Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Vedolizumab for treating moderately to severely active ulcerative colitis

Final scope

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 or a tumour necrosis factor-alpha antagonist.

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 128,400 people in England have ulcerative colitis.

Ulcerative colitis usually affects the rectum, and a variable extent of the colon proximal to the rectum. The 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 severity of ulcerative colitis may be classified based on criteria such as the modified Truelove and Witts severity index: mildly active ulcerative colitis is defined as fewer 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, and severe ulcerative colitis is defined as more than six bowel movements daily with systemic illness, as shown by tachycardia, fever, anaemia or a raised erythrocyte sedimentation rate. Severe ulcerative colitis (often termed ‘acute severe ulcerative colitis’) as defined by the Truelove and Witts severity index is a medical emergency that requires intensive inpatient treatment. The scope of this appraisal includes people with moderately to severely active ulcerative colitis; it does not include acute severe ulcerative colitis (that is, severe ulcerative colitis according to the Truelove and Witts severity index) that is a medical emergency. NICE recommendations for managing acute severe ulcerative colitis are found in

CG166 and NICE technology appraisal 163 (infliximab for acute exacerbations of ulcerative colitis).

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 (sulfasalazine, mesalazine, balsalazide or olsalazine) and corticosteroids. If the disease does not adequately respond to oral corticosteroids then an immunosuppressant (such as a calcineurin inhibitor) or a tumour necrosis factor-alpha inhibitor (TNF-alpha inhibitor inhibitor , such as infliximab or adalimumab) may be considered. Treatment to maintain remission may include aminosalicylates or thiopurines (such as mercaptopurine or azathioprine). Colectomy (with the creation of either an ileostomy or an ileo-anal pouch) is a treatment option for some patients, to improve the quality of life in chronic or treatment-refractory active disease or to treat cancer or pre-cancerous changes.

The technology

Vedolizumab (Entyvio, 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.

The European Medicines Agency's Committee for Medicinal Products for Human Use has recommended granting a marketing authorisation for vedolizumab for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor−alpha antagonist.

Intervention	Vedolizumab
Population	Adults with moderately to severely active ulcerative colitis (excluding those with acute severe ulcerative colitis that is a medical emergency and requires inpatient treatment) who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy (immunosuppressants and/or corticosteroids) or a TNF-alpha inhibitor.

Comparators	Established clinical management without vedolizumab, which may include a combination of aminosalicylates (sulfasalazine, mesalazine, balsalazide or olsalazine), corticosteroids (beclometasone, budesonide, hydrocortisone or prednisolone), thiopurines (mercaptopurine or azathioprine), calcineurin inhibitors (tacrolimus or ciclosporin), TNF-alpha inhibitors (infliximab, adalimumab or golimumab) and surgical intervention.
Outcomes	The outcome measures to be considered include: • mortality • measures of disease activity • rates of and duration of response, relapse and remission • rates of hospitalisation • rates of surgical intervention • time to surgical intervention • 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. The availability of any patient access schemes for the comparator technologies should be taken into account.

Other considerations	If evidence allows following subgroups will be considered: • People who have been previously treated with one or more TNF-alpha inhibitors and people who have not received prior TNF-alpha inhibitor therapy 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 (see below). Technology Appraisal No. 163, Dec 2008, 'Infliximab for acute exacerbations of ulcerative colitis'. Review proposal date TBC. Technology Appraisal No. 140, Apr 2008, 'Infliximab for subacute manifestations of ulcerative colitis'. Currently being reviewed (see below). 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 January 2015. Related Diagnostics Guidance: Diagnostics Guidance No. 11, October 2013, 'Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel'. 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'. Moved to static list in December 2013.

Related NICE recommendations and NICE pathways (continued)	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)', Anticipated publication date September 2014. 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 national 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