National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Vedolizumab for treating moderately to severely active ulcerative colitis

Response to consultee and commentator comments on the draft remit and draft scope

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	AbbVie	Yes	Thank you for your comment. No action required.
	South Kent Coast CCG and Thanet CCG	Yes, it would be appropriate to refer this topic to NICE for appraisal.	Thank you for your comment. No action required.
	Takeda UK	Yes.	Thank you for your comment. No action required.
	UK Clinical Pharmacy Association (UKCPA)	ok	Thank you for your comment. No action required.
Wording	AbbVie	Yes	Thank you for your comment. No action required.

Section	Consultees	Comments	Action
	Merck Sharp and Dohme	- The remit states that vedolizumab will be considered for the treatment of "adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy". - As the licence for vedolizumab is not yet known, and may or may not specify which interventions constitute conventional therapy, it is unclear what should be considered as conventional therapy for the purpose of this appraisal. - Within the comparators section (table on page 3) standard clinical management is described as including aminosalicylates, corticosteroids, immunosuppressants, tumour necrosis factor-alpha antagonists (anti-TNFs), and surgical intervention – MSD agrees that these treatments can be considered to be part of established clinical practice, however, it is not clear whether these aspects of standard clinical management are considered to be conventional therapy, as referred to in the remit. - For instance, if the anti-TNF infliximab was to be considered as conventional therapy (which evidence from current clinical practice and NICE guidance TA163 would support for the acute severe setting) then vedolizumab would be restricted to use post-infliximab. - It should also be considered that the on-going MTA for anti-TNFs (infliximab, golimumab, and adalimumab) in UC may issue a positive recommendation for an anti-TNF within the subacute setting (in addition to the currently-existing recommendation for infliximab in the acute severe setting) and therefore, anti-TNFs could be considered as conventional therapy for all patients with moderate to severe UC, limiting vedolizumab to use post-anti-TNF in all settings.	Thank you for your comments. Guidance will only be issued in accordance with the marketing authorisation for vedolizumab. Following discussion at the scoping workshop, the population for the appraisal has been defined more clearly in the remit, background and population sections. Attendees at the scoping workshop agreed that TNF-alpha inhibitors were appropriate comparators for this appraisal.
	South Kent Coast CCG and Thanet CCG	The wording and remit reflect the issues of clinical and cost-effectiveness.	Thank you for your comment. No action required.

Section	Consultees	Comments	Action
	Takeda UK	No. To appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely active ulcerative colitis in adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist.	The remit and population have been amended to include prior therapy with a TNF-alpha inhibitor.
	UKCPA	ok	Thank you for your comment. No action required.
Timing Issues	AbbVie	This appraisal timing should take account of the expected timelines for the appraisal of adalimumab, golimumab and infliximab in a multiple technology appraisal in this same indication.	Thank you for your comment. This topic has been scheduled into the NICE work programme with consideration of the need for timely guidance.
	Merck Sharp and Dohme	NICE is currently conducting an assessment of other biologic medicines in this indication. MSD believes that the appraisal for vedolizumab is not urgent and it is of greater importance to provide guidance for the medicines that are already available (or will be available prior to vedolizumab).	Thank you for your comment. This topic has been scheduled into the NICE work programme with consideration of the need for timely guidance.
	South Kent Coast CCG and Thanet CCG	It would be helpful if the publication of the TA is about the time, or soon after, launch of the drug in the UK market.	Thank you for your comment. This topic has been scheduled into the NICE work programme with consideration of the need for timely guidance.
	UKCPA	Needs to have UK licence first – do we know when this is expected? Ideally guidance to come out in line with publication of other monoclonal antibody reviews (infliximab, adalimumab) which are due for publication Feb 15 to know which order they should be given based on efficacy and/or cost effectivenss Might be useful to have results of CONSTRUCT trial (CYA vs infliximab in acute severe (UC)	Thank you for your comment. This topic has been scheduled into the NICE work programme with consideration of the need for timely guidance.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	AbbVie	The scope states that “the overall mortality in the UK is 0.8%”, but it is unclear whether this is UC specific mortality or mortality of the UK general population.	This statement has been removed for clarity.
	British Society of Gastroenterology (BSG)	The epidemiological aspects are correct. The background includes aspects of the impact of ulcerative colitis on schooling, work relationships and quality of life in general; such aspects should be considered when looking at treatment outcomes, albeit that the published data may simply be ‘quality of life’. The disease being reviewed should be better defined. The STA refers to moderately to severely active ulcerative colitis; the definitions of disease activity (page 1) moderately active UC adequately, but severe disease (as stated) defines acute severe disease: ie. patients who should be treated as in patients. A better definition of the sick out-patient with UC is needed, that might define a ‘severe’ outpatient in a similar way to the Mayo score (but without the need to perform sigmoidoscopy. A compromise might be to define moderate activity as per the BSG, a ‘non-acute severe’ as those patients having more than bloody bowel movements per day, but without tachycardia or fever. (Anaemia is not particularly useful in assessing severity in outpatients, unless it of new on-set). When managing outpatients, azathioprine / methotrexate are used as steroid sparing agents; they are no used to induce remission.	Thank you for your comments. The Appraisal Committee will consider the impact of ulcerative colitis on people with this disease (see section 3.1.4 of the NICE guide to the methods of technology appraisal). The background and population sections have been amended to define the relevant disease activities more clearly.

