Complete Summary

GUIDELINE TITLE

Infliximab for subacute manifestations of ulcerative colitis.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Infliximab for subacute manifestations of ulcerative colitis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Apr. 21 p. (Technology appraisal guidance; no. 140).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Subacute manifestations of moderately to severely active ulcerative colitis

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery
Family Practice

Gastroenterology
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of infliximab for the treatment of subacute manifestations of moderately to severely active ulcerative colitis

TARGET POPULATION

Patients with subacute manifestations of moderately to severely active ulcerative colitis

INTERVENTIONS AND PRACTICES CONSIDERED

The use of infliximab for the treatment of subacute manifestations of moderately to severely active ulcerative colitis was considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Health-related quality of life
    - Survival
    - Disease activity
    - Rates and duration of response, relapse, and remission
    - Rates of hospitalization
    - Reduction in use of corticosteroids
    - Rates of surgical intervention
    - Adverse effects of treatment
- 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Searches of Unpublished Data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 the West Midlands Health Technology Assessment Collaboration, University of Birmingham (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of Manufacturer's Approach

This is based on a formal critical appraisal recorded in Appendix 1 of the ERG report (see the "Availability of Companion Documents" field). An additional appraisal (Appendix 2 of the ERG report [see the "Availability of Companion Documents" field]) was conducted on the Cochrane review which was used as the foundation for the Schering-Plough review of clinical evidence. In addition two key included studies in both reviews were reappraised and the abstracted data rechecked, records of which processes are provided in Appendices 3 and 4 of the ERG report (see the "Availability of Companion Documents" field).

Description of Manufacturer's Search Strategy and Comment on whether the Search Strategy Was Appropriate

The search strategy of both the submission and the underlying Cochrane review were strong with respect to published data, but possibly slightly limited with respect to unpublished data. The ERG verified search strategies and checked for on-going studies (refer to Appendix 5 of the ERG report [see the "Availability of Companion Documents" field]). No major additional sources of evidence were identified.

On balance the ERG therefore felt it unlikely that major sources of relevant rigorous evidence on effectiveness had been omitted from consideration, although the ERG did have concerns that not all the pertinent data from these studies had been presented.

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

Broadly the inclusion/exclusion criteria for the submission were randomised controlled trials (RCTs) comparing infliximab with placebo, standard care appropriate to the severity of ulcerative colitis being suffered being available in both arms. This was felt by the ERG to be appropriate as the main evidence base for this single technology appraisal (STA).

The scope suggests that effectiveness studies comparing infliximab with surgery and ciclosporin were possible additional important sources of evidence. The ERG agreed with the submission that such evidence, drawn from RCTs or non-randomised comparisons was unlikely to exist and even if in existence was unlikely to be of assistance.

What Studies Were Included in the Submission and What Were Excluded

All 5 RCTs (reported in four articles) comparing infliximab with placebo were included. There was minimal detail on excluded studies. Arguably some discussion about the reasons for irrelevance of the two RCTs comparing infliximab with corticosteroids, included in the preceding Cochrane review, would have been useful.

Although all RCTs comparing infliximab with placebo were included, much greater emphasis was placed on the two large studies ACT I and ACT II. For instance, only data from ACT I and II was included in the meta-analysis. Although understandable given the much greater size of these studies, not fully considering the data from the smaller studies limits the generalisability of the review to the population and the circumstances considered in ACT I and II. A particular issue is that ACT I and II deal with ulcerative colitis treated in an outpatient setting. This has implications for the severity of ulcerative colitis being investigated, reflected in the low colectomy rates experienced in both treatment arms of ACT I and II. In contrast Jarnerot et al. examine the impact of infliximab in hospitalised patients, a setting where the use of infliximab also seems worth investigating, albeit clearly recognising that the clinical scenario is distinct. Arguments that the use of infliximab is "off-label" in the small studies like Jarnerot et al. seem unnecessarily restrictive.

The ERG found no studies which should have been included in the submission, although some aspects of the included studies were not reported as fully as needed.

Economic Evaluation

The manufacturer identified no published economic evaluations of infliximab in ulcerative colitis (UC) and this finding is supported by the ERG's own literature search.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Five randomised controlled trials (RCTs) (reported in four articles) were included

Cost-Effectiveness

- No published economic evaluations of infliximab were identified.
- The manufacturer of infliximab submitted a cost-effectiveness model.

