Complete Summary

GUIDELINE TITLE

Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Nov. 30 p. (Technology appraisal guidance; no. 132).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Primary (heterozygous-familial or non-familial) hypercholesterolemia

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To systematically evaluate and appraise the clinical effectiveness and cost-effectiveness of ezetimibe as combination therapy or monotherapy for the treatment of primary hypercholesterolemia (including heterozygous familial hypercholesterolemia) in the United Kingdom

TARGET POPULATION

Adults (18 years of age and older) with primary heterozygous-familial or non-familial hypercholesterolemia

INTERVENTIONS AND PRACTICES CONSIDERED

1. Ezetimibe monotherapy
2. Ezetimibe coadministered with statin therapy

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Survival
    - Fatal and non-fatal cardiovascular events
    - Adverse effects of treatment
    - Health-related quality of life (HRQoL)
    - Surrogate endpoints
        - Low-density lipoprotein-cholesterol (LDL-c)
        - Total cholesterol (Total-c)
        - High-density lipoprotein-cholesterol (HDL-c)
- 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Searches of Unpublished Data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 technology appraisal was prepared by the University of Sheffield School of Health and Related Research (ScHARR) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Identification of Studies

Sources Searched

Eleven electronic databases were searched providing coverage of the biomedical and grey literature and current research. The publications lists and current research registers of seven health services research related organisations were consulted via the World Wide Web (WWW). Keyword searching of the WWW was undertaken using the Google search engine. The submissions of evidence to NICE by sponsors were hand-searched as well as references of retrieved papers. A list of the sources searched is provided in Appendix 1 of the Assessment Report (see the "Availability of Companion Documents" field).

Keyword Strategies

Sensitive keyword strategies using free-text and, where available, thesaurus terms were developed to search the electronic databases. Synonyms relating to the intervention (e.g., ezetimibe, ezetrol, zetia, vytorin, inegy and Chemical Abstracts Service [CAS] Registry number or Enzyme Commission [EC] number: 163222-33-1) were combined with synonyms relating to the condition (e.g., hypercholesterolemia, hypercholesterolaemia). Keyword strategies for all electronic databases are provided in Appendix 1 of the Assessment Report (see the "Availability of Companion Documents" field).

Search Restrictions

A methodological filter aimed at restricting search results to randomised controlled trials (RCTs) was used in the searches of Medline and Embase. The search of pre-MEDLINE was restricted to the last 180 days to capture recent and unindexed Medline references. Date limits were not used on any other database. Language restrictions were not used on any database. All searches were undertaken between April to June 2006.

Inclusion and Exclusion Criteria

Two reviewers independently screened all titles and abstracts. Full paper manuscripts of any titles/abstracts that were considered relevant by either reviewer were obtained where possible. The relevance of each paper was assessed according to the criteria set out below. Trial flow chart is presented in Appendix 2

of the Assessment Report (see the "Availability of Companion Documents" field). Any disagreements were resolved by discussion.

Population

Adult patients (defined as >18 years of age) with primary (heterozygous familial and non-familial) hypercholesterolaemia were included in the review whereas adults with homozygous familial hypercholesterolaemia or homozygous sitosterolaemia were excluded.

Interventions

- For patients whose condition is not adequately controlled with a statin alone the intervention was ezetimibe (Ezetrol®, Merck Sharp and Dohme Limited/Schering-Plough Limited [MSD/SP]) co-administered with a statin or a fixed dose combination tablet containing ezetimibe and simvastatin (Inegy®, MSD/SP)
- For patients in whom a statin is considered inappropriate, or is not tolerated, the intervention is ezetimibe monotherapy (Ezetrol®, MSD/SP)

Comparators

The comparator treatment included the following:

- For patients whose condition is not adequately controlled with a statin alone the relevant comparator was optimal statin monotherapy or treatment with a statin in combination with other lipid regulating drugs (e.g., nicotinic acid, bile acid resins, or fibrates).
- For patients in whom a statin is considered inappropriate, or is not tolerated, the relevant comparator was an alternative lipid regulating agent (e.g., nicotinic acid, bile acid resins, or fibrates) or no treatment.

Outcomes

Data on the following outcomes were included: survival, fatal and non-fatal cardiovascular events, adverse effects of treatment and health-related quality of life (HRQoL). Where information on clinical end-points is unavailable, consideration were given to surrogate endpoints, such as low-density lipoprotein-cholesterol (LDL-c), total cholesterol (Total-c), and high-density lipoprotein-cholesterol (HDL-c).