Section	Consultees	Comments	Action
		It would be important to mention the potential negative impact on QOL associated with poor pouch function / infertility after surgery as well as QoL data associated with permanent ileostomy	The negative aspects of surgery may be considered by the committee during the appraisal, if appropriate.

Section	Consultees	Comments	Action
	Merck Sharp and Dohme	• MSD recognises that the prevalence and incidence data presented in this section are consistent with the data published in other NICE guidance (CG166) but would like to note that the data differ between this draft scope and the draft scope for the UC MTA. This could lead to variability in the way that consultees and commentators perceive the burden of disease and need for effective treatment options in each of the proposed appraisals. • In the first paragraph on page 2, the draft scope states that, referring to the subacute setting, "a tumour necrosis factor-alpha antagonist (such as infliximab or adalimumab) may be used in clinical practice." This can be interpreted as infliximab being accepted and used as conventional therapy within this setting despite, as the next sentence states, infliximab not having a positive recommendation from NICE for subacute UC (TA140). MSD would like to note that adalimumab also does not have a NICE recommendation for the subacute setting (TA262) and this should be stated here. • MSD realises that NICE guidance TA163 and CG166 recommend the use of ciclosporin in patients with acute severe UC but would like to reiterate that ciclosporin is not licensed for this indication. Further, evidence supporting its efficacy compared to standard of care is limited, it has not been shown to reduce colectomy, it has significant toxicities, food and drug interactions, a narrow therapeutic index, and slow onset of action in UC, supported by the 2012 ECCO guideline (Dignass et al., 2012).	Thank you for your comment. The scope has been updated to use the prevalence referred to in the MTA scope – that is, 240 per 100,000. The issues regarding TNF-alpha inhibitors were discussed in detail at the scoping workshop. Attendees agreed that TNF-alpha inhibitors were appropriate comparators for this appraisal. Comment noted. The Appraisal Committee can consider as comparators technologies that do not have a marketing authorisation for the indication defined in the scope, when they are considered to be part of established clinical practice for the indication in the NHS (see section 6.2.4 of the NICE guide to the methods of technology appraisal).
	South Kent Coast CCG and Thanet CCG	The information provided appears complete and accurate.	Thank you for your comment. No action required.
	Takeda UK	No comment.	No action required.

Section	Consultees	Comments	Action
	UKCPA	Needs to mirror statements & factual content of NICE CG 166	The epidemiology data and current treatment options have been amended for clarity and consistency with existing NICE guidance.
The technology/ intervention	BSG	Yes	Thank you for your comment. No action required.
	South Kent Coast CCG and Thanet CCG	The description is accepted as read.	Thank you for your comment. No action required.
	Takeda UK	Yes	Thank you for your comment. No action required.
	UKCPA	To make clear if this is for an acute exacerbation to induce remission and/or maintenance	In line with the anticipated marketing authorisation, the appraisal will include both induction and maintenance of remission. No action required.
Population	AbbVie	Yes, as long as both patient groups have been assessed during the course of vedolizumab clinical trials.	Following discussion at the scoping workshop, the disease activities and prior therapies included in the appraisal have been clarified.
	BSG	Vedolizumab has only been studies in 'sub-acute' (using NICE definition) moderate to severe UC There is no evidence that I am aware of to assess vedolizumab in acute severe colitis This emphasises the importance of defining what is meant by moderate-to severely active ulcerative colits.	Following discussion at the scoping workshop, the disease activities and prior therapies included in the appraisal have been clarified.

