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Infliximab for acute exacerbations of ulcerative colitis

**This guidance was developed using the
single technology appraisal process**

NICE technology appraisal guidance 163 Infliximab for acute exacerbations of ulcerative colitis

Ordering information

You can download the following documents from www.nice.org.uk/TA163

- The full guidance (this document).
- A quick reference guide for healthcare professionals.
- Information for people with ulcerative colitis and their carers ('Understanding NICE guidance').
- Details of all the evidence that was looked at and other background information.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1753 (quick reference guide)
- N1754 ('Understanding NICE guidance').

This guidance is written in the following context

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.

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1 Guidance

This guidance relates only to the use of infliximab within its marketing authorisation, for the treatment of acute exacerbations of severely active ulcerative colitis. It relates to an induction course of three doses of infliximab.

- 1.1 Infliximab is recommended as an option for the treatment of acute exacerbations of severely active ulcerative colitis only in patients in whom ciclosporin is contraindicated or clinically inappropriate, based on a careful assessment of the risks and benefits of treatment in the individual patient.
- 1.2 In people who do not meet the criterion in 1.1, infliximab should only be used for the treatment of acute exacerbations of severely active ulcerative colitis in clinical trials.

2 The technology

- 2.1 Infliximab (Remicade, Schering-Plough Ltd) is a tumour necrosis factor alpha (TNF- α) inhibitor and has a UK marketing authorisation for the treatment of moderately to severely active ulcerative colitis. Infliximab is indicated for intravenous use in adults whose ulcerative colitis has responded inadequately to conventional therapy (including corticosteroids and 6-mercaptopurine or azathioprine), or who are intolerant of or have medical contraindications to such therapies. The recommended dose of infliximab for the treatment of ulcerative colitis is 5 mg/kg body weight infused intravenously over a 2-hour period followed by additional 5 mg/kg infusions at 2 and 6 weeks after the first infusion, then every 8 weeks. The summary of product characteristics (SPC) states that continued therapy should be carefully reconsidered in patients who show no evidence of therapeutic benefit within this time period.
- 2.2 The most common adverse events reported during infliximab therapy, for all indications, include viral infections, serum sickness-

like reaction, headache, vertigo, dizziness, flushing, lower and upper respiratory tract infections, abdominal pain, diarrhoea, nausea, dyspepsia, increased transaminases, urticaria, rash, pruritus, hyperhidrosis, dry skin, infusion-related reactions, chest pain, fatigue and fever. Infliximab is contraindicated in people with moderate or severe heart failure and active infections. Before starting treatment, people must be screened for both active and inactive tuberculosis. The 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.

- 2.3 Infliximab (vial with powder for reconstitution) is available at a net price of £419.62 for a 100-mg vial (excluding VAT; 'British national formulary' [BNF] edition 55). The drug cost varies from patient to patient because the dose is adjusted to each patient's body weight. For example, for a person weighing 73 kg the cost per infusion (if no vial sharing is assumed) would be £1678.48, corresponding to four vials of 100 mg for a dose of 365 mg. Therefore, for a 'course' of infliximab, assuming three doses, the drug cost is £5035.44. Costs may vary in different settings because of negotiated procurement discounts.

3 The manufacturer's submission

The Appraisal Committee (appendix A) considered evidence submitted by the manufacturer of infliximab and a review of this submission by the Evidence Review Group (ERG; appendix B).

- 3.1 The manufacturer developed a systematic review of the literature on the use of infliximab and comparator drugs in the target population. Two randomised controlled trials (RCTs) comparing infliximab with placebo were included in the review. For the comparator drug, ciclosporin, two RCTs were included. Searches carried out by the ERG identified no additional RCTs for either

infliximab or ciclosporin. The ERG noted that the total number of participants in the studies was small.