Study Design

Phase III randomised controlled trials of at least 12 weeks duration were included on the ground that trials of less than 12 weeks duration are unlikely to inform on survival, cardiovascular disease (CVD) events, adverse events, or HRQoL due to lipid lowering treatments. In the absence of clinical endpoint data from trials, the Assessment Group identified and included data from RCTs of sufficient duration (i.e. at least 12 weeks) for surrogate endpoints. This decision was then validated by clinical experts' opinion and meta-analysis.

Reviews of primary studies were not included in the analysis, but retained for discussion and identification of additional trials. The following publication types were excluded from the review: non-randomised studies (except for adverse events); animal models; preclinical and biological studies; narrative reviews, editorials, opinions; non-English language papers and reports where insufficient methodological details are reported to allow critical appraisal of the study quality.

Handling of the Company Submission

Company submissions were screened for data additional to that identified in published studies retrieved from the literature search.

Cost-Effectiveness

Systematic Review of Existing Cost Effectiveness Evidence

Search Strategy

Studies were identified through searches of the following databases: Medline, Embase, Cochrane Library, National Health Service Economic Evaluation Database (NHSEED), NHS Centre for Review and Dissemination Database of Abstracts Reviews of Effectiveness (NSH CRD DARE), NHS CRD Health Technology Assessment (NHC CRD HTA), CINAHL, OHE HEED and Web of Science. Publications lists and current research registers of HTA organisations were consulted via the WWW. Hand-searching and citation searches of included studies and of the company submission were undertaken. All searches were undertaken between April and June 2006. A list of the sources consulted and the keyword strategies used are given in Appendix 22 of the Assessment Report (see the "Availability of Companion Documents" field).

Inclusion Criteria

- Cost effectiveness/cost-utility analyses
- Ezetimibe monotherapy
- Ezetimibe co-administered with statins
- The benefits in terms of life-years saved (LYS) or quality adjusted life-years (QALYs)
- Adult population (aged 18 years and over)

Exclusion Criteria

- Studies that do not report results in terms of incremental cost utility ratios (ICERs)

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Thirteen phase III randomized controlled trials meeting inclusion criteria were included: 12 published in peer-reviewed journal, one published in abstract form.

Cost-Effectiveness

- Existing literature – two full articles and one abstract
- A submission by Merck Sharp and Dohme Limited/Schering-Plough Limited

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

Clinical Effectiveness

Data Abstraction Strategy

Data relating to study design, quality, and results were extracted by one reviewer into a standardised data extraction form and independently checked for accuracy by a second. Any discrepancies were resolved by consensus. Where multiple publications of the same study were identified, data were extracted and reported as a single study.

Critical Appraisal Strategy

The quality of the included studies was assessed (unblinded) by one reviewer and independently checked for agreement by a second. Disagreements were resolved by consensus. The quality of the clinical effectiveness studies was assessed according to criteria based on those proposed by the National Health Service (NHS) Centre for Reviews and Dissemination. The purpose of this assessment was to give a narrative assessment of the potential for bias in the studies and, in the event that statistical synthesis (meta-analysis) was appropriate, to inform sensitivity analysis.

Methods of Data Synthesis

Data were tabulated and discussed in a narrative review. Where appropriate, meta-analyses were employed to estimate a summary measure of effect on relevant outcomes. All analyses were by intention-to-treat or modified intention-to-treat (analysis of subset of patients who received treatment as planned or at least some treatment). Efficacy results were reported as least squares (LS) mean percent change from baseline to study endpoint for comparison groups. Where appropriate, the standard deviations (SD) and 95% confidence intervals (CI) were calculated using the method documented in the Cochrane Handbook to perform meta-analyses of the published literature.

Meta-analyses were carried out using fixed and random effect models, with the Cochrane Collaboration Review Manager 4.2.3 software. Heterogeneity between trial results was explored through consideration of the study populations, methods and interventions, by visualization of the results and, in statistical terms, by chi^2 test for homogeneity and the I^2 measure. The chi^2 test measures the amount of variation in a set of trials. Small p-values imply that there is more heterogeneity present than would be expected by chance. Chi^2 is not a particularly sensitive test: a cut-off of $p<0.10$ is often used to indicate significance, but lack of statistical significance does not mean there is no heterogeneity. The I^2 measure is the proportion of variation that is due to heterogeneity rather than chance. Large values of I^2 suggest heterogeneity. I^2 values of 25%, 50%, and 75% could be interpreted as representing low, moderate, and high heterogeneity.