Section	Consultees	Comments	Action
	Merck Sharp and Dohme	• As stated in the previous comment on "wording", it is unclear what should be considered as conventional therapy for the purpose of this appraisal and therefore, what treatments the population will have received prior to being considered for vedolizumab. • In response to the first, third, and forth questions for consultation (page 5), MSD believes that the subacute and acute severe subgroups should be considered so that the guidance for vedolizumab is consistent with previously published guidance for infliximab – where two separate recommendations were made for each setting (TA140 and TA163). MSD do not recommend any further subgroups. • In separate points of the draft scope, consultees and commentators are asked to consider the population defined either in terms of "moderately active" or "severely active", or "subacute" or "acute severe". This leads to a lack of clarity and consistency around the population being appraised.	Following discussion at the scoping workshop, the disease activities and prior therapies included in the appraisal have been clarified.
	South Kent Coast CCG and Thanet CCG	The population appears appropriately defined. No other groups identified within that population that should be considered separately.	Comment noted. No action required.
	Takeda UK	No. For the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist.	The population has been amended accordingly.
	UKCPA	This could be first line monoclonal antibody prior to infliximab/adalimumab	Thank you for your comment. If appropriate the position of vedolizumab in the treatment pathway may be considered during the appraisal.
Comparators	AbbVie	Yes	Thank you for your comment. No action required.

Section	Consultees	Comments	Action
	BSG	Slightly confusingly in the comparator section on page 3 they say that standard therapy would involve anti TNF agents, however NICE does NOT recommend anti TNF agents in this patient group (as per earlier paragraph)	Thank you for your comment. At the scoping workshop it was agreed that TNF-alpha inhibitors are appropriate comparators in this population.
	Merck Sharp and Dohme	In response to the first part of the second question for consultation (page 5), MSD considers the interventions listed as comparators (table on page 3) to represent established clinical practice for moderately to severely active UC. Further, in response to the second part of the second question, MSD believes that treatment options and therefore comparators will differ according to disease severity, as dictated by published NICE guidance. However, MSD notes that consultees and commentators are only asked to consider comparators according to disease severity (moderately or severely active) when no consideration is given to which comparators would be most appropriate for each of the suggested subgroups (subacute and acute severe).	Thank you for your comments. At the scoping workshop it was agreed that it is not necessary to define specific comparators for specific disease states or patient populations. It was also agreed that the population should be restricted to moderately to severely active ulcerative colitis, excluding acute severe disease. The population has been amended accordingly.
	South Kent Coast CCG and Thanet CCG	Yes, the comparators identified are the standard treatments currently used in the NHS. Collectively, they comprise best alternative care. Bio-similar infliximab, if available, could also be a comparator.	Thank you for your comments. All TNF-alpha inhibitors available in England at the start of the appraisal (30 May 2014) have been included.
	Takeda UK	Yes	Thank you for your comment. No action required.

Section	Consultees	Comments	Action
	UKCPA	Duration of treatment – acute exacerbation and/or maintenance – comparing like for like TNF antags although licenced currently not fully NICE approved (IFX 3 doses only; ADA not NICE approved)	Thank you for your comments. The appraisal will include both induction and maintenance of remission. At the scoping workshop it was agreed that TNF-alpha inhibitors are appropriate comparators in this population.
Outcomes	AbbVie	Yes	Thank you for your comment. No action required.
	BSG	Yes	Thank you for your comment. No action required.
	Merck Sharp and Dohme	MSD notes that extra-intestinal manifestations of UC are discussed in the background section. Due to the gut-specific mechanism of action of vedolizumab, MSD would like to suggest that extra-intestinal manifestations of UC are an important outcome that should be considered within this appraisal. The rationale for this is that vedolizumab may represent a less effective treatment option for extra-intestinal manifestations compared to other currently available biologic treatments for UC.	Thank you for your comment. Attendees at the scoping workshop agreed not to include extra-intestinal manifestations of ulcerative colitis in the scope.
	South Kent Coast CCG and Thanet CCG	Yes, I believe the outcomes as described capture the most important benefits and harms.	Thank you for your comment. No action required.
	Takeda UK	Yes	Thank you for your comment. No action required.
	UKCPA	Mucosal healing Specify measures of disease activity	Thank you for your comment. Attendees at the scoping workshop agreed not to include mucosal healing and specific measures of disease activity in the scope.