- 3.2 The primary outcome in both the review of clinical effectiveness and the economic evaluation was the avoidance of colectomy. In the larger of the two infliximab studies (n = 45) 67% and 29% of patients treated with placebo and infliximab, respectively, had a colectomy within the first 3 months. Within 12 months, 71% and 42% of patients treated with placebo and infliximab, respectively, underwent colectomy. In the smaller infliximab study (n = 11), all three participants treated with placebo underwent colectomy whereas none of the three patients treated with infliximab at the licensed dose did so within the first 3 months. Both studies included people with severe acute ulcerative colitis that had not responded to intravenous corticosteroids. The larger study also included people with moderately severe ulcerative colitis. Infliximab was given as a single infusion at a dose of approximately 5 mg/kg in the larger study. In the smaller study, patients were randomly assigned to single doses of 5 mg/kg, 10 mg/kg or 20 mg/kg. Neither study used a multiple-dose regimen as specified in the SPC for infliximab.
- 3.3 The two studies investigating ciclosporin differed from each other in the populations included and in the comparator used. In one study, ciclosporin was compared with placebo in people with acute severe ulcerative colitis that had not responded to corticosteroids. In this respect it was similar to the infliximab studies. In this study (n = 20) 44% of people treated with placebo and 27% of those treated with ciclosporin underwent colectomy within the first 3 months. The second study, by D'Haens and coworkers, was different in that it compared ciclosporin with intravenous corticosteroid treatment in people who had not already received treatment with intravenous corticosteroids (n = 30). In this study, 20% of people treated with corticosteroids and 21% of those treated with ciclosporin underwent colectomy within the first 3 months, and 40% of the corticosteroid-

treated group and 36% of the ciclosporin-treated group underwent colectomy within 12 months.

3.4 To compare the effectiveness of infliximab with ciclosporin in the absence of a study comparing them directly, a mixed-treatment comparison (MTC) model was used to synthesise the relative treatment effects in respect of colectomy outcomes observed in the trials. The objective was to develop probabilities of colectomy that could be used in an economic evaluation comparing infliximab with ciclosporin. The probabilities of a patient undergoing colectomy were estimated to be 0.67, 0.23 and 0.58 for placebo, infliximab and ciclosporin, respectively, for the first 3 months. The respective probabilities during months 4–12 were 0.14, 0.27 and 0.18 for placebo, infliximab and ciclosporin. The ERG pointed out that it is likely that the model does not appropriately estimate the true effects of the different treatment options, particularly with respect to the effectiveness of ciclosporin. The estimate of colectomy rate in the MTC was nearly twice that actually observed in the RCTs of ciclosporin. In the ERG's view it was not appropriate to include the study by D'Haens and coworkers in this analysis because neither the population nor the comparator treatment was in line with the other infliximab and ciclosporin RCTs. In a further analysis undertaken by the ERG the exclusion of this study from the analysis of colectomy rate for months 0–3 reduced the estimated rate for ciclosporin from 0.58 to 0.48. According to the ERG, however, these probabilities were still much higher than would be expected in practice.

3.5 Neither of the infliximab RCTs reported any deaths and the frequency of adverse events appeared to be comparable between the infliximab and placebo groups. In these studies, two patients treated with infliximab had serious adverse events that required prolonged hospitalisation, and one had long-lasting bleeding. In the ciclosporin studies, no deaths were reported. Adverse events

reported in the ciclosporin groups included paresthesias, grand mal seizure and headaches.

3.6 A decision analytical model was used to simulate the progression of hypothetical cohorts of patients. The structure of this model was informed by the infliximab (first infusion was 5 mg/kg including concomitant intravenous corticosteroids) and ciclosporin (4 mg/kg daily, intravenously) RCTs, information on current UK clinical practice and expert opinion. People with severe active ulcerative colitis hospitalised for an acute exacerbation of the disease were considered in the economic evaluation. It was assumed that these patients had already received treatment with corticosteroids for 72 hours, and that this had not improved their condition adequately. They were tracked as they received one of four treatment strategies:

