Vedolizumab for treating moderately to severely active Crohn's Disease after prior therapy

NICE Appraisal Consultation Document, January 2015

Response on behalf of the UK Clinical Pharmacy Association (UKCPA)

We acknowledge with concern the proposed decision by NICE not to recommend vedolizumab in Crohn's Disease (CD) patients after prior therapy.

The drug has a different mode of action to the available biologic treatment for CD therefore allows clinicians to offer a further treatment alternative to patients failing available medical therapies, potentially avoiding high cost chronic ill health and repeated surgery.
We can particularly see the use of vedolizumab in the elderly patient with a higher risk of infection[1] due to its low ADR profile and for patients with high risk of cancer.

You asked the following questions:

- Has all of the relevant evidence been taken into account?

1. Current practice uses adalimumab and infliximab as treatment therapy in mild to severeCD usually after failing thiopurines but has an overall efficacy rate of about 40-50% only. Once failed on one anti-TNFs recapturing remission with a second anti-TNF succeeds in about 20% of patients.
   For patients with either primary failure to respond or loss of response there is no further medical treatment available and surgery is often of limited value and in many cases not indicated. These patients, approx. 10% of patients with CD, have to live with chronic ill health which often entails repeated high cost health care usage.
   Vedolizumab has proven to be superior to placebo in inducing remission at week 10 and more importantly in maintaining remission with 39% remission 43.5% response at week 52 offering an alternative to patients after anti-TNF therapy in Gemini II [2].
   From the Gemini II and III[3]trials it is obvious that the primary endpoint used traditionally for biologics in CD of response and remission at week 6 is not suitable for this novel molecule and that vedolizumab patients take longer to respond with slower onset of action and enhanced response at week 10.We feel that the current evidence support the use of vedolizumab in patients previously exposed to anti-TNFs where both trials showed a steady improvement in response between week 6 and maintenance of response at week 52 in Gemini II. Encouragingly Gemini III showed a high improvement rate for treatment failure patients between week 6 and 10 in comparison to treatment naïve patients who responded earlier in the treatment. This could be explained with treatment failure patients having more structural damage and needing longer to heal but there is no evidence that these patients would maintain their remission any less. It remains to be seen if the outcome of Gemini III patients at week 52 is similar to the results of Gemini II.

There is very little evidence available on the cost to the health system of CD patients that have failed anti-TFN treatment. As the practice in the UK is to use biologics once thiopurines have failed it is safe to assume that treatment failure patients are the difficult to treat group and of high cost to the NHS. Their limited option for treatment is currently steroids +/- surgery with the ensuing problems of longterm use of steroid and post-surgery morbidity.
If only a proportion of these refractory patients can be maintained in remission with vedolizumab it will be of great benefit to the economy and the health care system.
Crohn's and Colitis showcases clearly what it means to live with treatment resistant CD and the effect it has on patients live and their employment potential.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

2. It is currently not clear if the anti-TNF failure group is different to patients that respond to biologics but this should not be a reason to exclude access to an effective treatment for these patients. We are currently in the process of trying to stratify patients according to disease picture and response to treatment, but so far the evidence has been elusive.
   We feel that the cost of living with treatment resistant CD is higher than the current assumption of surgery etc. The effects on fertility, on employment potential and health care usage in this young patient group are underestimated.
   In addition the use of vedolizumab in patient groups that are not suitable for anti-TNFs due to their ADR profile such as elderly patients at risk of infections and patients with a history of cancer has not been taken into account. This may be a minority of patients but vedolizumab may just change their lives in the same way anti-TNFs have done.
   In view of the small numbers of treatment failure patients and the severity of the consequences of not responding to medical treatments it may be appropriate to apply less strict pharmaco-economic criteria as the effect of treatment failure has a profound and disabling impact on patients' lives beyond the healthcare setting.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

We have serious concerns that these patients would be denied an effective treatment based on insufficient evidence. There is a cohort of patients who had biologics in the past and having active disease would benefit from this novel therapeutic class with considerable reduction in ADRs.
In view of the burden to the society and the NHS these patients can pose we feel that vedolizumab should be accessible as a treatment option with clear guidance on review and suggested stopping rules.

We would like to urge the committee to review the decision to exclude patients with CD previously exposed to anti-TNFs from vedolizumab therapy as this may be the only medical alternative to surgery and chronic ill health with the life changing impact this has on patients.

References:

1. Cottone K et al. Age is a risk factor for severe infections and mortality in patient given anti-TNF therapy for IBD. Clinical Gastroenrerol Hepatol.2011;9:30-35
2. Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel JF, Sands BE, et al. Vedolizumab as induction and maintenance therapy for Crohn' disease. N Engl J Med. 2013;369(8):711-721.
3. Sands BE, Feagan BG, Rutgeerts P, et al. Effects of vedolizumab induction therapy for patients with Crohn's disease in whom tumor necrosis factor antagonist treatment failed. Gastroenterology 2014;147:618-27.