NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Vedolizumab for treating moderately to severely active ulcerative colitis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely active ulcerative colitis in adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy.

Background

Ulcerative colitis is the most common inflammatory bowel disease. The cause of ulcerative colitis is unknown. Hereditary, infectious and immunological factors have been proposed as possible causes. It can develop at any age, but peak incidence is between the ages of 15 and 25 years, with a second, smaller peak between 55 and 65 years. It has been estimated that around 146,000 people in the UK have ulcerative colitis.

Ulcerative colitis usually affects the rectum, and a variable extent of the colon proximal to the rectum. The classic symptoms of ulcerative colitis are bloody diarrhoea, colicky abdominal pain, urgency and tenesmus. Some patients may have extra-intestinal manifestations involving joints, eyes, skin and liver. Ulcerative colitis is a lifelong disease that is associated with significant morbidity; symptoms can relapse and then go into remission for months or even years. Around 50% of people with ulcerative colitis will have at least one relapse per year. About 80% of these are mild to moderate and about 20% are severe. Complications of ulcerative colitis may include haemorrhage, perforation, stricture formation, abscess formation and anorectal disease. People with long-standing disease have an increased risk of bowel cancer. The overall mortality in the UK is 0.8%.

Mildly active ulcerative colitis is defined as less than four bowel movements daily. Moderately active ulcerative colitis is defined as more than four daily bowel movements but where the patient is not systemically ill. Severe ulcerative colitis is defined as an attack in which a person has more than six bowel movements daily, and is systemically ill as shown by tachycardia, fever, anaemia or a raised erythrocyte sedimentation rate. NICE clinical guideline 166 ‘Ulcerative colitis: Management in adults, children and young people’ (CG166) recognises subacute ulcerative colitis as a moderately to severely active ulcerative colitis that would normally be managed in an outpatient setting and does not require hospitalisation or the consideration of urgent surgical intervention.

The aim of treatment in active disease is to address symptoms of urgency, frequency and rectal bleeding, and thereafter to maintain remission. Initial management depends on clinical severity, extent of disease and the person's preference, and may include topical or oral aminosalicylates and corticosteroids. For people with subacute manifestation of ulcerative colitis, CG166 recommends oral prednisolone as an initial treatment option. If the disease does not adequately respond to oral corticosteroids then an immunosuppressant (such as tacrolimus, methotrexate or ciclosporin) or a tumour necrosis factor-alpha antagonist (such as infliximab or adalimumab) may be used in clinical practice. NICE technology appraisal 140 does not recommend infliximab for the treatment of subacute manifestations of moderately to severely active ulcerative colitis. In acute severe ulcerative colitis, CG166 recommends initial management with intravenous corticosteroids. If there is no improvement or worsening of symptoms despite corticosteroid treatment, the guideline recommends adding intravenous ciclosporin or undertaking surgery. For people who cannot tolerate intravenous corticosteroids or in whom it is contraindicated, CG166 recommends initial management with ciclosporin. NICE technology appraisal 163 recommends infliximab for treating acute exacerbations when ciclosporin is contraindicated or inappropriate. Once the symptoms are in remission, treatment involves regular doses of aminosalicylates, or oral immunosuppressants (azathioprine or mercaptopurine) to reduce the risk of relapse. People with ulcerative colitis may need a colectomy (with the creation of either an ileostomy or an ileo-anal pouch) to control acute severe disease, to improve the quality of life in chronic active disease or to treat cancer or pre-cancerous changes.

The technology

Vedolizumab (brand name unknown, Takeda) is a humanized 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. Vedolizumab is administered by intravenous infusion.

Vedolizumab does not currently have a UK marketing authorisation for the treatment of ulcerative colitis. It has been studied in clinical trials compared with placebo in adults with moderately to severely active ulcerative colitis who are intolerant of, or whose disease has had an inadequate response or loss of response to at least one conventional therapy.

Intervention	Vedolizumab
Population	Adults with moderately to severely active ulcerative colitis who are intolerant of, or whose disease has had an inadequate response or loss of response to at least one conventional therapy.

Comparators	Standard clinical management without vedolizumab, which may include a combination of aminosalicylates, corticosteroids, immunosuppressants, tumour necrosis factor-alpha antagonists and surgical intervention.
Outcomes	The outcome measures to be considered include: • measures of disease activity • rates of and duration of response, relapse and remission • rates of surgical intervention • time to surgical intervention • mortality • adverse effects of treatment (including leakage and infections following surgery) • 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	If evidence allows following subgroups will be considered: • People with a subacute manifestation of ulcerative colitis • People with an acute exacerbation of ulcerative colitis Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE pathways	Related Technology Appraisals: Technology Appraisal No. 262, July 2012, 'Adalimumab for the treatment of moderate to severe ulcerative colitis (terminated appraisal). Currently being reviewed. Earliest anticipated date of publication February 2015.

	Technology Appraisal No. 163, Dec 2008, 'Infliximab for acute exacerbations of ulcerative colitis'. Review Date TBC. Technology Appraisal No. 140, Apr 2008, 'Infliximab for subacute manifestations of ulcerative colitis'. Currently being reviewed. Earliest anticipated date of publication February 2015. Technology Appraisal in preparation, 'Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262), Earliest anticipated date of publication February 2015. Related Guidelines: Clinical Guideline No. 166, June 2013, 'Ulcerative colitis: Management in adults, children and young people'. Review Proposal Date TBC. Clinical Guideline No. 118, March 2011, 'Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas'. Review Proposal Date March 2014. Related Interventional Procedures: Interventional Procedure No. 126, June 2005 'Leukapheresis for inflammatory bowel disease'. Moved to static list in June 2008. Related Quality Standards: Quality Standard in Preparation, 'Inflammatory bowel disease (to cover Ulcerative colitis and Crohn's disease)', Publication TBC. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Ulcerative colitis overview, Pathway created: June 2013. http://pathways.nice.org.uk/pathways/ulcerative-colitis

Related NHS England policy	'Improving the health and well-being of people with long term conditions. World class services for people with long term conditions: information tool for commissioners', January 2010. http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_111187.pdf

Questions for consultation

Should the appraisal consider the use of vedolizumab for the treatment of acute and/or sub-acute manifestations of moderately to severely active ulcerative colitis?

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

- Which treatments are considered to be established clinical practice in the NHS for moderately to severely active ulcerative colitis?
- Are the comparators for vedolizumab likely to be different for moderately active ulcerative colitis and severely active ulcerative colitis?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom vedolizumab 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 ulcerative colitis?

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.

NICE intends to appraise vedolizumab 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 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.