



Complete Summary

GUIDELINE TITLE

Telbivudine for the treatment of chronic hepatitis B.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Telbivudine for the treatment of chronic hepatitis B. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Aug. 26 p. (Technology appraisal guidance; no. 154).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Chronic hepatitis B

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology

Infectious Diseases
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost effectiveness of telbivudine for the treatment of chronic hepatitis B

TARGET POPULATION

Patients with chronic hepatitis B

Note: This guidance does not apply to people with chronic hepatitis B who also have hepatitis C, hepatitis D or human immunodeficiency virus (HIV).

INTERVENTIONS AND PRACTICES CONSIDERED

Telbivudine (not recommended)

MAJOR OUTCOMES CONSIDERED

- Clinical Effectiveness
 - Suppression of hepatitis B virus deoxyribonucleic acid (HBV DNA) <5 log copies/mL plus *either* clearance of detectable hepatitis B e antigen (HBeAg) *or* alanine aminotransferase (ALT) normalization
 - Viral response
 - Biochemical response
 - HBeAg loss/seroconversion
 - Virologic breakthrough
 - Viral resistance
 - Histologic response
 - Adverse events
- 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Searches of Unpublished Data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 Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Southampton Health Technology Assessment Centre, University of Southampton (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of Manufacturer's Approach

Description of Manufacturer's Search Strategy

The manufacturer ran searches in Ovid including Medline, Embase, Cochrane (Cochrane Database of Systematic Reviews [CDSR] and Cochrane Central Register of Controlled Trial [CTR]), Database of Abstracts of Reviews of Effectiveness (DARE) and the American College of Physicians (ACP) Journal Club database, as well as Novartis' own in-house database. No evidence of searches of Medline in Progress (MEIP) is documented within the manufacturer's submission (MS), and therefore the minimum database search criteria for undertaking clinical effectiveness searches as specified by NICE was not adhered to. Other sources searched are described as a manual search of relevant publications, other in-house trials and the telbivudine registration dossier, but no results or details of the outcome of these searches are provided. In addition, it is not stated if the searches were restricted to English language. Additional databases that could have been searched to obtain clinical evidence include Institute for Scientific Information (ISI) proceedings and Biosis.

The searches were run in two stages. The main search (search strategies for the clinical effectiveness and indirect comparison searches) was run in January 2007, whilst an updated replication of the searches was run from January to September 2007 in order to meet the requirements for an Australian submission. No further update searches from September 2007 were performed for this submission.

The search terms used are the minimum suitable for precise searches, but not the sensitive results required for a systematic review. For the population group, use of 'Hepatitis B' rather than 'Chronic Hepatitis B' as an exploded Medical Subject Headings (MeSH) term would have ensured greater comprehensiveness of a systematic search. A limited number of synonyms are also used in the text search. Searching on the word string 'chronic hepatitis B' as a phrase limits the results as the words may not be used in that order in the text. The drug search was for three interventions – telbivudine, lamivudine and adefovir. The MS does not state why adefovir was included in the search, and the Evidence Review Group (ERG) finds its inclusion inconsistent when it has not been considered in the submission. Entecavir was not included as a search term. An acceptable randomised controlled trial (RCT) filter was applied to the search strategy, and is sufficient for finding very precise and focused results; however, it does not meet the Cochrane standards of RCT sensitivity. The download is further limited by excluding all review papers that are not meta-analyses.

The ERG re-ran the Ovid Medline search from 1950 to Week 2 November 2007 and the numbers retrieved were similar to those of the manufacturer.

Statement of the Inclusion/Exclusion Criteria Used in the Study Selection and Comment on Whether They Were Appropriate

The MS specified the following inclusion criteria for the review of the literature:

- Population: patients with chronic hepatitis B
- Intervention: telbivudine (Sebivo)
- Comparator: lamivudine (also include adefovir)
- Outcomes: primary and secondary outcomes (changes in hepatitis B virus deoxyribonucleic acid [HBV DNA], hepatitis B e antigen [HBeAg], hepatitis B e antibody [HBeAb], hepatitis B surface antigen [HBsAg], hepatitis B surface antibody [HBsAb], alanine aminotransferase [ALT])
- Study design: RCTs