- Infliximab: the first infusion was 5 mg/kg on day 4, including concomitant intravenous corticosteroid treatment for an additional 7 days during the hospital stay. In addition, responders also received two 5-mg/kg doses of infliximab at weeks 2 and 6 following the first infusion.
- Ciclosporin: patients were given a 4-mg/kg daily dose of intravenous ciclosporin starting on day 4 for 7 days. Following discharge from hospital, ciclosporin responders were switched to oral ciclosporin (2 mg/kg/day) for 3 months.
- Standard care: patients continued treatment with intravenous corticosteroids for an additional 7 inpatient days.
- Surgical intervention.

3.7 The time horizon used in the base case was 1 year. The course of the disease was represented by post-hospitalisation outcomes including medical remission, surgical remission and surgical complications. Treatment outcomes were characterised in the model as short term (0–3 months) and medium term (4–12 months). In the first 3 months, treatment with infliximab,

ciclosporin or standard care either caused the ulcerative colitis to respond to treatment and go into remission, or the treatment failed and patients underwent colectomy. For the rest of the base-case analysis (4–12 months), patients whose disease went into initial remission either stayed in remission or the response was lost and they underwent surgery. An analysis extrapolated up to 10 years was also conducted to address the long-term treatment effect. Overall, the ERG considered that the structure of the manufacturer's economic model appropriately addressed the acute phase of the disease. However, the model did not take into account the costs and disutilities associated with adverse events. The ERG noted this was especially important because trials of infliximab in patients with ulcerative colitis described 'serious adverse events'. Mortality was also not included in the model.

3.8 The parameter estimates used in the model were obtained from clinical studies of infliximab and ciclosporin, and other sources. Although the baseline risk of disease progression was estimated using the placebo arm from the larger infliximab study, this was inconsistently stated in the manufacturer's submission. The primary source for the base-case utilities was an unpublished study based on the Health Outcomes Data Repository (HODaR), which was conducted using the EQ-5D instrument in patients with ulcerative colitis in south Wales. These were supplemented with utilities from another study in which utilities were estimated using the time trade-off method. Estimates of healthcare resource use and concomitant medication use were based on the opinions of a panel of UK gastroenterologists. The costs of all drugs were calculated based on the average doses used in the clinical trials and on pack sizes listed in the BNF. Drug administration costs were obtained from the NHS reference costs.

3.9 Univariate sensitivity analyses were performed considering variations in treatment effect, patient weight, utility estimates,

infiximab administration cost, hospitalisation period and infiximab infusion doses. Probabilistic sensitivity analyses were conducted to assess the uncertainty of the cost-effectiveness estimates by assigning distributions around the primary outcome (colectomy), secondary outcome (post-surgery complications), utility estimates and unit costs. The ERG considered that the sensitivity analyses were appropriate, although they noted that the colectomy rates associated with the alternative treatment arms were not varied as part of the univariate analyses. The incremental cost-effectiveness ratios (ICERs) were shown by the ERG to be most sensitive to these colectomy rates. Also, the probabilistic sensitivity analysis placed distributions around selected parameters only.

- 3.10 The base-case cost-effectiveness estimates presented in the manufacturer's submission were £11,589 per additional quality-adjusted life year (QALY) gained for infiximab compared with standard care; £18,425 per additional QALY gained for infiximab compared with ciclosporin; and £13,407 per additional QALY gained for infiximab compared with surgery. These ICERs after minor corrections by the ERG rose to £12,307, £19,922 and £14,427, respectively. When the ERG excluded the study by D'Haens and coworkers (which the ERG considered was included in the analysis inappropriately; see 3.3 and 3.4), the ICER for infiximab versus ciclosporin increased considerably from £19,922 to £48,367 per QALY gained. Following consultation, further analyses were presented by the manufacturer to reflect the uncertainty around the estimate of the colectomy rate during months 4–12 following treatment with ciclosporin. In the original analysis, the colectomy rate for this period was based on the study by D'Haens and coworkers. If this study was excluded, then there was no other estimate available for this parameter. The manufacturer presented analyses assuming a high value (0.48, the same as the estimate for months 0–3 following ciclosporin treatment) and a low value (0.143, based on the estimate for

months 4–12 following standard care). When the high value was assumed, the ICER for infliximab versus ciclosporin was reduced to £9300 per QALY. Conversely when the low value was assumed, the ICER increased to £52,000 per QALY.

