



Complete Summary

GUIDELINE TITLE

Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza. London (UK): National Institute for Clinical Excellence (NICE); 2003 Feb. 30 p. (Technology appraisal guidance; no. 58).

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.

- [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.

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SCOPE

DISEASE/CONDITION(S)

Influenza

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Pediatrics
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To examine the clinical and cost-effectiveness of zanamivir, oseltamivir, and amantadine in children and adults with influenza

TARGET POPULATION

Children and adults with influenza who are considered to be "at risk"

At-risk adults and children 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

INTERVENTIONS AND PRACTICES CONSIDERED

1. Zanamivir
2. Oseltamivir

Amantadine was considered but not recommended for treatment of influenza.

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
 - Time to symptom alleviation
 - Time to return to normal activities
 - Hospitalisation
 - Adverse effects of treatment
 - Complications requiring use of antibiotics
- 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).

Search Strategy

A number of online electronic databases were searched to ensure complete ascertainment of published reports on the neuraminidase inhibitors (Nis): MEDLINE (1966 through December 2001), EMBASE (1980 through December 2001) and the Integrated Science Citation Index (via Manchester Information and Associated Services) (1981 through December 2001). These were supplemented with searches of the National Library of Medicine (PUBMED) and the Health

Economic Evaluations Database (HEED) of the Office of Health Economics. The main subject terms are given in Table 3.1 of the Assessment Report (see the "Availability of Companion Documents" field), and used to search title, abstract, and keyword sections of the references.

The search findings were checked against a number of registers and online databases (Table 3.2 of the Assessment Report [see the "Availability of Companion Documents" field]).

Journals whose contents and archives were searched are given in Table 3.3 of the Assessment Report (see the "Availability of Companion Documents" field).

In addition to the electronic database search strategy, the following further measures were taken in order to maximise the chances of finding all the relevant studies.

1. Scrutiny of reference lists of identified articles
2. Scrutiny of reference sections of the major textbook of "Nicholson KG, Webster RG & Hay AJ (1998). Textbook of Influenza. Oxford: Blackwell Science"
3. Scrutiny of reference lists of two National Institute for Clinical Excellence reports on the use of Zanamivir and also the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) reports on the use of Oseltamivir and Zanamivir for the treatment of influenza
4. Meetings with representatives from both Roche and GlaxoSmithKline were set up to ascertain if any additional trials, not identified through other methods, existed (i.e., "unpublished" or "in print" or "on-going"). Also to gain further information where the published information on known trials was unclear.
5. Searching of pre-existing personal databases

Inclusion and Exclusion Criteria

All trials evaluating the treatment of influenza by neuraminidase inhibitors (zanamivir or oseltamivir) were considered for inclusion in this systematic review. To be selected for the systematic review, leading to further examination for inclusion in the meta-analyses, trials had to meet all the criteria outlined below.

Inclusion criteria for NI systematic review

1. It had to be a randomised, double-blind trial
2. Patients had to have contracted (or suspected to have contracted) naturally occurring influenza (i.e., all trials where patients were deliberately given experimental influenza were excluded, since this does not relate to the efficacy of NIs in clinical practice, of interest here)
3. At least one clinical outcome measure of relevance had to be reported. Those considered relevant are:
 - Time to alleviation of symptoms
 - Time to alleviation of major influenza symptoms
 - Time to eradication of major signs and symptoms
 - Time to return to normal activities
 - Number of days symptoms scored none/mild
 - Complications requiring use of antibiotics

- Adverse events due to treatment
 - Hospitalisations
4. The NI had to be administered using the formulation submitted for licensing approval.
 5. Data had to be available before 31/12/2001.
 6. Necessary trial information had to be available in English.

An additional systematic review of the effectiveness of amantadine for treatment and prophylaxis use for influenza A in children and the elderly was also undertaken. See Chapter 5 of the Assessment Report (see "Availability of Companion Documents" field) for further details.

NUMBER OF SOURCE DOCUMENTS

Zanamivir

44 different trials evaluating zanamivir for the treatment of influenza were identified. Since the results of trials:

- i. NAIA2008 and NAIB2008, and
- ii. NAIA2005 and NAIB2005

are reported as combined in most data sources they are treated as two trials rather than four trials (i.e., NAIA/B2008 and NAIA/B2005) in this review, reducing the number of trials to 42. Of these, 11 trials had data available and met the criteria for inclusion in the systematic review.

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.

