NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA140; Infliximab for subacute manifestations of ulcerative colitis and TA163; Infliximab for the treatment of acute exacerbations of ulcerative colitis

TA140 was issued April 2008 with a review date of February 2011

TA163 was issued December 2008 with a review date of December 2011

Background

At the GE meeting of 22 March 2011 it was agreed we would consult on the review plans for this guidance. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

Proposal put to consultees:	A decision to review TA163 should be deferred until the completion of the GETAID CYSIF and CONSTRUCT trials. A decision to review TA140 should be deferred until the completion of the single technology appraisal of adalimumab for the second-line treatment of moderate to severe ulcerative colitis (referred November 2010).
Rationale for selecting this proposal	There are several ongoing clinical trials that are due to report in 2011 and 2012. The relevant trials include GETAID CYSIF study and CONSTRUCT and these compare infliximab with ciclosporin. This comparison was a recommendation for further research in TA163. An appraisal of adalimumab for the second-line treatment of moderate to severe ulcerative colitis has recently been referred. This is the same place in the treatment pathway as addressed in TA140. It is proposed that a decision to review infliximab is deferred until the outcome of this appraisal is known, so that, if appropriate it can be proposed that the appraisals are reviewed together.

GE is asked to consider the original proposal in the light of the comments received from consultees and commentators, together with any responses from the appraisal team. It is asked to agree on the final course of action for the review.

Recommendation post consultation:	A decision to review TA163 should be deferred until the completion of the GETAID CYSIF and CONSTRUCT trials. A decision to review TA140 should be deferred until the completion of the single technology appraisal of adalimumab for the second-line treatment of moderate to severe ulcerative colitis (referred November 2010).

Respondent	**Response to proposal**	**Details**	**Comment from Technology Appraisals**
British Society of Gastroenterology	Agree	I am happy that NICE have taken the right decision in postponing this appraisal until there is more data available and until Adalimumab has been studied	Comment noted. No change to the review proposal made.
Medicines and Healthcare products Regulatory Agency	No objection	We are not aware of any evidence that is likely to have an impact on the proposal	Comment noted. No change to the review proposal made.
Royal College of Physicians	Agree	The RCP agrees with the NICE proposal to defer the review until there is more data available.	Comment noted. No change to the review proposal made.
Royal College of Pathologists	No comment	Please note that the Royal College of Pathologists has no comments to make.	Comment noted. No change to the review proposal made.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Healthcare Improvement Scotland	No comment	NHS Quality Improvement Scotland (which will become Healthcare Improvement Scotland on 1 April 2011) has no comment to make on the proposals regarding the reviews of TA140 and 163.	Comment noted. No change to the review proposal made.
NHS Oxfordshire	Agree	TA 163 – Proposal to defer the review until the clinical trials have reported – we agree that this is the appropriate choice.	Comment noted. No change to the review proposal made.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
NHS Oxfordshire	Disagree	TA 140 – If I understand the proposals mentioned, the STA for adalimumab will go ahead and it is too late to combine it as an MTA with infliximab, although they are both at the same point in the pathway. NICE's preferred proposal seems to be to wait until the TA on adalimumab is due for review and to review both drugs at the same time. The difficulty for us, as NHS commissioners responsible for the best use of the allocated budget is that the use of anti-TNFs within gastroenterology is a very high spend area, appears to be increasing and we would be very worried if the existence of two separate TAs suggested to clinicians that they might be used sequentially rather than as alternatives (unless there were good clinical evidence to support this and we are not aware of any). To wait for two or more years before the two were reviewed together could impose considerable financial burdens on NHS commissioners. Incorporation of the TAs into the forthcoming clinical guideline on ulcerative colitis – NHS Oxfordshire normally welcomes precise advice within clinical guidelines on the appropriate use of drugs and their place in the patient pathway. However, we agree that where the evidence is likely to be overtaken during the lifetime of the clinical guideline it is inappropriate.	Comment noted. No change to the review proposal made. The single technology appraisal of adalimumab for the second-line treatment of moderate to severe ulcerative colitis was referred in November 2010 and, as correctly stated, it is too late to combine it as an MTA with infliximab. Due to the funding directive applied to technology appraisal guidance, unless there is sufficient reason given by consultees and commentators justifying inclusion in a clinical guideline, new technologies are generally appraised in the technology appraisal process, if prioritised for appraisal during topic selection.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Public Health Wales NHS Trust	Agree	The Public Health Wales NHS Trust agrees with the proposals to defer TA140 & 163.	Comment noted. No change to the review proposal made.
Royal College of Nursing	No objection	Nurses caring for people with ulcerative colitis reviewed this consultation document on behalf of the Royal College of Nursing. They consider that the guidance should be updated with any current knowledge and reviewed in the light of any new evidence.	Comment noted. No change to the review proposal made.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Merck Sharp & Dohme	Agree	MSD welcomes the opportunity to comment on NICEs proposal for the review of TA140 and TA163. We have a query around the wording of the NICE recommendation that: - A decision to review TA140 should be deferred until the outcome of the recently referred STA of adalimumab for the second line treatment of moderate to severe ulcerative colitis is known. If appropriate, it can be proposed that the appraisals are reviewed together. Our interpretation of this recommendation is that NICE will conduct an STA of adalimumab for the second line treatment of moderate to severe ulcerative colitis. Only after this appraisal has been completed may it be proposed that the appraisals are reviewed together. Assuming this is the correct interpretation, our comments are as follows: - MSD are not pursuing an extension to the license indication for infliximab in UC at this time. There have been a few publications supporting the use of infliximab in ulcerative colitis since the original technology appraisal (TA140). However we do not believe that there is any new data which would warrant a re-review at this time. Ongoing clinical studies on infliximab in UC are expected to report in 2012, at which time we believe a review of this guidance would be appropriate.	Comment noted. The interpretation is correct.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
		- MSD support the Institute's proposal that the review of TA163 should be deferred until the completion of ongoing clinical studies. - We do not believe that any important organisations have been missed or included inappropriately from the matrix.	

