NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Vedolizumab for treating moderate to severe active Crohn´s disease after prior therapy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderate to severe active Crohn´s disease in people who are intolerant of, or whose disease has not responded or is resistant to either conventional therapy or a tumour necrosis factor-alpha (TNF-α) antagonist.

Background

Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract (gut) that may affect any part of the gut from the mouth to the anus. People with Crohn's disease have recurrent attacks, with acute exacerbations ('flares') in between periods of remission or less active disease. These flares may affect any part of the gut and are defined by location (terminal ileal, colonic, ileocolic, upper gastrointestinal), or by the pattern of the disease (inflammatory, fistulising, or stricturing).

The clinical features of Crohn's disease are variable and are determined partly by the site of the disease. The symptoms include diarrhoea, abdominal pain and weight loss. Constitutional symptoms include malaise, lethargy, anorexia, nausea, vomiting and low-grade fever.

Crohn's disease can be complicated by the development of strictures (a narrowing of the intestine), obstructions, fistulae and perianal disease. Other complications include acute dilation, perforation and massive haemorrhage, and carcinoma of the small bowel or colon.

There are currently at least 115,000 people in the UK with Crohn´s disease. The incidence of Crohn's disease is greatest in people aged between 15 and 30 years. However, it may affect people of any age and 15% of people with the disease are over the age of 60 at diagnosis. Mortality among people with Crohn's disease is only slightly higher than that in the general population.

Crohn's disease is not medically or surgically curable. Treatment aims to control manifestations of Crohn's disease to reduce symptoms, and to maintain or improve quality of life while minimising short- and long-term adverse effects. Clinical management depends on disease activity, site, behavior of disease (inflammatory, fistulising or stricturing), response to previous medications, side-effect profiles of medications and extra-intestinal manifestations.

NICE clinical guideline 152 recommends monotherapy with a glucocorticosteroid (prednisolone, methylprednisolone or intravenous hydrocortisone) to induce remission in people with a first presentation or a single inflammatory exacerbation of Crohn's disease in a 12-month period. Budesonide or 5-aminosalicylate are considered for some people who decline, cannot tolerate or in whom a conventional glucocorticosterioid is contraindicated. When 2 or more inflammatory exacerbations are experienced in a 12-month period, azathioprine, mercaptopurine and methotrexate may be considered as add-on treatments to conventional glucocorticosterioids or budesonide to induce remission of Crohn's disease. NICE technology appraisal 187 recommends infliximab and adalimumab as treatment options for adults with severe active Crohn's disease whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy.

In addition to pharmacological treatment, between 50 and 80% of people with Crohn's disease will require surgery during the course of their disease. The main reasons for surgery are strictures causing obstructive symptoms, lack of response to medical therapy, and complications such as fistulae and perianal disease.

The technology

Vedolizumab (brand name unknown,Takeda UK) is a humanised IgG_1 monoclonal antibody derived from a newly engineered cell line. It is targeted against the $\alpha_4\beta_7$ integrin, which is expressed in certain white blood cells and is responsible for recruiting these cells to inflamed bowel tissue. It is administered by intravenous infusion.

Vedolizumab does not currently have a UK marketing authorisation for treating moderate to severe active Crohn´s disease in people who are intolerant of, or whose disease has not responded or is resistant to either conventional therapy or a TNF-α antagonist. It has been studied in clinical trials compared with placebo in adults with moderate to severe active Crohn´s disease who are intolerant of, or whose disease has had an inadequate response or loss of response to at least 1 conventional therapy or a TNF-α antagonist.

Intervention(s)	Vedolizumab
Population(s)	People with moderate to severe active Crohn´s disease who are intolerant of, or whose disease has not responded or is resistant to either conventional therapy or a TNF-α antagonist

Comparators	For people with moderate active Crohn's disease: • Conventional treatment strategies without vedolizumab (including no treatment, dietary intervention, drug treatment with conventional glucocorticosteroids [prednisolone, methylprednisolone, and hydrocortisone] alone or in combination with azathioprine, mercaptopurine or methotrexate; aminosalicylates; budesonide alone or in combination with azathioprine, mercaptopurine or methotrexate) For people with severe active Crohn's disease: • Conventional treatment strategies without vedolizumab (as described above) • TNF-α antagonists (infliximab or adalimumab and biosimilars)
Outcomes	The outcome measures to be considered include: • disease activity (remission, response, relapse) • surgery • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 187, May 2010, 'Infliximab (review) and adalimumab for the treatment of Crohn's disease (including a review of technology appraisal guidance 40)'. Guidance on static list. Related Guidelines: Clinical Guideline No. 152, October 2012, 'Crohn´s disease: management in adults, children and young people'. Review Proposal Date TBC. Related Interventional Procedures: Interventional Procedure No. 288, February 2009, 'Extracorporeal photopheresis for Crohn's disease'. Related NICE Pathways: NICE Pathway: Crohn´s disease overview, Pathway created: October 2012 http://pathways.nice.org.uk/pathways/crohns-disease
Related NHS England policy	None

Questions for consultation

Have all relevant comparators for vedolizumab been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for moderate to severe active Crohn's disease?
- Are conventional treatment strategies correctly defined?
- Are infliximab and adalimumab currently used in clinical practice for treating moderate active Crohn's disease?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider vedolizumab will fit into the existing NICE pathway for Crohn's disease?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which vedolizumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)

Subject to referral by the Department of Health, the invite for participation in this technology appraisal is anticipated for after January 2014, when new arrangements for the pricing of pharmaceuticals are expected to be in place. Consequences for this appraisal will be explored through further consultation on the scope pre-invitation.