These criteria do not specify several of the outcomes outlined in the decision problem, particularly viral resistance and histological improvement. In terms of the patient population, the criteria do not specify that patients should have persistently raised ALT levels and histological evidence of active inflammation and/or fibrosis as per the licensed indication, although these are stipulated in the patient inclusion criteria for the GLOBE trial. RCTs where telbivudine and the main comparator were not in separate trial arms were excluded, as were abstracts and studies reviewing quality of life data. The MS did not specifically state whether systematic reviews would be considered, and neither is there discussion of whether conference proceedings would be included or excluded. Clarification of inclusion was sought from the manufacturer and the reply received stated that abstracts and systematic reviews were eligible for inclusion but not conference proceedings. However, abstracts were still listed in the table of exclusion criteria.

The patient inclusion/exclusion criteria for the GLOBE trial are clearly stated in the MS report, are appropriate and fulfil the specific criteria of the product licence.

The methodology adopted by the manufacturer for screening references for inclusion appears to have been appropriate. Two reviewers assessed the citations at the title and abstract stage, ordered relevant full trial papers and screened them against the eligibility criteria. Disagreement was resolved through discussion.

The MS does not provide any inclusion/exclusion criteria for the indirect treatment comparisons, nor are there any details about the identification and selection of studies.

Cost-Effectiveness

The MS states that no formal search of the cost-effectiveness literature on treatments for chronic hepatitis B was undertaken given the recent date of the review reported in the Health Technology Assessment (HTA) monograph. Since the HTA monograph reports that the searches (including cost effectiveness and quality of life searches) for the review were conducted up to April 2005, more

than two years prior to the manufacturer's submission to NICE, update searches would have been appropriate.

Refer to section 3.1 of the ERG report (see the "Availability of Companion Documents" field) for further information regarding the manufacturer's approach to clinical effectiveness and cost effectiveness searches.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

One randomized controlled trial (RCT) met the inclusion criteria. The manufacturer's submission (MS) also identified two studies for an indirect comparison.

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

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 Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Southampton Health Technology Assessment Centre, University of Southampton (see the "Availability of Companion Documents" field).

Clinical Effectiveness

The manufacturer's submission (MS) provides no details about the data extraction and quality assessment procedure.

Description and Critique of Manufacturer's Approach to Validity Assessment

The MS provides a formal appraisal of the validity of the included trial using the quality assessment criteria developed by NICE. The process of applying quality criteria was not reported in the MS. The ERG queried this with the manufacturer

but no further details were provided. Also, no formal quality assessment was undertaken on the comparator trials.

Description and Critique of the Statistical Approach Used

Achievement of therapeutic response (the primary outcome) was reported as proportion of patients, % absolute difference with 95% confidence interval (CI), and *p* values. The majority of the secondary outcomes were presented as proportions of patients only, with *p* values. The difference (%) and 95% confidence intervals are reported in the full trial report but not the MS.

The intention to treat (ITT) population was defined as comprising all randomised subjects, presumed to have had at least one dose of study medication and at least one baseline observation. A true ITT analysis should include all randomised patients, regardless of having received treatment. This analysis excluded six randomised patients that failed to return for baseline visits and therefore did not receive any study drug. Three other patients are reported as not having any baseline data. Missing data was treated as "no response" in the ITT analysis.

The results of the key efficacy points were broken down for sub-groups (hepatitis B e antigen [HBeAg]-positive and negative patients) by treatment and race/ethnicity and were reported in percentages. *P* values were reported, but no statistical comparison was carried out between Asian and Caucasian patients. The sub-group analysis on key efficacy parameters for HBeAg-positive patients with alanine aminotransferase (ALT) $\geq 2 \times$ ULN was undertaken, but it is unclear whether the trial was powered for this analysis. No statistical comparison between treatment groups was made for the safety data/adverse events.

Indirect Comparison

The indirect comparison with entecavir (also compared to lamivudine) carried out by the manufacturer is methodologically poor and should be treated with caution. As only one telbivudine study was included in the MS, no meta-analysis was undertaken.

Despite the manufacturer stating that a formal indirect comparison would not be valid given the lack of meta-analyses, a statistical indirect comparison is nonetheless conducted. It is the opinion of the ERG that this approach is not valid.

A random effects model was used for most outcomes analysed 'to allow for heterogeneity between studies'. However, for HBeAg loss and seroconversion a fixed effects model was used due to there 'only being two trials (with four arms) to provide data'. The ERG considers this inappropriate.