Cost-Effectiveness

Systematic Review of Existing Cost Effectiveness Evidence

Quality Assessment Strategy

The Eddy checklist on mathematical models for technology assessments in combination with the British Medical Journal checklist for economic evaluations was used to assess the quality of studies.

Published Cost Effectiveness Analyses

The two papers and the abstract included in the review describe country specific evaluations using a core economic model developed by Cook et al. The core model used is also used to inform the economic evaluation for the industry submission.

Review of the Merck Sharp and Dohme Limited/Schering-Plough Limited (MSD/SP) Economic Evaluation

Two models were submitted by the MSD/SP analysts. In keeping with the MSD/SP report, the main health economic model is referred to as the "Cook" model in this report, while the second model is referred to as the "Basic" model. The Cook model is an adaptation of the existing model (built in Excel using Visual Basic programming) used in all the publications described in section 6.1. of the Assessment Report (see the "Availability of Companion Documents" field). This model was designed to explore the cost effectiveness of ezetimibe in patients with

raised cholesterol levels and examines the potential benefits of treatment using changes in total cholesterol (Total-c) and high-density lipoprotein-cholesterol (HDL-c). The primary objective of the second model submitted was to determine "if a very simple model, developed from key clinical results can be used to predict approximately the results of the more sophisticated modelling exercise." The Basic model examines the potential benefits of treatment using changes in low-density lipoprotein-cholesterol (LDL-c).

Independent Economic Assessment by ScHARR

A Markov model was developed to explore the costs and health outcomes associated with a lifetime of treatment using a UK NHS perspective. The Framingham risk equations are used to derive baseline risks. Effectiveness of treatments is modelled using a reported link between chemically induced LDL-c reductions and cardiovascular events. Distribution across event types is based on UK specific incidence and prevalence rates. Meta-analyses of published randomised controlled trial (RCT) data are used to inform efficacy of treatments in lowering LDL-c levels. Input parameters are characterised by probability distributions and Monte Carlo simulations performed to reproduce this uncertainty in the results. Results are presented in terms of cost per quality-adjusted life years (QALYs).

Refer to Sections 5 and 6 of the Assessment Report (see the "Availability of Companion Documents" field) for additional information on methods used to analyze the evidence.

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 reviewed the literature and the submitted manufacturers' analyses, and generated its own economic model.

The Committee discussed the results of the economic analyses from the manufacturer's models and the Assessment Group's model. It concluded that the Assessment Group's model represented the most appropriate analysis on which to base its decision regarding the use of ezetimibe. This was because the Assessment Group's model was based on the effect on cardiovascular risk of reductions in cholesterol concentrations as a result of drug treatment. By contrast, the algorithms from the Framingham study, used in the main model submitted by the manufacturer, were based on the cardiovascular risk associated with a

particular cholesterol concentration. The Committee also considered which time horizon was the most appropriate for the economic analysis. It agreed that a time horizon based on the costs and health outcomes associated with a lifetime of treatment should be assumed, given that ezetimibe is a lifelong treatment and benefits may occur well into the future.

See Sections 4.2 and 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 should be read in conjunction with National Institute for Health and Clinical Excellence (NICE) guidance on the initiation of statin therapy (NICE technology appraisal guidance 94) (see the National Guideline Clearinghouse [NGC] summary of the NICE technology appraisal, Statins for the prevention of cardiovascular events). NICE has published clinical guidelines on the management of blood pressure and blood lipids in people with type 2 diabetes (Inherited clinical guideline H) and secondary prevention for patients following a myocardial infarction (NICE clinical guideline 48) (see the NICE Web site). The following clinical guidelines are under development: lipid modification; familial hypercholesterolaemia; type 2 diabetes (update). This guidance should be read in the context of the relevant clinical guideline, when available.

- Ezetimibe monotherapy is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who would otherwise be initiated on statin therapy (as per NICE guidance TA 94 in adults with non-familial hypercholesterolaemia [see the NGC summary of the NICE technology appraisal, Statins for the prevention of cardiovascular events]) but who are unable to do so because of contraindications to initial statin therapy.