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

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Description and Critique of Manufacturer's Approach to Validity Assessment

There is very limited information about how this was conducted in the submission. Although there appears to have been no recognised framework used to assess the threats to validity, the commentary does consider all the main aspects of randomised controlled trial (RCT) quality which one would expect a systematic review to examine. The ERG has confirmed that key included studies (ACT I and II and Jarnerot et al.) are substantially free from threats to internal validity as claimed. Additional information, not present in the published report of ACT I and II, reassuring about the quality of randomisation and blinding was obtained from the original trial reports and was consistent with the Schering-Plough submission. Although not highlighted in the submission, the ERG concurred with the preceding Cochrane review by Lawson et al., that information on randomisation and blinding was limited in the study by Jarnerot et al., and noted too that this study had been terminated early because of slow recruitment.

Description and Critique of Manufacturer's Outcome Selection

The submission provides information on most of the outcomes mentioned in the scope and on which data appears to have been collected in the included studies. An exception is information collected on EuroQol-5 dimensions (EQ-5D) in ACT I which only appears in the clinical trial report provided by Schering-Plough as additional information. This is useful in helping to gauge not just the statistical significance of the effect on quality of life occurring in the trial, but also the size of this effect too.

Information on colectomy rates is not clearly reported, particularly that relating to the ACT studies. There is inconsistency between the rates in ACT I and II and between the rates claimed at 54 weeks in ACT I and the information provided in the trial reports for the rate at 30 weeks.

The process of data abstraction is poorly described. The ERG have confirmed that for the data for one of the key studies (ACT I and II) there are some major data abstraction errors. Fortunately these errors do not seriously affect the interpretation of the clinical evidence, as the direction of effect is unaltered. The meta-analysis of the results of ACT I and II is affected, and the correct values are indicated in the next section.

Describe and Critique the Statistical Approach Used

The summary of the results in which results on common outcomes at similar time-points are presented together is the weakest component of the Clinical Evidence Section. The approach is basically qualitative, but there is little systematic attempt to draw out the overall patterns of results, and particularly to deal with the different scenarios (subacute and acute/"rescue") the included studies represent. Fortunately the limited number of included studies makes it possible for the reader to identify what the patterns are without much assistance.

There is some use of meta-analysis in summarising the results of ACT I and II alone. Unfortunately there are errors in this indicated in the table titled Corrections to: "Table 16. Pooled Results from ACT I/II trials" in the ERG report (see the "Availability of Companion Documents" field).

As already indicated, this does not alter the interpretation of the clinical evidence greatly. Some estimates of effect were underestimated. The major change concerns the estimates of heterogeneity which was very marked in the original analyses. There is still some heterogeneity in the revised analyses, particularly in the estimate of effect on clinical remission at 8 weeks. Although less noteworthy than originally, it is still an issue worth highlighting, particularly as ACT I and II were studies with virtually identical design.

Summary of Results

There is no succinct summary of results, and there is no attempt to consider whether the overall pattern of results differs depending on the circumstances in which infliximab is given.

The ERG offer a summary of results, based on the information presented in the submission (refer to section 4.2.1 of the ERG report [see the "Availability of Companion Documents" field]).

Critique of Submitted Evidence Syntheses

Concerning the primary research this seems generally robust, particularly for the subacute setting. There is some uncertainty about what the effects on colectomy rates are. However, the main challenge is understanding the magnitude of the effect of infliximab on a patient's health-related quality of life. The evidence on effectiveness in the acute situation is less robust, primarily because the number of patients investigated is still relatively small. However, the two studies in this category both apparently had problems recruiting patients.

The more important provisos concern the limitations of the method used to review the available research in the submission. These include:

- Poor recording of review method
- Errors in data abstraction
- Poor summary of included studies and errors in meta-analysis
- Failure to investigate heterogeneity between the results of the ACT studies
- No clear indication how the results of the included studies might vary between the subacute and "rescue" scenarios
- Possible over exaggeration of the measured effect on health-related quality of life in the ACT I and II studies
- Possible under emphasis of potential for infliximab to affect risk of malignancy in a group already at increased risk of malignancy.