Refer to Section 3 of the ERG report (see the "Availability of Companion Documents" field) for additional information.

Economic Evaluation

Overview of Manufacturer's Economic Evaluation

The manufacturer's submission to NICE includes a report of an economic evaluation undertaken by the manufacturer, for the NICE Single Technology Appraisal (STA) process. The cost-effectiveness of telbivudine for patients with chronic hepatitis B whose ALT ≥ 2 x upper limit of normal, but who have not developed cirrhosis, is estimated using two different economic models. The first, referred to as the viral load model, is the manufacturer's preferred approach and is used for both HBeAg-positive and HBeAg-negative patients. The second – seroconversion model – has been included for consistency with the recent Health Technology Assessment (HTA) report of adefovir and pegylated interferon and is for HBeAg-positive patients only.

Both the viral load and seroconversion models are based on state transition models. The structure of the models and the methodology used to evaluate the cost-effectiveness are similar to those used in previous economic evaluations of anti-viral treatments for patients with chronic hepatitis B – although the disease progression model adopted in the viral load model is more complex than in previous evaluations.

Sensitivity Analyses

The MS does not report one-way sensitivity analyses for either the viral load or seroconversion models. The results of probabilistic sensitivity analyses are treated as base case results, with limited discussion of uncertainty.

Model Validation

The MS does not report on attempts to establish the viral load model's internal validity (no discussion of consistency checks or checks of coding accuracy). The validation reported is limited to checking the outputs of the model at two years against the trial results, but no detail is provided.

The MS does not report on attempts to establish the seroconversion model's internal validity (no discussion of consistency checks or checks of coding accuracy). The approach to establishing external consistency of this model was to compare results with those in the HTA monograph for the assessment group model and those reported by the manufacturer of adefovir.

Refer to Section 4 of the ERG report (see the "Availability of Companion Documents" field) for additional information.

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 manufacturer's submission presented an analysis of the cost effectiveness of telbivudine in patients with chronic hepatitis B whose serum alanine aminotransferase (ALT) levels are more than or equal to twice the upper normal limit. Two Markov state-transition models were provided in the manufacturer's submission: a seroconversion model (applicable to only hepatitis B e antigen [HBeAg]-positive disease) and a viral load model (applicable to both HBeAg-positive and HBeAg-negative disease). Both models used a lifetime horizon.

The viral load model submitted by the manufacturer assumed that patients entered the model in the chronic hepatitis state without cirrhosis. Health states associated with disease progression were divided by serum ALT and viral load levels, resulting in a large number of possible health states. Consequently the data available from the GLOBE trial to populate the viral load model were sparse. In an attempt to deal with this, the manufacturer used values of 0.0 and 0.5 (which they referred to as 'non-informative priors') to correct for the probabilities of health-state transitions for which there were one or more zero observations and no data available.

The base-case analysis of the viral load model (based on probabilistic sensitivity analysis) comparing telbivudine with lamivudine and assuming a 'non-informative prior' of 0.0 produced an incremental cost-effectiveness ratio (ICER) of 15,377 pounds sterling per additional quality-adjusted life year (QALY) gained for HBeAg-positive disease; the corresponding ICER with a 'non-informative' prior of 0.5 was 8,542 pounds sterling per additional QALY gained. For HBeAg-negative disease, the ICER for a comparison of telbivudine with lamivudine with a 'non-informative prior' of 0.0 was 20,256 pounds sterling per additional QALY gained. The corresponding ICER with a 'non-informative prior' of 0.5 was 27,801 pounds sterling per additional QALY gained.

Deterministic base-case analyses (requested from the manufacturer) of the viral load model comparing telbivudine with lamivudine, with a 'non-informative prior' of 0.0, produced an ICER of 12,278 pounds sterling per additional QALY gained for HBeAg-positive disease. The corresponding ICER, with a 'non-informative prior' of 0.5, was 8,669 pounds sterling per additional QALY gained. For HBeAg-negative disease, the ICER for a comparison of telbivudine with lamivudine was 20,383 pounds sterling per additional QALY gained with a 'non-informative prior' of 0.0; the corresponding ICER, with a 'non-informative prior' of 0.5, was 57,419 pounds sterling per additional QALY gained.

