influenza.

BIBLIOGRAPHIC SOURCE(S)

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 STATUS

This is the current release of the guideline.

** 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.

- 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.

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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
Physician Assistants
Physicians
Public Health Departments
Utilization Management

GUIDELINE OBJECTIVE(S)

To establish the clinical and cost effectiveness of amantadine, oseltamivir and zanamivir for the treatment and prevention of influenza

TARGET POPULATION

- At-risk people* aged 13 years or older who are not effectively protected by vaccination and who have been exposed to someone with influenza-like illness (ILI) and are able to begin prophylaxis within 48 hours of exposure
- At-risk people*, aged 13 years and older and who can begin prophylaxis within 48 hours, whether or not they have been vaccinated, if they live in a residential care establishment where a resident or staff has ILI.

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

INTERVENTIONS AND PRACTICES CONSIDERED

1. Oseltamivir

2. Amantadine (considered but not recommended)
3. Community-based virological surveillance

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness of:
    - Amantadine for post-exposure and seasonal prophylaxis
    - Oseltamivir for post-exposure and seasonal prophylaxis
- Adverse effects
- 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 Departments of Epidemiology and Public Health & Microbiology and Immunology, University of Leicester and ScHARR, University of Sheffield (see the "Companion Documents" field).

A systematic review and meta-analysis of the randomized evidence was undertaken to investigate the effectiveness of oseltamivir and zanamivir for treatment and prophylaxis used for influenza A and B. Where necessary, pharmaceutical companies were contacted for additional information not available from the published literature. An additional systematic review of the effectiveness of amantadine for treatment and prophylactic use for influenza A in children and the elderly was also undertaken.

Economic decision models were constructed to examine the cost-effectiveness and cost-utility of the alternative strategies for treating and preventing influenza A and/or B. This was informed by the systematic reviews outlined above and additional sources of information where required.

NUMBER OF SOURCE DOCUMENTS

Zanamivir

44 different trials evaluating zanamivir for the treatment of influenza were identified; of these, 11 trials had data available and met the criteria for inclusion in the systematic review

Eleven zanamivir prevention trials were identified, of which five met all of the inclusion criteria

Oseltamivir

17 different trials evaluating oseltamivir for the treatment of influenza were identified; of these, 9 trials had data available and met the criteria for inclusion in the systematic review

Seven oseltamivir prophylaxis trials were identified, of which four randomized controlled trials met all of the inclusion criteria

Children

Eight amantadine prevention trials were identified, of which three met all of the inclusion criteria

Four studies were identified that examined amantadine treatment in children; two were included in the review

Elderly

Seven amantadine prophylaxis trials were identified, of which two randomized clinical trials met all of the inclusion criteria

There were no studies identified that met the inclusion criteria and addressed amantadine treatment in the elderly

Cost Effectiveness

Seven published studies were identified that examined the cost-effectiveness of one or both of oseltamivir or zanamivir

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

Decision Analysis
Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

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Economic decision models were constructed to examine the cost-effectiveness and cost-utility of the alternative strategies for treating and preventing influenza A and/or B. This was informed by the systematic reviews outlined above and additional sources of information where required.

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

Cost Effectiveness

For the prophylaxis of influenza, the Assessment Report found one cost-effectiveness study of oseltamivir. In addition, the two manufacturers of the technologies provided analyses for this appraisal, and the Assessment Group developed its own models for both seasonal and post-exposure prophylaxis, and commented on models in the literature.

The estimated cost effectiveness in the models varied considerably, depending on the assumptions made for some of the key parameters. The most important of these was whether a reduction in mortality was included. One variant of the model prepared by the Assessment Group examined the scenario where a benefit is assumed from averting death. The percentage reduction in post-influenzal pneumonia attributed to antiviral drug treatment was estimated, and the same percentage reduction in pneumonia deaths was inferred. Because pneumonia is the most common cause of death from complications of influenza, this provided a

reasonable method of extrapolating the beneficial effect (for the purposes of cost effectiveness) of the antiviral drugs.

Different studies have made different assumptions about plausible values of several key variables, to which the estimates of cost effectiveness within the models are very sensitive. Apart from the inclusion or otherwise of the effect of the drugs on mortality, when used for prophylaxis, the key variables were:

- whether prophylaxis extends for the whole time that influenza is circulating (seasonal prophylaxis) or only for the few days following contact with a person with influenza-like illness (ILI) symptoms (post-exposure prophylaxis)
- whether the person/group of people has been vaccinated
- the effectiveness of the vaccine and the attack rate of the virus

See Section 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

This guidance pertains only to circumstances where it is known that either influenza A or influenza B is circulating in the community (see Section 1.7 of the original guideline document).

- Oseltamivir is recommended for the post-exposure prophylaxis of influenza in at-risk people aged 13 years or older who are not effectively protected by vaccination and who have been exposed to someone with influenza-like illness (ILI) and are able to begin prophylaxis within 48 hours of exposure. People who are not effectively protected by vaccination include those who have not been vaccinated since the previous influenza season, or for whom:

    - Vaccination is contraindicated, or has yet to take effect.
    - Vaccination has been carried out but the vaccine is not well matched to the strain of influenza virus circulating. (The Department of Health and the Welsh Assembly Government, acting on information from the Health Protection Agency, issue advice nationally each year on whether the vaccine and the circulating influenza virus are well matched.)

