NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely 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, behaviour of disease (inflammatory, fistulising or stricturing), response to previous treatments, side-effect profiles of treatments and extra-intestinal manifestations, such as uveitis and arthritis.

NICE clinical guideline 152 recommends monotherapy with a corticosteroid (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-aminosalicylates are considered for some people who decline, cannot tolerate or in whom a conventional corticosteroid 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 corticosteroids 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. At the time of NICE technology appraisal 187, marketing authorisations for infliximab and adalimumab did not include treating adults with moderately active Crohn's disease and so moderately active disease is not covered by that guidance. The marketing authorisations for infliximab and adalimumab have subsequently been expanded to include treating people with both moderately and severely active disease that whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments).

For people who choose to have maintenance treatment, NICE clinical guideline 152 recommends azathioprine or mercaptopurine as monotherapy to maintain remission when previously used with a conventional corticosteroid or budesonide to induce remission. Azathioprine or mercaptopurine may also be considered for maintaining remission in people who have not previously received these drugs. Methotrexate may be used to maintain remission only in people who needed methotrexate to induce remission, or in people for whom azathioprine or mercaptopurine maintenance treatment is not suitable.

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 (Entyvio,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 has received a positive opinion from the Committee for Medicinal Products for Human Use for 'the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist'.

Intervention(s)	Vedolizumab
Population(s)	Adults with moderately to severely active Crohn's disease in whom the disease has responded inadequately to, or is no longer responding to, either conventional therapy or a TNF-α antagonist, or who are intolerant to either of them.
Comparators	For people with moderately to severely active Crohn's disease: • Conventional treatment strategies without vedolizumab (including antibiotics, drug treatment with conventional corticosteroids alone or in combination with azathioprine, mercaptopurine or methotrexate; aminosalicylates; budesonide alone or in combination with azathioprine, mercaptopurine or methotrexate) Additionally, for people with moderately to severely active Crohn's disease who have not previously received a TNF-α antagonist and for whom this treatment would be suitable: • TNF-α antagonists (infliximab and adalimumab)
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. Biosimilars are not expected to be in established NHS practice at the time of appraisal and are not included as comparators.
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 national policy	None

Questions for consultation

The list of comparator treatments for vedolizumab has been updated. Has the group for whom TNF-α would be used been appropriately defined?

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 vedolizumab 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 vedolizumab 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.