No response received from:

Patient/carer groups	General
• Afiya Trust • Black Health Agency • Bladder and Bowel Foundation • Chinese National Healthy Living Centre • Colostomy Association • Counsel and Care • Crohn's and Colitis UK • Equalities National Council • Ia: Ileostomy and Internal Pouch Support Group • IBD Club • Muslim Council of Britain • Muslim Health Network • Ostomy Lifestyle Centre	• Board of Community Health Councils in Wales • British National Formulary • Care Quality Commission • Commissioning Support Appraisals Service • Department of Health, Social Services and Public Safety for Northern Ireland • National Association of Primary Care • NHS Alliance • NHS Commercial Medicines Unit • NHS Confederation • Scottish Medicines Consortium

• South Asian Health Foundation • Specialised Healthcare Alliance • Ulcerative Colitis UK <u>Professional groups</u> • Association of Coloproctology of Great Britain and Ireland • Association of Surgeons of Great Britain and Ireland • British Association for Services to the Elderly • British Geriatrics Society • Primary Care Society for Gastroenterology • Royal College of Anaesthetists • Royal College of General Practitioners • Royal College of Surgeons • Royal Pharmaceutical Society • Royal Society of Medicine • United Kingdom Clinical Pharmacy Association <u>Others</u> • Department of Health • NHS Devon • Welsh Assembly Government	<u>Possible comparator manufacturers</u> • AAH Pharmaceuticals (sulfasalazine, azathioprine, ciclosporin, mesalazine) • Abbott laboratories (adalimumab) • Actavis UK (azathioprine, sulfasalazine) • Almirall (balsalazide) • Arrow generics (azathioprine) • Almus pharmaceuticals (azothiaprine, sulfasalazine) • Aspen Europe (azathioprine, mercaptopurine) • Dexcel-Pharma (ciclosporin) • Dr Falk Pharma UK (mesalazine, mercaptopurine) • Ferring Pharmaceuticals (mesalazine) • Focus Pharmaceuticals (azathioprine) • Forest Laboratories UK (prednisolone –foam and enema) • Genesis pharmaceuticals (sulfasalazine) • Kent Pharmaceuticals (sulfasalazine, azathioprine, mesalazine) • Meda Pharmaceuticals (hydrocortizone -foam) • Metwest pharmaceuticals (sulfasalazine) • Mylan (sulfasalazine, azathioprine, ciclosporin) • Novartis Pharmaceuticals (ciclosporin) • Pfizer (sulfasalazine) • Ranbaxy UK (sulfasalazine) • Rosemont Pharmaceuticals (sulfasalazine) • Sandoz (azathioprine, mesalazine, sulfasalazine) • Shire Pharmaceuticals (mesalazine) • Teva UK (azathioprine, sulfasalazine, mesalazine)

	• Tilomed (azathioprine) • UCB Pharmaceuticals (olsalazine) • Warner Chilcott UK (mesalazine) • Waymade (sulfasalazine, mesalazine, mercaptopurine) <u>Relevant research groups</u> • CORE (Digestive Disorders Foundation) • MRC Clinical Trials Unit • National Institute for Health Research • Policy Research Institute on Ageing and Ethnicity • Research Institute for the Care of Older People <u>Assessment Group</u> • Assessment Group tbc • National Institute for Health Research Health Technology Assessment Programme

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25 May 2011