Amantadine

Four studies were identified that examined amantadine treatment in children. Two were included in the review. There were no studies identified that met the inclusion criteria and addressed amantadine treatment in the elderly.

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

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 technology appraisal was prepared by the School of Health and Related Research (SchARR), University of Sheffield. (See the "Availability of Companion Documents" field.)

Assessment of Study Validity

Previous reports have applied the JADAD trial quality scoring system to assess study validity (see Appendix 3B of the Assessment Report [see the "Availability of Companion Documents" field]). This was considered problematical to the point of misleading because:

1. Varying degrees of published information were available in English (i.e., conference abstracts, U.S. Food and Drug [FDA] reports, formal publications, personal correspondence with pharmaceutical companies)
2. Where necessary, data was re-analysed at our request by the pharmaceutical companies. Intention-to-treat (total population and influenza positive population) analyses were always requested irrespective of any results that may have been published previously.

For the reasons outlined above, in this review low JADAD scores primarily indicate lack of clarity in the trial descriptions available (the Assessment Group used whatever data sources available to calculate these scores -- see point 1 above). Therefore, no JADAD cut-off point was applied as an additional exclusion criterion. However, since all trials had to be randomised and double-blinded for inclusion in this review, a quality threshold is maintained.

Data Extraction Strategy

Data from the studies identified for inclusion in the systematic review were extracted using a data extraction form. Data was extracted on the patient groups considered by each trial and the summary statistics for the efficacy outcomes of interest (details are provided in Chapter 3 of the Assessment Report [see the "Availability of Companion Documents" field]). Data was obtained from a variety of sources including the published literature, FDA reports (<http://www.fda.gov/cder/approval/index.htm>), previous health technology assessments, and directly from pharmaceutical companies.

Data Analysis

Where sufficient information was available, results from different studies were combined using meta-analysis for each neuraminidase inhibitor (NI) compound separately using the outcome measures defined in section 3.1.3 of the

Assessment Report (see the "Availability of Companion Documents" field). Separate analyses were carried out on intent to treat (ITT) populations for each patient subgroup and for all individuals and those confirmed influenza positive. Random effects models were used throughout to take into account any statistical heterogeneity that may exist. All meta-analyses were performed using the STATA software package (<http://www.stata.com>). Note the practice of combining medians rather than means is non-standard, however, justified for time to event data, as it is the more clinically relevant outcome in this case (as discussed in section 3.1.3.3 of the Assessment Report [see the "Availability of Companion Documents" field]). For the complication endpoints considered by this review, previous pooled analyses were used since these contained more data than available to the Assessment Group. Note these analyses were conducted by pooling the individual patient level data from the different studies (rather than combining effect sizes from each study in a meta-analysis). Since such analyses are marginal (i.e., equivalent to constructing one large 2 by 2 table of all the data combined), they have the potential to be misleading. As a safeguard against this, meta-analyses were carried out on the limited data available, which produced results that were consistent with the marginal analyses results in all cases.

Sensitivity analyses were performed to test the robustness of the results to various assumptions made in the analysis. Hence, additional meta-analyses were performed on the subsets defined by (i) data published in peer-reviewed journals only, and (ii) a JADAD quality score of 4 or 5 only (see Tables 3.8 and 3.11 of the Assessment Report (see the "Availability of Companion Documents" field)).

For information about the methods to analyze the evidence about amantadine, see Chapter 5 of the Assessment Report (see "Availability of Companion Documents" field).

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 Report found seven cost-effectiveness studies for the treatment of influenza: for zanamivir, two for the National Institute for Health and Clinical Excellence (NICE) appraisal in 2000, one on behalf of the Canadian Coordinating Office of Health Technology Assessment (CCOHTA), and one in association with Glaxo Wellcome; for oseltamivir, one for CCOHTA and one in association with Roche; and for both zanamivir and oseltamivir, one with an association with Glaxo Wellcome. In addition, the three manufacturers of the technologies provided

analyses for this appraisal, and the Assessment Group also developed its own model, and commented on models in the literature.

See Section 4.3 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 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 pertains only to circumstances where it is known that either influenza A or influenza B is circulating in the community.