The ERG appraisal has sought to compensate for these limitations within the constraints of the process. Ideally an independent systematic review would have been undertaken in parallel with the Schering-Plough submission.

Refer to Sections 4.1 and 4.2 and Appendices 1, 2, 3, and 4 of the ERG report (see the "Availability of Companion Documents" field) for more information on clinical effectiveness.

Economic Evaluation

Overview of Manufacturer's Economic Evaluation

The report of the cost-effectiveness work focuses almost entirely on the *de novo* model and economic evaluation undertaken by the manufacturer.

A Markov model has been built using Microsoft Excel to compare two treatment strategies, infliximab versus standard care, in terms of costs and quality-adjusted life years (QALYs). The patient group modelled has moderate to severe active ulcerative colitis (UC) and includes patients "who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies." The main submission only considered patients in this category (although the manufacturer's clarification response

included results for patients who are more severe, where surgery is the comparator considered). This modelling was undertaken, in part, using data from the ACT trials.

Two separate treatment strategies have been evaluated, strategies A and B, which differ in the assumption made about continuation of infliximab therapy. Strategy A modelled the continuation of infliximab in treatment responders who achieved and maintained remission or mild health states. In contrast, strategy B considered a narrower therapy continuation group defined as responders who achieve and maintain remission.

Sensitivity Analyses

Extensive one-way sensitivity analysis was undertaken to consider variation in utility values, time horizon of the model, the assumption concerning an average patient's weight, and discount rates.

Model Validation

The electronic version of the model was made available to the ERG in an executable form. The model has been run using the inputs stated in the manufacturer's report, and the same results have been obtained. The workings of the model have been audited and whilst the ERG have found some errors in programming, none of them are serious in that they do not change the results in a meaningful way.

Critique of Approach Used

Model Type and Structure

The use of a Markov model is appropriate as the disease is characterised by progression over time and so a modelling approach that can deal with transition between states and the timing of events is required.

A further issue relates to the consideration of adverse events in the model. The only adverse events considered explicitly in the model are those that led to discontinuation of the study drug. Other events described in ACT trial papers as 'serious adverse events', 'infections requiring antimicrobial treatment', and 'serious infections' (bacterial infection, etc.) are not accounted for in the model. The only model health state that considers adverse events is the temporary discontinuation state. Thus, any costs or dis-utilities associated with such serious adverse events associated with infliximab use have been ignored.

Sensitivity Analysis

The sensitivity analysis has explored the robustness of results to variation in some of the key parameters. The probabilistic sensitivity analysis (PSA) has been undertaken in a very partial manner, with distributions placed around selected parameters only. Further, the selection of normal distributions for the utility data appears arbitrary and has the potential to lead to values outside the acceptable range (e.g., utility values greater than 1). Errors in the interpretation of the PSA

and calculation of the cost-effectiveness acceptability curve (CEAC) have been identified and detailed.

Refer to Section 5 of the ERG report (see the "Availability of Companion Documents" field) for additional information on economic evaluation.

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

A state-transition cost-effectiveness model was developed by the manufacturer to evaluate the cost effectiveness of infliximab plus standard care when compared with standard care alone in subacute manifestations of ulcerative colitis. The model follows a cohort of hypothetical patients with moderate or severe ulcerative colitis, from entry through to 10 years, with patients being tracked as they move between the nine states of the model in each of the 8-week cycles. The three pre-surgery disease states in the model are defined using the Mayo score (remission: Mayo 0 to 2; mild: Mayo 3 to 5; and moderate/severe: Mayo 6 to 12). Two separate treatment strategies were evaluated. Strategy A modelled the continuation of infliximab treatment in patients whose condition showed a clinical response to the induction regimen of infliximab and maintained mild disease or remission. Strategy B modelled infliximab treatment continuation only in patients whose disease was in remission after the induction regimen and maintained remission after the subsequent doses.