Section	Consultees	Comments	Action
Economic analysis	AbbVie	None at present	Thank you for your comment. No action required.
	BSG	As far as is possible, the long term costs of surgical intervention should be considered. It will be difficult to estimate long term costs for vedolizumab from the available data	Comment noted. The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect all important differences in costs or outcomes between the technologies being compared (see section 5.1.15 of the NICE guide to the methods of technology appraisal). No action required.
	South Kent Coast CCG and Thanet CCG	Cost per QALY is as expected. Suggest the time horizon should include the duration of remission if possible.	Comment noted. The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect all important differences in costs or outcomes between the technologies being compared (see section 5.1.15 of the NICE guide to the methods of technology appraisal). No action required.
	Takeda UK	No comment	No action required.
	UKCPA	See above	Thank you for your comment. No additional action required.
Equality and Diversity	AbbVie	No	Thank you for your comment. No action required.
	BSG	Nil	Thank you for your comment. No action required.

Section	Consultees	Comments	Action
	South Kent Coast CCG and Thanet CCG	No issues concerning equality are identified.	Thank you for your comment. No action required.
	Takeda UK	No comment	Thank you for your comment. No action required.
Innovation	BSG	Yes – this will be a step change new therapeutic class. Given the lack of available therapies in this clinical scenario, it has the potential to impact substantially on management of refractory sub-acute UC. Need to consider all the negative impacts of surgery – including poor pouch function / pouch failure / reduced fecundity. Also the long-term costs associated with pouch and/or stoma surgery Phase II and III trial data. In addition, QoL data relating to pouch / stoma surgery	Thank you for your comments. The innovative nature of vedolizumab will be considered by the committee during the appraisal.
	South Kent Coast CCG and Thanet CCG	As a new cell line biologic agent and additional biologic for the treatment of UC it has the potential to be innovative particularly if it distinguishes itself in terms of speed of response and duration of remission.	Thank you for your comments. The innovative nature of vedolizumab will be considered by the committee during the appraisal.
	Takeda UK	Takeda UK considers vedolizumab innovative defined by its unique mechanism of action and published data outcomes for efficacy and safety[1] in its potential to make a significant and substantial impact on health-related benefits and address current unmet need. There is a significant unmet need for new treatments for ulcerative colitis patients who fail conventional therapies and for those who fail to respond, lose response, or cannot tolerate current systemically acting tumour necrosis factor-alpha (TNFα) antagonists. Specifically, there are unmet needs for ulcerative colitis therapies	Thank you for your comments. The innovative nature of vedolizumab will be considered by the committee during the appraisal.

Section	Consultees	Comments	Action
		demonstrating a favourable safety profile, as well as improved efficacy on key endpoints such as mucosal healing, durable remission, and corticosteroid-free remission, when compared to conventional therapy or tumour necrosis factor-alpha (TNFα) antagonists currently in use. The United States Food and Drug Administration (FDA) have granted "Priority Review" status for the Biologics License Application for vedolizumab for the treatment of adults with moderately to severely active ulcerative colitis. An application can receive Priority Review designation if it is for a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness relative to conventional treatments. Approximately 55% of patients report flare-up of symptoms every few months, while 9% have monthly flare-ups and a further 9% experience weekly problems[2]. The clinical course of ulcerative colitis is marked by exacerbation and remission with an estimated 30–60% of people with ulcerative colitis experiencing at least one relapse per year[3]. About 80% of these are mild to moderate and about 20% are severe[3]. Ulcerative colitis is a chronic condition and is associated with significant morbidity. Approximately 25% of people with ulcerative colitis will have one or more episodes of acute severe colitis in their lifetime[3]. Of these, 20% will need a colectomy on their first admission and 40% on their next admission[3]. Although mortality rates have improved steadily over the past 30 years, acute severe colitis still has a mortality rate of up to 2%[3]. 166 deaths from ulcerative colitis were registered in England and Wales during 2011 (ICD-10 K51)[4]. In 2011-12, there were 38,745 admissions for ulcerative colitis (ICD-10 K51) in England and Wales , resulting in 75,265 bed days and 46,652 finished consultant episodes[5].	