The manufacturer's economic analysis based on the seroconversion model (HBeAg-positive disease only) gave an ICER of 13,193 pounds sterling per additional QALY gained (95% confidence interval [CI] 7,788 to 25,194 pounds sterling) for a comparison of telbivudine alone (followed by best supportive care [BSC] if appropriate) with BSC alone. A comparison of telbivudine followed by adefovir dipivoxil and then BSC against BSC alone gave an ICER of 15,684 pounds sterling per additional QALY gained (95% CI 9,491 to 28,151 pounds sterling). Adefovir dipivoxil followed by telbivudine and then BSC compared with BSC alone gave an ICER of 18,388 pounds sterling per additional QALY gained (95% CI 11,707 to 30,357 pounds sterling). Adefovir dipivoxil followed by lamivudine and then BSC compared with BSC alone gave an ICER of 17,398 pounds sterling per additional QALY gained (95% CI 11,063 to 28,322 pounds sterling).

The Evidence Review Group (ERG) carried out scenario analyses on the viral load model (with a 'non-informative prior' of 0.0) using non-constant age-specific utilities, increasing the proportion of cirrhotic patients at treatment initiation to 15% and applying model calibration factors (for risk of advanced liver disease). The cumulative effects of varying these parameters for HBeAg-positive disease gave an ICER of 16,100 pounds sterling per additional QALY gained. The corresponding ICER for HBeAg-negative disease was 26,200 pounds sterling per additional QALY gained.

- The ERG conducted exploratory scenario analyses on the seroconversion model
- Assuming no treatment with telbivudine for people with decompensated liver disease
- Removing treatment-resistant patients from the denominators used to calculate transition probabilities for HBeAg seroconversion
- Increasing the proportion of cirrhotic patients at the start of treatment to 15%
- Assuming treated people with cirrhosis seroconvert at the same rate as people with treated non-cirrhotic chronic hepatitis B

The cumulative effects of varying the first three parameters gave an ICER of 20,200 pounds sterling per additional QALY gained for telbivudine followed by adefovir compared with lamivudine followed by adefovir in the HBeAg-positive group. Adding the last assumption results in an ICER of 8,400 pounds sterling per additional QALY gained for the same comparison. The cumulative effects of varying the first three parameters gave an ICER of 22,500 pounds sterling per additional QALY gained for telbivudine alone compared with lamivudine alone. Adding the last assumption results in an ICER of 10,800 pounds sterling per additional QALY gained for the same comparison.

The ERG conducted a probabilistic sensitivity analysis using the viral load model with a 'non-informative prior' of 0.0 only. It replaced constant health-state utilities with non-constant age-specific utilities and applied the model calibration factors for risk of advanced liver disease listed in the appendices to the manufacturer's submission. This reduced the probability of telbivudine being cost effective for any given willingness to pay (cost-effectiveness) threshold when compared with lamivudine. For the HBeAg-positive group, the probabilities that telbivudine was cost effective at willingness to pay thresholds of 20,000 and 30,000 pounds sterling per additional QALY gained were 0.53 and 0.82, respectively. For the HBeAg-negative group, the probabilities of telbivudine being cost effective at willingness to pay thresholds of 20,000 and 30,000 pounds sterling per additional QALY gained were 0.01 and 0.54, respectively. The ERG also conducted a probabilistic sensitivity analysis using the seroconversion model, and the results differed from the manufacturer's analysis: in particular, lamivudine is optimal over a wider range of willingness to pay, with lamivudine followed by adefovir being optimal over a cost-effectiveness threshold range of 22,000 to 24,000 pounds sterling per additional QALY, whereas telbivudine was the optimal strategy over this range in the manufacturer's probabilistic sensitivity analysis. At higher cost-effectiveness thresholds (greater than 25,000 pounds sterling per QALY gained), telbivudine followed by adefovir remained the optimal strategy.

The Appraisal Committee considered that the transparency of the viral load model for assessing the cost effectiveness of telbivudine for the treatment of HBeAg-negative patients was reduced by the lack of detail in the manufacturer's submission about which parameters were used. The Committee concluded that, in light of the uncertainty about the cost effectiveness of telbivudine in HBeAg-negative chronic hepatitis B and the sensitivity analyses presented by the ERG, telbivudine could not be recommended as a cost-effective use of National Health Service (NHS) resources.