- 3.11 Full details of all the evidence are in the manufacturer’s submission and the ERG report, which are available from www.nice.org.uk/TA163

4 Consideration of the evidence

- 4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of infliximab, having considered evidence on the nature of acute exacerbations of severely active ulcerative colitis and the value placed on the benefits of infliximab by people with the condition, those who represent them, and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources.
- 4.2 The Committee understood that the symptoms of ulcerative colitis may fluctuate in severity and often the disease can remain inactive for some time. In patients who present with severe exacerbations, hospital admission is often necessary.
- 4.3 The Committee heard from the clinical specialists that if acute severe ulcerative colitis does not respond to treatment with intravenous corticosteroids within 72 hours, patients are very likely to require urgent colectomy. In these circumstances, infliximab or ciclosporin may be used in an attempt to avoid the need for surgery. The Committee understood that although these strategies may reduce the need for urgent colectomy, the likelihood of colectomy as an elective procedure may still remain in the long term. The Committee further understood from the patient experts that it is important psychologically for patients to delay colectomy in order to have time to consider and come to terms with the

implications of major surgery and the possibility of the provision of a stoma.

4.4 The clinical specialists told the Committee that a single dose of infliximab is often used in clinical practice to treat acute severe ulcerative colitis in order to delay or avoid urgent colectomy after failure of intravenous corticosteroids. The Committee appreciated that this approach clearly differs from the regimen specified in the SPC for infliximab for ulcerative colitis, which involves at least three doses for induction.

4.5 The clinical specialists described to the Committee the current management of acute ulcerative colitis using ciclosporin. They expressed the view that there was widespread concern among clinicians treating acute ulcerative colitis about the adverse effects of ciclosporin in this indication, particularly the risk of serious infections and the associated risk of mortality. The clinical specialists also indicated that ciclosporin is not used routinely in all centres because of these concerns. However, the Committee noted that the evidence on the relative safety of infliximab in this setting was not adequately researched given the small sizes of the available studies. The Committee was mindful of the results of the indirect comparison presented in the manufacturer's submission. Specifically, the Committee discussed whether the estimated colectomy rates following the use of ciclosporin were in line with those observed in clinical practice. The Committee considered that the manufacturer's submission overestimated the clinical effectiveness of infliximab compared with ciclosporin based on the probability of colectomy because:

- the clinical benefit of ciclosporin in the appropriate population (that is, those resistant to intravenous steroids) was underestimated in the manufacturer's submission, and

- the effectiveness of placebo in the clinical trials may have been overestimated, because of possible confounding due to the use of ciclosporin as a 'rescue therapy' in patients whose disease failed to respond to placebo treatment.

The Committee noted the critical importance of the comparative colectomy rates for infliximab and ciclosporin in the cost-effectiveness analysis. Although noting the concerns of the clinical specialists, the Committee concluded that ciclosporin was clinically effective and an appropriate comparator for infliximab in this setting. The Committee also considered the views of patients about the potential adverse effects associated with drug treatments for acute severe ulcerative colitis, and their need to receive full information about these options.