Section	Consultees	Comments	Action
		Current medical therapy has important limitations; aminosalicylates[6-8] are only modestly effective; glucocorticoids can cause unacceptable adverse events and do not provide a benefit as maintenance therapy. Tumour necrosis factor (TNF) antagonists, although efficacious,[9,10] predispose patients to serious infection.[11] 1 Feagan et al. Vedolizumab as Induction and Maintenance Therapy for Ulcerative Colitis N Engl J Med 2013;369:699-710. 2 National Association for Colitis & Crohn's Disease. New European survey of people with colitis and Crohn's disease highlights that "brits needs to communicate better". 3 National Institute for Health and Clinical Excellence. Management of ulcerative colitis. Clinical guideline in development. Expected June 2013. 4 Office for National Statistics. Deaths registered in England and Wales, Series DR 2011. http://www.ons.gov.uk 5 NHS Hospital episode statistics. NHS England 2011-12 HES data 2012. 6. Ford AC, Khan KJ, Achkar JP, Moayyedi P. Efficacy of oral vs. topical, or combined oral and topical 5-aminosalicylates, in ulcerative colitis: systematic review and meta-analysis. Am J Gastroenterol 2012;107:167-76. 7. Sutherland L, Roth D, Beck P, May G, Makiyama K. Oral 5-aminosalicylic acid for maintaining remission in ulcerative colitis. Cochrane Database Syst Rev 2000; 2:CD000544. 8. Sutherland L, Roth D, Beck P, May G, Makiyama K. Oral 5-aminosalicylic acid for inducing remission in ulcerative colitis. Cochrane Database Syst Rev 2000;2: CD000543. 9. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N EnglJ Med 2005;353:2462-76. [Erratum, N EnglJ Med J 2006;354:2200.] 10. Sandborn WJ, van Assche G, Reinisch W, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe	

Section	Consultees	Comments	Action
		ulcerative colitis. Gastroenterology 2012;142:257-65. 11. Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab,a tumor necrosis factor α–neutralizing agent. N Engl J Med 2001;345:1098-104.	
	UKCPA	Different target to other monoclonal antibodies currently licenced Need to know dosing schedule	Thank you for your comments. The innovative nature of vedolizumab will be considered by the committee during the appraisal.
Other considerations	AbbVie	None	Thank you for your comment. No action required.
	BSG	Could consider comparison between anti TNF naive (more effective) and anti TNF exposed (although the latter would not be that common in the UK) when assessing health benefit. This may allow the position of the therapy within the treatment pathway to be clarified Vedolizumab would be predominantly used for steroid dependant / refractory or azathioprine refractory disease	The subgroups have been amended accordingly.
	South Kent Coast CCG and Thanet CCG	No other considerations identified.	Thank you for your comment. No action required.
	Takeda UK	Takeda UK anticipate the EMA Marketing Authorisation for Vedolizumab will be: "For the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist." The GEMINI clinical trial programme was designed to compare the efficacy and safety of Vedolizumab against placebo for induction and maintenance of moderately to severely active ulcerative colitis.	The remit and population have been amended to match the anticipated marketing authorisation.

Section	Consultees	Comments	Action
NICE Pathways	AbbVie	Given that vedolizumab drug exposure to date is limited to its utilisation in clinical trials only, it may be most commonly used in anti-TNF failures.	Thank you for your comment. If appropriate the position of vedolizumab in the treatment pathway may be considered during the appraisal.
	Merck Sharp and Dohme	In response to the fifth question for consultation (page 5), MSD notes that it is difficult to properly consider the place of vedolizumab in the treatment pathway, before the MTA for UC produces guidance around the role of anti-TNFs. However, as discussed in the comment on "wording", MSD believes that infliximab can be considered as conventional therapy and therefore vedolizumab should be used post-infliximab.	Thank you for your comment. If appropriate the position of vedolizumab in the treatment pathway may be considered during the appraisal.
Questions for consultation	AbbVie	The additional questions are answered below.	Thank you for your comment. Please see below.
Additional comments on the draft scope.	AbbVie	**Q1. Should the appraisal consider the use of vedolizumab for the treatment of acute and/or sub-acute manifestations of moderately to severely active ulcerative colitis?** The appraisal should consider the use of vedolizumab as per patient presentations studied in vedolizumab clinical trials and in line with the proposed scope of the MTA of anti-TNF agents to ensure consistency with both pieces of guidance. **Are the comparators for vedolizumab likely to be different for moderately active ulcerative colitis and severely active ulcerative colitis?** No, but different comparators should be considered for sub-acute and acute manifestations of moderately to severely active UC.	Thank you for your comments. Following discussions at the scoping workshop, the disease severities included in the appraisal have been defined as moderately to severely active ulcerative colitis, excluding acute severe disease.

