

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

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

**Final 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- $\alpha$ ) 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<sub>1</sub> 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 a marketing authorisation in the UK 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 (TNF $\alpha$ ) antagonist’.

<b>Intervention(s)</b>	Vedolizumab
<b>Population(s)</b>	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- $\alpha$ antagonist, or who are intolerant to either of them.
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• 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)</li> <li>• TNF-<math>\alpha</math> antagonists (infliximab and adalimumab)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• disease activity</li> <li>• surgery</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>Biosimilars are not expected to be in established NHS practice at the time of appraisal and are not included as comparators.</p>

<b>Other considerations</b>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p> <p>If evidence allows, the following subgroups should be considered:</p> <ul style="list-style-type: none"> <li>• People who have not previously received a TNF-<math>\alpha</math> antagonist</li> <li>• People for whom a TNF-<math>\alpha</math> antagonist has failed</li> <li>• People for whom TNF-<math>\alpha</math> antagonists are not suitable because of intolerance or contraindication.</li> </ul>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Technology Appraisals:</p> <p>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.</p> <p>Related Guidelines:</p> <p>Clinical Guideline No. 152, October 2012, 'Crohn's disease: management in adults, children and young people'. Review Proposal Date TBC.</p> <p>Related Interventional Procedures:</p> <p>Interventional Procedure No. 288, February 2009, 'Extracorporeal photopheresis for Crohn's disease'.</p> <p>Related NICE Pathways:</p> <p>NICE Pathway: Crohn's disease overview, Pathway created: October 2012</p> <p><a href="http://pathways.nice.org.uk/pathways/crohns-disease">http://pathways.nice.org.uk/pathways/crohns-disease</a></p>
<b>Related national policy</b>	<p>None</p>