National Institute for Health and Care Excellence

Health Technology Evaluation

Etrasimod for treating moderately to severely active ulcerative colitis

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Crohn's and Colitis UK	The NICE guideline on Ulcerative Colitis and Quality Standard on Inflammatory Bowel Disease are outdated and do not reflect current best practices and the experience of people with Ulcerative Colitis. We would ask that NICE update the guideline and quality standard urgently given it is the basis on which this drug will be appraised.	Thank you, the comment has been acknowledged and concerns relating to NICE guideline and quality standards will be shared internally. This technology has been selected to be appraised as a cost-comparison.
	Pfizer	Yes.	Thank you, the comment has been noted. This technology has been selected to be appraised as a cost-comparison.

Section	Stakeholder	Comments [sic]	Action
Wording	Crohn's and Colitis UK	None provided.	N/A
	Pfizer	Since the marketing authorisation process is still ongoing, please change 'To appraise the clinical and cost effectiveness of etrasimod within its proposed marketing authorisation for treating moderately to severely active ulcerative colitis.'	Thank you for your comment. This is standard wording used on all scopes. This wording is broad and based on the publicly available trial population. No changes made.
Additional comments on the draft remit	Crohn's and Colitis UK	There are limited treatment options available in treating moderate to severe ulcerative colitis. It is important that patients have the widest possible options available to them, particularly given what we are increasingly coming to understand in terms of the importance of personalised treatments.	Thank you, the comment has been noted and will be considered in the appraisal of etrasimod.
	Pfizer	No comments.	N/A

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Crohn's and Colitis UK	The aim of treatment is for people to live their best-possible lives, not just achieve remission. As currently written the background does not capture the significant unmet need for treatments within this patient cohort. There is currently no medical or surgical cure for Crohn's Disease. The range of options available for treating	Thank you for your comment. The background section has been amended.

Section	Consultee/ Commentator	Comments [sic]	Action
		Crohn's Disease remain far from optimal for patients, a substantial number of whom experience lack of response (primary or secondary) and/or adverse reactions to biologic as well as conventional therapies. For example, up to one third of patients with IBD are intolerant to thiopurines and a further 10% are unresponsive to them.[1,2] In the majority of patients who do respond, the benefits take three to six months to appear. Significant risks of thiopurines including non-Hodgkin's lymphoma (as high as 4-5-fold compared with unexposed IBD patients and further increased when used in combination with anti-TNFs). Other side effects include early hypersensitivity reactions such as fever and pancreatitis, bone marrow suppression and hepatotoxicity requiring frequent lab monitoring during treatment.[3,4] Furthermore, up to 40% of patients treated with anti-TNF therapy do not respond to induction therapy.[5] In the approximately one-third of patients who do achieve remission with anti-TNF therapy, between 10%-50% lose response over time.[6] 1. Fraser, A.G, Orchard, T.R, Jewell, D.P. (2002). The efficacy of azathioprine for the treatment of inflammatory bowel disease: a 30 year review. Gut, 50: 485–9. 2. Candy, S, Wright, J, Gerber, M, et al., (1995) A controlled double blind study of azathioprine in the management of Crohn's disease. Gut, 37: 674–8. 3. Siegel, C.A, Marden, S.M, Persing, S.M, et al., (2009). Risk of lymphoma associated with combination anti-tumor necrosis factor and immunomodulator therapy for the treatment of Crohn's disease: a meta-analysis. Clin Gastroenterol Hepatol, 7:874–881	

Section	Consultee/ Commentator	Comments [sic]	Action
		4. Jorquera, A, Solari, S, Vollrath, V. et al., (2012). Phenotype and genotype of thiopurine methyltransferase in Chilean individuals. Rev Med Chil, 140:889–895 5. Rutgeerts, P, Van Assche, G, Vermeire S. (2004). Optimizing anti-TNF treatment in inflammatory bowel disease. Gastroenterology, 126(6):1593-610. 6. Roda, G. (2016). Loss of Response to Anti-TNFs: Definition, Epidemiology, and Management. Clin Transl Gastroenterol, 7 (1), e135.	
	Pfizer	First paragraph Please replace 'It has been estimated that between 1 in 200 and 1 in 420 people in England have ulcerative colitis, of whom about 52% have moderate to severe disease.' With 'It has been estimated that ulcerative colitis affects around 1 in 420 people[1], which equates to about 134,000 people in England[2]. About 52% have moderate to severe disease[3]. Supporting reference: 1. Crohn's and Colitis UK – About Crohn's and Colitis, Ulcerative Colitis [accessed September 2022] 2. Office for National Statistics – population estimates [accessed September 2022] 3. National Institute for Health and Care Excellence, Costing statement: Ulcerative colitis, June 2015 [accessed September 2022].	Thank you for your comment. The prevalence estimates have been updated using information from the Crohn's and Colitis UK website.