The base-case cost-effectiveness estimates presented in the manufacturer's submission were 33,866 pounds sterling per additional quality-adjusted life year (QALY) gained for strategy A, and 25,044 pounds sterling per additional QALY gained for strategy B. For both strategies, extensive univariate sensitivity analyses were performed, which considered variations in time horizon, utility values, surgery rates, discount rates and average patient weight. Probabilistic sensitivity analyses were conducted to assess the uncertainty of the cost-effectiveness estimates by assigning distributions around some of the transition probabilities, the health-state utility estimates and some of the unit costs. These showed that: for strategy A, if willingness to pay for an additional QALY gained is 20,000 pounds sterling or 30,000 pounds sterling, infliximab has an 11.4% or 33.9% probability of being cost effective, respectively; for strategy B, for a willingness to pay of 20,000 pounds sterling or 30,000 pounds sterling per additional QALY gained, infliximab has a 21.3% or 40.1% probability of being cost effective, respectively.

Overall, the Evidence Review Group (ERG) considered that the model and the analysis presented adequately reflected the outpatient scenario, although there

were some important issues that were not fully addressed. The ERG considered that although the model structure appeared to be generally appropriate for the subacute outpatient setting, it did not include the cost and health-related quality of life (HRQoL) impact of the serious adverse events reported in the trials.

The ERG considered that the justification provided for using utility data from studies other than ACT I and ACT II, despite these being the main sources of clinical data for the modelling work, was not reasonable. In the ERG's view, the univariate sensitivity analyses performed highlighted the importance of the utility estimates in driving the cost-effectiveness results, because the highest incremental cost-effectiveness ratio (ICER) for both strategies is seen when the utility data from the ACT I trial are used (60,750 pounds sterling and 53,504 pounds sterling per additional QALY gained for strategy A and strategy B, respectively). Therefore, the judgement about which set of utility data is most plausible is of critical importance when estimating cost effectiveness.

The ERG conducted further exploratory analyses to address a discrepancy between the criteria used to identify responders in the trials and the criteria used in the model to define health states: trial criteria (using both the total score and the subscores of the Mayo scale) to define response at week 8 were used to identify responders whereas the criteria used to define the health states in the model used only the total Mayo score. In these exploratory analyses, the ERG also attempted to address the fact that the transitions between the standard-care health states (to where patients whose condition does not respond to infliximab or placebo progress) are inappropriately based only on the placebo patients in the trials who had a clinical response at week 8. These exploratory analyses resulted in increased ICERs for the base case when considering the two strategies (approximately 38,000 pounds sterling and 33,000 pounds sterling per additional QALY gained for strategy A and strategy B, respectively). However, the ERG stated that these estimates would need to be considered cautiously because the full data that would be needed to follow all the patients throughout the trials were not available.

The Committee discussed the limitations of and the degree of uncertainty within the economic model presented. It considered the uncertainties in the assumptions about the time horizon of the model and the low numbers of patients supporting the estimates of the transition probabilities between health states. The Committee noted the base-case cost-effectiveness estimates of approximately 38,000 pounds sterling and 33,000 pounds sterling per additional QALY gained for strategies A and B (respectively) presented by the ERG in their exploratory analyses, and the results of the extensive sensitivity analyses performed. The Committee considered that although the proposed treatment continuation strategy, which selected patients whose ulcerative colitis remitted (strategy B), was more cost effective than the alternative continuation strategy (strategy A), when compared with standard care in the outpatient setting, neither approach was within a range of cost effectiveness that would usually be considered a cost-effective use of NHS resources.

In summary, the Committee considered that, on the basis of current evidence on the clinical effectiveness of infliximab and the best available estimates of cost effectiveness, the ICER for infliximab for the treatment of subacute manifestations of ulcerative colitis would lie between 33,000 pounds sterling and 61,000 pounds

sterling per additional QALY. The Committee therefore concluded that the use of infliximab for the treatment of moderately to severely active ulcerative colitis where disease activity would normally be managed in an outpatient setting could not be considered a cost-effective use of National Health Service (NHS) resources, and so could not recommend its use.

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 relates only to the use of infliximab for subacute manifestations of moderately to severely active ulcerative colitis. The guidance does not cover the use of infliximab for acute manifestations of moderately to severely active ulcerative colitis.

Guidance

Infliximab is not recommended for the treatment of subacute manifestations of moderately to severely active ulcerative colitis.