- Zanamivir and oseltamivir are not recommended for the treatment of influenza in children or adults unless they are considered to be "at risk."
- At-risk adults and children 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
- Amantadine is not recommended for the treatment of influenza.
- Within their licensed indications, zanamivir and oseltamivir are recommended for the treatment of at-risk adults who present with influenza-like illness (ILI) and who can start therapy within 48 hours of the onset of symptoms.
- Within its licensed indications, oseltamivir is recommended for the treatment of at-risk children who present with ILI and who can start therapy within 48 hours of the onset of symptoms.
- Community-based virological surveillance schemes should be used to indicate when influenza virus is circulating in the community. Community-based virological surveillance schemes, such as those organised by the Royal College of General Practitioners and the Public Health Laboratory Service, should be used to indicate when influenza virus is circulating in the community. Such schemes should ensure that the onset of the circulation of influenza virus (A or B) within a defined area is identified as rapidly as possible.

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 use of zanamivir and oseltamivir in "at risk" children and adults with influenza

POTENTIAL HARMS

Zanamivir

In clinical trials, zanamivir is generally well tolerated, with the number, type and severity of adverse events being similar to those with placebo. Zanamivir has not been extensively tested in people with severe asthma or other chronic respiratory diseases, unstable chronic illnesses or compromised immune systems. In post licensing experience, there have been very rare reports of allergic reactions such as facial and oropharyngeal oedema, rash, and urticaria.

Oseltamivir

In clinical trials, oseltamivir 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 3–7% higher rate of nausea and up to 2% 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 skin rashes.

For full details of side effects and contraindications, see the Summary of Product Characteristics, available at <http://emc.medicines.org.uk/>.

CONTRAINDICATIONS

CONTRAINDICATIONS

Zanamivir is contraindicated in women who are breastfeeding. It should be used with caution in people with asthma or chronic pulmonary disease because of risk of bronchospasm, in people with unstable chronic illness or compromised immune systems and during pregnancy. If people with asthma or chronic pulmonary disease are prescribed zanamivir, they should be made aware of the risks and have a fast-acting bronchodilator available.

For full details of side effects and contraindications, see the Summary of Product Characteristics, available at <http://emc.medicines.org.uk/>.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- It is recommended that at-risk groups and healthcare personnel dealing with people in at-risk groups on a face-to-face basis are vaccinated against influenza before the beginning of every winter.
- The present National Health Service (NHS) policy of active influenza vaccination provides an opportunity for a targeted approach to the use of antiviral drugs for influenza in the at-risk population. Information about the availability and appropriate use of the medicine could be incorporated into local and national influenza treatment campaigns.

- This guidance is likely to have an impact on primary healthcare services, both during the day and after hours, compared with no prescribing of drugs for the treatment of influenza, but little additional impact compared with the provisions of National Institute for Health and Clinical Excellence (NICE) Guidance No. 15, November 2000. Policies put in place at that time should still be followed where appropriate, but should now also incorporate some provisions for treatment of at-risk children.
- In considering local implementation arrangements, health authorities and primary care organisations 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 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 triaging by a practice nurse or other healthcare professional with reference to a protocol where 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
- The following criteria are suggested to measure compliance locally with the guidance set out in the guideline (see "Major Recommendations" field). Further details on audit criteria are presented in Appendix D of the original guideline document.
 - When influenza is circulating, an at-risk adult (for the purposes of the guidance, 12 years or older) who presents with influenza-like illness (ILI) and who can start therapy within 48 hours of the onset of symptoms is treated with zanamivir or oseltamivir.
 - When influenza is circulating, an at-risk child who presents with ILI and who can start therapy within 48 hours of the onset of symptoms is treated with oseltamivir.
 - Oseltamivir is not provided for the treatment of influenza in children or adults who are not considered to be at risk, and zanamivir is not provided for the treatment of influenza in adults who are not considered to be at risk and is not provided for children (under the age of 12 years).
 - Amantadine is not provided for the treatment 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

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza. London (UK): National Institute for Clinical Excellence (NICE); 2003 Feb. 30 p. (Technology appraisal guidance; no. 58).

ADAPTATION

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

DATE RELEASED

2003 Feb

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; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Professor Carol Black (up to June 2002) Consultant Physician, Royal Free Hospital & University College London; Professor John Brazier, Health

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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:

- Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Feb. 2 p. (Technology appraisal 58). 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 HTA Programme.

2002 Apr 29. 493 p. 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: N0199. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria are available in Appendix D of the [original guideline document](#).

PATIENT RESOURCES

The following is available:

- Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza. Information for the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Feb. 8 p. (Technology appraisal 58).

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: N0200. 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 August 2, 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). This summary was updated by ECRI Institute on April 9, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Relenza (zanamivir).

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