- Ezetimibe monotherapy is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who are intolerant to statin therapy (as defined below).
- Ezetimibe, coadministered with initial statin therapy, is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who have been initiated on statin therapy (as per NICE guidance TA 94 in adults with non-familial hypercholesterolaemia [see the NGC summary of the NICE technology appraisal, Statins for the prevention of cardiovascular events]) when:
    - Serum total or low-density lipoprotein (LDL) cholesterol concentration is not appropriately controlled (as defined below) either after appropriate dose titration of initial statin therapy or because dose titration is limited by intolerance to the initial statin therapy (as defined below)

      and

    - Consideration is being given to changing from initial statin therapy to an alternative statin.
- When the decision has been made to treat with ezetimibe coadministered with a statin, ezetimibe should be prescribed on the basis of lowest acquisition cost.
- For the purposes of this guidance, appropriate control of cholesterol concentrations should be based on individualised risk assessment in accordance with national guidance on the management of cardiovascular disease for the relevant populations.
- For the purposes of this guidance, intolerance to initial statin therapy should be defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in compliance with therapy being compromised. Adverse effects include evidence of new-onset muscle pain (often associated with levels of muscle enzymes in the blood indicative of muscle damage), significant gastrointestinal disturbance or alterations of liver function tests.

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 ezetimibe for the treatment of primary (heterozygous-familial or non-familial) hypercholesterolemia

POTENTIAL HARMS

The adverse effects of ezetimibe monotherapy are usually mild and transient and most commonly include headache, abdominal pain, and diarrhoea. When coadministered with a statin, the most common adverse effects include gastrointestinal disturbances, headache, fatigue, and myalgia (muscle pain).

For full details of adverse effects and contraindications, see the summaries 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 available evidence. 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.
- Uncertainties:

  The main area of clinical uncertainty concerns the association between the ezetimibe induced reductions in low-density lipoprotein-cholesterol (LDL-c) observed in the short-term randomised controlled trials (RCTs) and corresponding reductions in cardiovascular events. The long term safety and adverse event profile, particularly when taken in combination with other treatments is also unknown. The treatment effect in different populations, in particular those who have not achieved lipid targets on optimal statin treatment or those who cannot tolerate statins is also uncertain. There is also limited data to confirm that the observed effectiveness of ezetimibe in the clinical trials transfers to produce corresponding reductions in lipids when prescribed in clinical practice. The proportion of individuals who are willing to switch from monotherapy to multi-drug therapies is unknown, and the associated impact on compliance to treatment when prescribing multi-lipid lowering therapies for life is unknown.

  All the above impact on the assumptions required to produce results from economic evaluations. As discussed elsewhere in the Assessment Report (see the "Availability of Companion Documents" field) the three pivotal areas of uncertainty in the economic modelling are the assumption that changes in surrogate outcomes will provide corresponding reductions in cardiovascular events, the assumption that extremely short term reductions in LDL-c levels will be maintained over very long time horizons, and the lack of evidence on potential differences in effectiveness rates for different treatment strategies.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations 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 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 NICE website (www.nice.org.uk/TA132; see also the "Availability of Companion Documents" field).
    - Audit criteria to monitor local practice
    - A costing statement explaining the resource impact of this guidance

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

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
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Nov. 30 p. (Technology appraisal guidance; no. 132).

ADAPTATION

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

DATE RELEASED

2007 Nov

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

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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:

- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Nov. 2 p. (Technology appraisal 132). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Nov. 14 p. (Technology appraisal 132). Available in Portable Document Format (PDF) from the NICE Web site.
- Costing statement: Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Nov. 3 p.

(Technology appraisal 132). Available in Portable Document Format (PDF) from the NICE Web site.

- Ezetimibe for the treatment of hypercholesterolaemia. Assessment report guide. 2006 Dec 8. 310 p. Available in Portable Document Format (PDF) from the NICE Web site.
- Amendments to methodologies and revised results for the ScHARR economic model - 16th February, 2007. 2007 Feb 16. 41 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: N1402. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Nov. 4 p. (Technology appraisal 132).

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 NHS Response Line 0870 1555 455. ref: N1403. 11 Strand, London, WC2N 5HR.

NGC STATUS

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