Overall, the Committee agreed that there was evidence that telbivudine was likely to be more clinically effective and have a more favourable resistance profile than lamivudine monotherapy in patients with HBeAg-positive disease. However, it did not agree with the manufacturer that the evidence presented on the cost effectiveness of telbivudine in the subgroup of patients with serum ALT levels greater than or equal to twice the upper limit of normal could be used as a reliable basis for decision-making in patients with HBeAg-positive disease.

Refer to Sections 3 and 4 of the original guideline document for details of the economic analyses provided by the manufacturer, the ERG comments, and the Appraisal Committee considerations.

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 does not apply to people with chronic hepatitis B who also have hepatitis C, hepatitis D or human immunodeficiency virus (HIV).

Telbivudine is not recommended for the treatment of chronic hepatitis B.

People currently receiving telbivudine should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

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 recommendation regarding the use of telbivudine for the treatment of chronic hepatitis B

POTENTIAL HARMS

The most common side effects associated with telbivudine include dizziness, headache, cough, diarrhoea, nausea, abdominal pain, rash, fatigue and increased levels of blood creatine phosphokinase, alanine aminotransferase (ALT) and amylase. Uncommon side effects include malaise, arthralgia, myalgia, peripheral neuropathy and myopathy.

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

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 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//TA154) [see also the "Availability of Companion Documents" field].
 - A costing statement explaining the resource impact of this guidance
 - 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

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Telbivudine for the treatment of chronic hepatitis B. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Aug. 26 p. (Technology appraisal guidance; no. 154).

ADAPTATION

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

DATE RELEASED

2008 Aug

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 David Barnett, Professor of Clinical Pharmacology, University of Leicester; Dr David W Black, Director of Public Health, Derbyshire County PCT; Dr Carol Campbell, Senior Lecturer, University of Teesside; Dr Peter Clarke, Consultant Medical Oncologist, Clatterbridge Centre for Oncology; Dr Christine Davey, Senior Researcher, North Yorkshire Alliance R & D Unit; Dr Mike Davies, Consultant Physician, Manchester Royal Infirmary; Dr Dyfrig Hughes, Reader in Pharmacoeconomics, Centre for the Economics of Health and Policy in Health, Bangor University; Dr Catherine Jackson, Clinical Lecturer in Primary Care Medicine, Alyth Health Centre; Dr Peter Jackson, Clinical Pharmacologist, Sheffield Teaching Hospitals NHS Foundation Trust; Professor Peter Jones, Pro Vice Chancellor for Research & Enterprise, Keele University; Ms Rachel Lewis, Practice Development Facilitator, Manchester PCT; Professor Jonathan Michaels, Professor of Vascular Surgery, University of Sheffield; Dr Eugene Milne, Deputy Medical Director, North East Strategic Health Authority; Dr Simon Mitchell, Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester; Dr Richard Alexander Nakielny, Consultant Radiologist, Royal Hallamshire Hospital, Sheffield; Dr Katherine Payne, Health Economics Research Fellow, University of Manchester; Dr Philip Rutledge, GP and Consultant in Medicines Management, NHS Lothian; Mr

Miles Scott, Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust; Dr Surinder Sethi, Consultant in Public Health Medicine, North West Specialised Services Commissioning Team; Professor Andrew Stevens, Chair of Appraisal Committee C; Mr William Turner, Consultant Urologist, Addenbrookes Hospital

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:

- Telbivudine for the treatment of chronic hepatitis B. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Aug. 2 p. (Technology appraisal 154). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Telbivudine for the treatment of chronic hepatitis B. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Aug. 1 p. (Technology appraisal 154). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Telbivudine for the treatment of chronic hepatitis B. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 5 p. (Technology appraisal 154). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Telbivudine as treatment for chronic hepatitis B. Evidence Review Group report. Southampton Health Technology Assessments Centre (SHTAC); 2008 Feb 5. 119 p. (Technology appraisal 154). 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: N1662. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Telbivudine for chronic hepatitis B. Understanding NICE guidance. Information for people who use NHS services. London (UK): National Institute for Health

and Clinical Excellence (NICE); 2008 Aug. 4 p. (Technology appraisal 154). 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: N1663. 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 Institute on December 19, 2008.

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