For the purposes of this guidance, a subacute manifestation of moderately to severely active ulcerative colitis is defined as disease that would normally be managed in an outpatient setting and that does not require hospitalisation or the consideration of urgent surgical intervention.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate recommendation regarding the use of infliximab for the treatment of subacute manifestations of moderately to severely active ulcerative colitis

POTENTIAL HARMS

The most common adverse events reported during infliximab therapy include acute infusion-related reactions, infections, and delayed hypersensitivity reactions. Before treatment begins, people must be screened for active and inactive tuberculosis. The Summary of Product Characteristics (SPC) lists a number of uncommon but serious adverse events related to infliximab's immunomodulatory activity.

For full details of side effects and contraindications, see the SPC.

CONTRAINDICATIONS

CONTRAINDICATIONS

Infliximab is contraindicated in people with moderate or severe heart failure and active infections.

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.

Key Issues

For both the clinical effectiveness and cost-effectiveness components, the key issues mirror the areas of uncertainty. Of these the interpretation of the importance of the quality of life changes in the sub-acute situation and the assessment of the adequacy of the evidence of effectiveness of infliximab in the acute hospital-based situation are pre-eminent.

Refer to the Evidence Review Group (ERG) Report (see the "Availability of Companion Documents" field) for additional information on weaknesses and areas of uncertainty in the manufacturer's submission.

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//TA140 [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

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Infliximab for subacute manifestations of ulcerative colitis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Apr. 21 p. (Technology appraisal guidance; no. 140).

ADAPTATION

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

DATE RELEASED

2008 Apr

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; Professor A E Ades, MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol; Dr Amanda Adler, Consultant Physician, Cambridge University Hospitals Trust; Anne Allison, Nurse Clinical Adviser, Healthcare Commission; Dr Tom Aslan, General Practitioner, Stockwell, London; Professor David Barnett (*Chair*), Professor of Clinical Pharmacology, University of Leicester; Mrs Elizabeth Brain, Lay Member; Professor Karl Claxton, Professor of Health Economics, Department of Economics & Related Research, University of York; Dr Richard Cookson, Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Professor Christopher Eccleston, Director, Pain Management Unit, University of Bath; Dr Paul Ewings, Statistician, Taunton & Somerset NHS Trust, Taunton; Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford; Mr John Goulston, Director of Finance, Barts and the London NHS Trust; Ms Linda Hands, Clinical Reader in Surgery, University of Oxford; Dr Rowan Hillson, Consultant Physician, Diabeticare, The Hillingdon Hospital; Professor Philip Home (*Vice Chair*), Professor of Diabetes Medicine, Newcastle University; Dr Terry John, General Practitioner, The Firs, London; Professor Richard Lilford, Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmingham; Dr Simon Maxwell, Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Queens Medical Research Institute, University of Edinburgh; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Ms Judith Paget, Chief Executive, Caerphilly Local Health Board, Wales; Dr Ann Richardson, Lay Member; Mr Mike Spencer, General Manager, Clinical Support Services, Cardiff and Vale NHS Trust; Dr Simon Thomas, Consultant Physician, General Medicine and Clinical Pharmacology, Newcastle Hospitals NHS Trust; Mr David Thomson, Lay Member; Dr Luke Twelves, General Practitioner, Ramsey Health Centre, North Huntingdon; Dr Norman Vetter, Reader, Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff; Dr Paul Watson, Director of Commissioning, East of England Strategic Health Authority

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:

- Infliximab for subacute manifestations of ulcerative colitis. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Apr. 2 p. (Technology appraisal 140). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Infliximab for subacute manifestations of ulcerative colitis. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Apr. 1 p. (Technology appraisal 140). Available in Portable Document Format (PDF) from the NICE Web site.
- Infliximab for subacute manifestations of ulcerative colitis. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 4 p. (Technology appraisal 140). Available in Portable Document Format (PDF) from the NICE Web site.
- Evidence review group report commissioned by the NHS R&D HTA programme on behalf of NICE. Infliximab for ulcerative colitis. Evidence review group report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007. 113 p. (Technology appraisal 140). 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: N1559. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Infliximab for subacute ulcerative colitis. Understanding NICE guidance. Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Apr. 4 p. (Technology appraisal 140). 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: N1560. 11 Strand, London, WC2N 5HR.

NGC STATUS

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