Section	Consultees	Comments	Action
	South Kent Coast CCG and Thanet CCG	No other comments.	No action required.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Healthcare Improvement Scotland
GlaxoSmithKline
Department of Health
Royal College of Nursing

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Vedolizumab for treating moderately to severely active ulcerative colitis [ID691]

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (post-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
1.	Ileostomy and Internal Pouch Support Group	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. Ileostomy and Internal Pouch Support Group has been added to the matrix of consultees and commentators under 'patient group'.

2.	Independent Age	Independent Age		Removed	Independent Age (formerly Counsel and Care) has asked not to be included in matrices relating to clinical issues. This is a charity that focuses largely on a more social than a medical model of care. Independent Age has been removed from the matrix of consultees and commentators under 'patient groups'.
3.	Research Institute for the Care of Older People (RICE)	NICE Secretariat		Removed	RICE is mainly interested in research on dementia and Alzheimer's and does not fit the inclusion criteria. It has been removed from the matrix of consultees and commentators under 'research groups'

4.	Arrow Generics (azathioprine)	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. Arrow Generics (azathioprine) has been added to the matrix of consultees and commentators under 'comparator manufacturer'.
5.	LPC Medical (prednisolone)	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. LPC Medical (prednisolone) has been added to the matrix of consultees and commentators under 'comparator manufacturer'.

6.	Metwest Pharmaceuticals (prednisolone)	NICE Secretariat		Added	This organisation have an area of interest closely related to this appraisal topic and meet the selection criteria to participate in this appraisal. Metwest Pharmaceuticals (prednisolone) has been added to the matrix of consultees and commentators under 'comparator manufacturer'.
7.	Sanofi (hydrocortisone)	NICE Secretariat		Added	This organisation have an area of interest closely related to this appraisal topic and meet the selection criteria to participate in this appraisal. Sanofi (hydrocortisone) has been added to the matrix of consultees and commentators under 'comparator manufacturer' .

8.	Amdipharm (prednisolone)	Amdipharm Company Ltd		Removed	This manufacturer has requested to be removed as they are not adequately resourced to participate in the appraisal. Therefore they have been removed from the matrix of consultees and commentators under 'comparator manufacturer'
9.	• Bristol-Myers Squibb (hydrocortisone) • Galderma (hydrocortisone)	NICE Secretariat		Removed	These manufacturers do not make hydrocortisone and therefore have been removed from the matrix of consultees and commentators under 'comparator manufacturer'.
10.	• Dermal laboratories (hydrocortisone) • Janssen (hydrocortisone) • LEO Pharma (hydrocortisone)	NICE Secretariat		Removed	These manufacturers make a hydrocortisone cream and therefore have been removed from the matrix of consultees and commentators under 'comparator manufacturer'.

11.	Focus Pharmaceuticals (beclometasone dipropionate)	NICE Secretariat		Removed	This manufacturer makes beclometasone for inhalation and therefore has been removed from the matrix of consultees and commentators under 'comparator manufacturer'.
12.	GlaxoSmithKline (hydrocortisone, beclometasone dipropionate)	NICE Secretariat		Removed	This manufacturer makes hydrocortisone ear drops and beclometasone for inhalation and therefore has been removed from the matrix of consultees and commentators under 'comparator manufacturer'.
13.	• Hospira UK (methotrexate) • Orion Pharma (methotrexate)	NICE Secretariat		Removed	These manufacturers make methotrexate which is not listed as a comparator on the final scope and therefore have been removed from the matrix of consultees and commentators under 'comparator manufacturer'.

14.	Chemidex Pharma (prednisolone, hydrocortisone)	NICE Secretariat		Removed	NICE understands that this company is a distributor, not a manufacturer. Therefore it has been removed from the matrix of consultees and commentators under 'comparator manufacturer'.
15.	Warner Chilcott (mesalazine)	NICE Secretariat		Removed	Warner Chilcott (mesalazine) has been taken over by Actavis and therefore has been removed from the matrix of consultees and commentators under 'comparator manufacturer'