- 4.6 The clinical specialists advised the Committee that, of those people with acute severe ulcerative colitis that was refractory to intravenous corticosteroids, approximately half would, with medical management (infliximab or ciclosporin), avoid colectomy in the short term (that is, during the course of the initial hospital admission) and approximately one quarter would avoid it in the long term. The Committee also discussed how appropriate it was to include the comparison of ciclosporin with corticosteroids in newly treated acute ulcerative colitis in the manufacturer's submission in the synthesis of relative treatment effects; both the population (people in whom a course of corticosteroids had not yet been tried) and the comparator (intravenous corticosteroids) studied in this trial differed from those in the other clinical trials included in the synthesis. The Committee agreed with the ERG that the inclusion of the comparison of ciclosporin with corticosteroids was inappropriate. Therefore, the Committee accepted the ERG's corrected predicted probabilities of colectomy for patients treated with ciclosporin for the first 3 months as the best available estimate. Because of the lack of any direct comparison between infliximab

and ciclosporin, the Committee considered that the comparative effectiveness of ciclosporin and infliximab in acute ulcerative colitis was subject to considerable uncertainty and that it could not estimate the true clinical effectiveness of infliximab relative to ciclosporin based on the evidence available. The Committee concluded that there was insufficient evidence to assume a clinical benefit of infliximab over ciclosporin and was persuaded by the clinical specialists that the colectomy rates with the two drugs were likely to be similar.

- 4.7 The Committee considered the economic analysis presented by the manufacturer and noted that the manufacturer's base-case analysis suggested that the ICER for infliximab relative to ciclosporin was £18,400 per QALY gained. However, the Committee also noted that when the ERG made corrections to the model and excluded the study they considered inappropriate from the analysis of the effectiveness of ciclosporin for the first 3 months, the ICER rose to £48,400 per QALY gained. The Committee observed that in this analysis, the estimate of the colectomy rate during months 4–12 following ciclosporin treatment had been taken from the study that had been excluded. The Committee was aware that there was no alternative estimate of this parameter and therefore considered the effect that varying this parameter had on the estimate of effectiveness. They noted sensitivity analyses presented by the manufacturer showing that when a high value of the colectomy rate was assumed (0.48), the ICER for infliximab versus ciclosporin was reduced (£9300 per QALY) and conversely when a low value was assumed (0.143) the ICER increased (£52,000 per QALY). The Committee considered that it was extremely unlikely that the colectomy rate during months 4–12 would be as high as 0.48, recalling their earlier discussions with the clinical experts that suggested that those patients who did not respond to ciclosporin would be likely to have a colectomy within the first few weeks following presentation. The Committee agreed that the lower

estimates of colectomy rate during months 4–12 were more likely, and that the ERG reanalysis giving an ICER of £48,400 per QALY represented the best available reflection of the cost effectiveness of infliximab relative to ciclosporin.

4.8 The Committee appreciated that the cost effectiveness of infliximab would be sensitive to the number of doses given. It noted that the economic analysis presented by the manufacturer assumed that all patients received the full induction course of three doses even if they underwent urgent colectomy. The Committee believed that the average course would be fewer than three doses because those who underwent colectomy would not receive further infliximab, and some people would discontinue treatment for other reasons. The Committee noted that if the average number of doses of infliximab was reduced from three to two and a half, while keeping the initial colectomy rates used in the model constant, then the ICER for the comparison with ciclosporin would fall from over £48,000 to approximately £33,000 per QALY gained; if the number of doses was assumed to be two then the ICER for infliximab compared with ciclosporin was approximately £20,000 per QALY gained. However, the Committee considered that on the evidence available to it the actual average number of doses used in clinical practice was uncertain.

4.9 The Committee also noted that there was further uncertainty around the ICERs, in that the univariate sensitivity analyses for the comparison of infliximab with ciclosporin resulted in ICERs ranging from £1400 to £64,500. The former value occurred when all responders were assumed to continue in remission with no colectomy after the first year, and the latter when all patients were assumed to undergo colectomy within the first cycle of the economic model (0–3 months) after the first year. In addition, the Committee noted that not including adverse events and mortality in the manufacturer's economic analyses increased the uncertainty

around the relative cost-effectiveness estimates. Because the available evidence did not show infliximab to be more clinically and cost effective than ciclosporin, the Committee felt unable to recommend it as a treatment option in people for whom ciclosporin is suitable. The Committee stated that further research is needed in order to establish a more accurate representation of the relative clinical and cost effectiveness of infliximab and ciclosporin. The Committee therefore concluded that using infliximab in research would reduce this uncertainty.