Section	Consultee/ Commentator	Comments [sic]	Action
	Pfizer	Second paragraph Please update the sentence to read 'the symptoms of ulcerative colitis include bloody diarrhoea, **colicky abdominal pain**, urgency, tenesmus, fatigue and anaemia.'	The background section has been amended
	Pfizer	Third paragraph No comment Fourth paragraph No comment	Thank you for your response.
	Pfizer	Fifth paragraph Please replace 'Surgery may be considered as emergency treatment for severe ulcerative colitis that does not respond to drug treatment. People may also choose to have elective surgery for unresponsive or frequently relapsing disease that is affecting their quality of life. The scope of this appraisal does not include severe ulcerative colitis that is a medical emergency requiring intensive inpatient treatment.' with 'Intravenous ciclosporin or surgery is recommended for people who cannot tolerate or decline intravenous corticosteroids, for people in whom intravenous corticosteroids are contraindicated or in addition to corticosteroids for people who have been given intravenous corticosteroids and have had little or no improvement within 72 hours or a worsening of symptoms at any time. Surgery maybe considered as emergency treatment	Thank you for your response. The description of the treatment pathway in the background section has been removed as not directly relevant to the decision problem.

Section	Consultee/ Commentator	Comments [sic]	Action
		for severe ulcerative colitis that does not respond to drug treatment. People may also choose to have elective surgery for unresponsive or frequently relapsing disease that is affecting their quality of life. The scope of this appraisal does not include severe ulcerative colitis that is a medical emergency requiring intensive inpatient treatment'	
	Pfizer	<u>The technology – paragraph one</u> Please remove **induction** from the following sentence with the following, as the trials go beyond the induction phase. 'It has been studied in clinical trials compared with placebo as an **induction** therapy in people with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.' Additionally, please add 'Etrasimod is a sphingosine 1-phosphate (S1P) receptor modulator that interacts with S1P receptors and is administered orally.'	The technology section has been amended. However we no longer include a description of the technology in our scopes.
Population	Crohn's and Colitis UK	None provided	N/A
	Pfizer	First paragraph Please update the population to read 'People with moderately to severely active ulcerative colitis'	Thank you for the comments. The population has been amended to:

Section	Consultee/ Commentator	Comments [sic]	Action
			People with moderately to severely active ulcerative colitis when conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment. This is in line with NICE guidance for relevant comparators in this scope.
Subgroups	Crohn's and Colitis UK	None provided	N/A
	Pfizer	None provided	N/A
Comparators	Crohn's and Colitis UK	We are concerned that the use of steroids as a comparator may imply that for those who cycle through available treatment options without success, steroids are an alternative treatment. "Corticosteroids have no proven efficacy in maintaining remission in IBD and should not be used for this purpose." The BSG guidelines set out clear stipulations on the best practice of prescribing steroid therapies given their diminishing returns, harsh side effects and risk of dependency. Corticosteroids can induce remission, but they do not heal mucosa. There is no evidence to support the benefits of high-dose steroids and they have side	Thank you for the comment. Conventional therapies have been removed from the comparator list.

Section	Consultee/ Commentator	Comments [sic]	Action
		effects. Approximately 50% of patients experience short-term corticosteroid-related adverse events such as acne, oedema, sleep and mood disturbance, glucose intolerance and dyspepsia.	
	NHS England	There should be an additional comparator added subject to NICE evaluation - mirikizumab for treating moderately to severely active ulcerative colitis [ID3973]	Thank you for your comment. Mirikizumab has been included as a comparator (subject to NICE evaluation).
	Pfizer	No comment	N/A
Outcomes	Crohn's and Colitis UK	Improved medicine adherence and self-management.	Thank you for the comment, these have not been included in the outcome list for consistency with other scopes in this disease area.
	Pfizer	None provided.	N/A
Equality	Crohn's and Colitis UK	There is an advantage to a further treatment option which can be administered at home, which avoids the need for patients to take time off work or education and could potentially improve adherence. The mode of administration could also benefit those with disabilities in terms of reducing the need to travel to hospital. Being able to take their treatment at home may also benefit cultures where it may be harder to speak openly about the condition or for those living in remote communities.	Thank you, equality comments have been noted.

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		Certain medications attract prescription costs in England. These costs can be prohibitive to groups of patients, acting as a barrier to well-being and adherence.	
	Pfizer	None provided.	N/A
Other considerations	Crohn's and Colitis UK	Biologics are administered via sub-cutaneous injection and/or infusion, which can be inconvenient and uncomfortable, so there is a clear benefit to patients from an additional treatment option which is an oral tablet.	Thank you, treatment administration benefits have been noted.
	Pfizer	None provided.	N/A
Questions for consultation	Crohn's and Colitis UK	None provided.	N/A
	Pfizer	None provided.	N/A
Additional comments on the draft scope	Crohn's and Colitis UK	None provided.	N/A
	Pfizer	None provided.	N/A

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

None