NICE
Appraisal consultation document
Vedolizumab for treating moderately to severely active ulcerative colitis

Response on behalf of the British Society of Gastroenterology

The BSG has considered the ACD following from the initial STA committee meeting considering vedolizumab treatment in moderate to severe ulcerative colitis (UC). We broadly welcome the recommendation that vedolizumab is used in this condition, recognising that this drug represents a novel treatment modality with gut selectivity that will be a significant advance for the subgroup of patients with UC who have failed conventional therapy.

We wish to make the following comments that should be considered in the Final Appraisal Determination, regarding the preliminary recommendation that vedolizumab should not be offered to patients who have failed anti-TNF therapy:

1) **Clinical experience of response to vedolizumab after anti-TNF failure.** The patient expert at the committee on Oct 28th who was on vedolizumab therapy, had previously failed both conventional therapy, and also anti-TNF treatment. It was noted in the committee meeting, that he had had a life-changing response to therapy, enabling him to return to normal life, free of drug side-effects and without having to resort to colectomy. Under the current recommendations in the ACD, this patient would not be offered vedolizumab. Like this patient, there will be a group who have used anti-TNF therapy previously, and who could respond. (This includes patients who have been in clinical trials receiving anti-TNF drugs). They should not be excluded from using this drug without strong evidence.
2) **Scientific rationale for poorer response in anti-TNF failure patients**. There is as yet no evidence that patients whose UC fails to respond to anti-TNF drugs, should have a reduced response to vedolizumab. It is recognised that clinical trial patients with IBD who have previously failed anti-TNF drugs are different to those who are anti-TNF naïve. The reasons for this are many, including longer disease duration since diagnosis, and potential for increased presence of symptoms unrelated to inflammation (such as co-existing functional diarrhoea). Careful exclusion of these causes will leave patients with primary or secondary failure of anti-TNF drugs, who have no reason to be more likely to fail vedolizumab than anti-TNF naïve patients.
3) **Difference between response and remission rates in anti-TNF naïve and anti-TNF failure patients.** It is acknowledged in the ACD (section 4.8) that vedolizumab is effective in both groups. In the maintenance period in GEMINI 1, section 3.5 stated 'In the population who had not had a TNF-alpha inhibitor before, 46% of people having 8-weekly vedolizumab and 19% people having placebo had clinical remission (percentage difference 26.8, 95% CI 12.4 to 41.2). In the population in whom treatment with a TNF-alpha inhibitor had failed, 37% of people having 8-weekly vedolizumab and 5.3% of people having placebo had remission (percentage difference 31.9, 95% CI 10.3 to 51.4). We recognise that there were fewer patients overall in GEMINI 1 who had failed anti-TNF drugs (41% of the total) and the study was not powered to examine end-points for this subgroup. This uncertainty should not

exclude this group however, without clear evidence to show this group differs fundamentally.

4) **Vedolizumab as first-line biological therapy in moderate to severe UC failing conventional therapy**. The implications of the current recommendations in this ACD are to use vedolizumab ahead of anti-TNF drugs in patients failing conventional therapy, in whom surgery is not appropriate. The situation differs in acute severe colitis however. Anti-TNF treatment is approved in acute severe UC (NICE TA163), and the outcome of the MTA on anti-TNF therapy in moderate to severe UC is awaited. Whilst there are no head to head comparisons of the two drug classes, it is clear from the GEMINI 1 data(1), and from the published data on infliximab in UC (2), that the response to infliximab is likely to be much more rapid than vedolizumab. In the acute severe UC situation it seems more appropriate to use infliximab, but responders to anti-TNF therapy in this acute severe situation may subsequently lose response, and it would seem inappropriate then to exclude them from using vedolizumab at some future date, when they have moderate to severe disease non-responsive to conventional therapy.

References

1. Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel JF, Sandborn WJ, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699-710.
2. Laharie D, Bourreille A, Branche J, Allez M, Bouhnik Y, Filippi J, et al. Ciclosporin versus infliximab in patients with severe ulcerative colitis refractory to intravenous steroids: a parallel, open-label randomised controlled trial. Lancet. 2012;380(9857):1909-15.