- 4.10 The Committee heard from the clinical specialists that some patients requiring treatment for acute ulcerative colitis would have other conditions that may mean that ciclosporin was contraindicated or inappropriate. The Committee noted that ciclosporin was not licensed for the treatment of ulcerative colitis and that the contraindications listed in the SPCs for ciclosporin related to its use in the other conditions for which it has been approved (in transplantation and in inflammatory conditions including skin conditions, rheumatoid arthritis and nephrotic syndrome). The Committee was aware that the contraindications to short-term use of ciclosporin in the treatment of acute ulcerative colitis may differ from those to the longer-term use of ciclosporin in conditions listed in the SPC. It was also aware that the decision about whether ciclosporin was contraindicated or inappropriate would have to be a matter for clinical judgement, based on a careful assessment of the risks and benefits of treatment in the individual patient. In addition, the Committee appreciated that the nature of the patient's acute presentation, their history of ulcerative colitis and their current use of immunomodulators may also have a bearing on the appropriateness of ciclosporin. The Committee was persuaded that there could be situations in which clinicians and patients judged that the potential risks from using ciclosporin in acute ulcerative colitis outweighed the likely clinical benefits. The Committee noted that in those situations, the ICER for infliximab

relative to standard care from the manufacturer's submission was £11,600 per QALY gained and the ICER relative to immediate surgery was £13,400 per QALY gained. Even after the ERG corrections to the model, these ICERs were similar: £12,300 and £14,400 per QALY gained, respectively. The Committee concluded that infliximab would be a cost-effective use of NHS resources if ciclosporin is contraindicated or clinically inappropriate based on an assessment of the risks and benefits.

5 Implementation

- 5.1 The Healthcare Commission assesses the performance of 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 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.
- 5.2 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 that requires local health boards and NHS trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- 5.3 NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TA163).
- Costing statement explaining the resource impact of this guidance.
 - Audit support for monitoring local practice.

6 Recommendations for further research

- 6.1 The Committee recommended that infliximab and ciclosporin should be directly compared, exploring the clinical effectiveness of the two therapies in the treatment of acute exacerbations of severely active ulcerative colitis.
- 6.2 The Committee noted that there are two ongoing studies relevant to this guidance:
- A study comparing ciclosporin with infliximab in steroid-refractory severe attacks of ulcerative colitis (sponsored by the Group d'Etude Thérapeutique des Affections Inflammatoires Digestif [GETAID]).
 - A study comparing the effectiveness of ciclosporin with infliximab in the management of acute ulcerative colitis refractory to intravenous corticosteroids (CONSTRUCT – comparison of infliximab and ciclosporin in steroid resistant ulcerative colitis; a trial), School of Medicine, Swansea University.

7 Related NICE guidance

Published

- Infliximab for subacute manifestations of ulcerative colitis. NICE technology appraisal guidance 140 (2008). Available from www.nice.org.uk/TA140

8 Review of guidance

- 8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.
- 8.2 The guidance on this technology will be considered for review in December 2011.

Andrew Dillon
Chief Executive
December 2008

Appendix A: Appraisal Committee members and NICE project team

A *Appraisal Committee members*

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice chair. Each branch considers its own list of technologies, and ongoing topics are not moved between the branches.