      Exposure to ILI is defined as being in close contact with someone who lives in the same home environment as a person who has been suffering from symptoms of ILI.

- At-risk people are defined, for the purpose of this guidance, as those who are in at least one of the following groups.

  People who:

    - have chronic respiratory disease (including asthma and chronic obstructive pulmonary disease)
    - have significant cardiovascular disease (excluding people with hypertension only)
    - have chronic renal disease
    - are immunocompromised
    - have diabetes mellitus
    - are aged 65 years or older
- Oseltamivir is recommended for the post-exposure prophylaxis of influenza in at-risk people, aged 13 years and older and who can begin prophylaxis within 48 hours, whether or not they have been vaccinated, if they live in a residential care establishment where a resident or staff member has ILI. For the purposes of this guidance, a residential care establishment is defined as a place where the at-risk person resides in the long term in order to be provided with continuing care alongside a number of other individuals.
- Oseltamivir is not recommended for post-exposure prophylaxis in healthy people up to age 65 years.
- Oseltamivir is not recommended for the seasonal prophylaxis of influenza.
- Amantadine is not recommended for either post-exposure or seasonal prophylaxis of influenza.
- Community-based virological surveillance schemes should be used to determine when influenza virus is circulating in the community. Such schemes, including those organised by the Royal College of General Practitioners and the Health Protection Agency, should ensure that the onset of the circulation of influenza virus (A or B) within a defined area is identified as rapidly as possible. In Appendix D of the original guideline document, definitions and numerical values of threshold levels for different categories of influenza activity are given.

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 for prophylaxis of influenza
- Reduced rates of influenza

POTENTIAL HARMS

Adverse Events

Oseltamivir

In clinical trials, oseltamivir at the licensed dosage is generally well tolerated, but has been associated with a somewhat higher rate of nausea and vomiting compared with placebo, although the differences are not large (a 3 to 7 percentage point higher rate of nausea and up to 2 percentage points higher rate of vomiting with oseltamivir compared with placebo). During post-licensing experience, there have been very rare reports of elevated liver enzymes and hepatitis, and of skin rashes.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance has been prepared in the expectation that vaccination against influenza is undertaken in accordance with national guidelines. Vaccination is the most effective way of preventing illness from influenza, and the drugs described in this guidance are not a substitute for 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 available evidence. 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 appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- In considering local implementation arrangements, the National Health Service (NHS) will wish to take account of previous advice from the Department of Health and the National Assembly of Wales (now the Welsh Assembly Government) following the National Institute for Health and Clinical Excellence (NICE) Guidance No. 15 and any further advice from these bodies following the extension of guidance in the current document. Local action might include some or all of the following.
    - Telephone advice and information by a practice nurse or other healthcare professional with reference to a protocol containing appropriate and standard diagnostic questions
    - Patient Group Directions for direct supply by nurses and pharmacists from community pharmacies, including those working from NHS walk-in centres in England
    - NHS prescriptions issued by general practitioners (GPs) in the standard way following consultations or home visits
- GPs should review their current practice and policies for the care of at-risk people who have been exposed to influenza-like illness (ILI) to take into account the guidance (see the "Major Recommendations" field).
- Local guidelines, protocols or care pathways that refer to the care of at-risk people who have been exposed to ILI should incorporate the guidance.
- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C of the original guideline document.
    - Oseltamivir is prescribed for the post-exposure prophylaxis of influenza in the following circumstances.
        - The individual is at-risk, is aged 13 years or older, is not effectively protected by vaccination, has been exposed to someone with ILI and is able to begin prophylaxis within 48 hours of exposure, or
        - The individual is at-risk and lives in a residential care establishment where a resident or staff member has ILI, whether or not the individual has been vaccinated.
    - Oseltamivir is not prescribed for post-exposure prophylaxis in a healthy individual who is up to age 65 years.
    - Oseltamivir is not prescribed for the seasonal prophylaxis of influenza.
    - Amantadine is not prescribed for either post-exposure or seasonal prophylaxis of influenza.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Foreign Language Translations
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 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).

ADAPTATION

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

DATE RELEASED

2003 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: Dr Jane Adam, Radiologist, St George's Hospital, London; Dr Sunil Angris, General Practitioner, Waterhouses Medical Practice, Staffordshire; Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Professor John Brazier, Health Economist, University of Sheffield; Professor John Cairns, Professor of Health Economics, Health Economics Research Unit, Institute of Applied Health Sciences, University of Aberdeen; Professor Mike Campbell, Statistician, Institute of General Practice & Primary Care, Sheffield; Dr Mark Chakravarty, Head of Government Affairs and NHS Policy, Procter and Gamble

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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.

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 and amantadine for the prophylaxis of influenza. Summary. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Sep. 2 p. (Technology appraisal 67). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Systematic review and economic decision modelling for the prevention and treatment of influenza A and B. Assessment report. NHS R&D HTA Programme; 2002 Apr 29. 493 p. Available in Portable Document Format

(PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0293. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria can be found in Appendix C of the original guideline document.

PATIENT RESOURCES

The following is available:

- The use of oseltamivir and amantadine to prevent influenza. Understanding NICE guidance - information for the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Sep. 10 p. (Technology appraisal 67).

Electronic copies: Available in English and Welsh 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: N0294. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on June 26, 2006. This summary was updated by ECRI on November 21, 2006 following the FDA advisory on Tamiflu. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Tamiflu (oseltamivir phosphate).

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Date Modified: 9/22/2008