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.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Professor A E Ades

Professor of Public Health Science, Department of Community Based Medicine, University of Bristol

Dr Amanda Adler

Consultant Physician, Cambridge University Hospitals Trust

Ms Anne Allison

Nurse Clinical Adviser, Healthcare Commission

Dr Tom Aslan

General Practitioner, The Hampstead Group Practice, London

Professor David Barnett (Chair)

Professor of Clinical Pharmacology, Leicester Royal Infirmary

Dr Matt Bradley

Head of HTA and Business Environment, Sanofi-Aventis

Mrs Elizabeth Brain

Lay Member

Mr David Chandler

Lay Member

Dr Karl Claxton

Professor of Health Economics, Department of Economics & Related Research, the University of York

Dr Simon Dixon

Reader in Health Economics, University of Sheffield

Mrs Fiona Duncan

Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool

Dr Paul Ewings

Statistician, Taunton & Somerset NHS Trust, Taunton

Mr John Goulston

Chief Executive, Barking, Havering and Redbridge Hospitals NHS Trust

Ms Eleanor Grey

Lay Member

Dr Richard Harling

Director of Public Health, Worcestershire PCT and Worcestershire County Council

Professor Philip Home (Vice Chair)

Professor of Diabetes Medicine, Newcastle University

Dr Vincent Kirkbride

Consultant Neonatologist, Regional Neonatal Intensive Care Unit, Sheffield

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

Dr Rubin Minhas

General Practitioner

Dr Ann Richardson

Lay Member

Mrs Angela Schofield

Chairman, Bournemouth and Poole Teaching PCT

Mr Mike Spencer

General Manager, Facilities and Clinical Support Services, Cardiff and Vale NHS Trust

Mr Cliff Snelling

Lay Member

Dr Simon Thomas

Consultant Physician and Reader in Therapeutics, Newcastle Hospitals NHS Foundation Trust and Newcastle University

Mr David Thomson

Lay Member

Mr William Turner

Consultant Urologist, Addenbrooke's Hospital

Dr Norman Vetter

Reader, Department of Primary Care and Public Health, School of Medicine, University of Cardiff

B ***NICE project team***

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Georgios Vamvakas

Technical Lead

Janet Robertson

Technical Adviser

Eloise Saile

Project Manager

Bijal Chandarana

Project Manager from September 2008

Appendix B: Sources of evidence considered by the Committee

A The Evidence Review Group (ERG) report for this appraisal was prepared by the Department of Public Health and Epidemiology University of Birmingham:

- Bryan S et al. Infliximab for the treatment of acute exacerbations of ulcerative colitis, June 2008.

B The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). Organisations listed in I were also invited to make written submissions. Organisations listed in II gave their expert views on infliximab for the treatment of acute exacerbations of ulcerative colitis by providing a written statement to the Committee. Organisations listed in I and II have the opportunity to appeal against the final appraisal determination.

I Manufacturer/sponsor:

- Schering Plough

II Professional/specialist and patient/carer groups:

- National Association for Colitis and Crohn's Disease (NACC)
- Association of Coloproctology of Great Britain and Ireland
- British Society of Gastroenterology
- Royal College of Nursing
- Royal College of Pathologists
- Royal College of Physicians

III Other consultees

- Department of Health
- Medway PCT
- Welsh Assembly Government

IV Commentator organisations (did not provide written evidence and without the right of appeal)

- British National Formulary
- Department of Health, Social Services and Public Safety for Northern Ireland
- NHS Quality Improvement Scotland
- Novartis Pharmaceuticals UK Ltd
- West Midlands Health Technology Assessment Collaboration
- National Collaborating Centre for Nursing and Supportive Care

C The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They gave their expert personal view on infliximab for the treatment of acute exacerbations of ulcerative colitis by attending the initial Committee discussion and providing written evidence to the Committee. They were also invited to comment on the ACD.

- Professor Jon Rhodes, nominated by Royal College of Physicians – clinical specialist.
- Professor David Rampton, nominated by Royal College of Physicians – clinical specialist.
- Richard Driscoll (Director), nominated by The National Association for Colitis and Crohn's Disease – patient expert.
- Mr Stuart Berliner (Director), nominated by The National Association for Colitis and Crohn's Disease – patient expert.