National Institute for Health and Care Excellence

Health Technology Evaluation

Mirikizumab for treating moderate to severe active ulcerative colitis [ID3973]

Response to stakeholder organisation comments on the final remit and final 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evaluation route	CCUK	The NICE guideline on Ulcerative Colitis and Quality Standard on Inflammatory Bowel Disease are outdated and do not reflect current best practices and the experience of people with Ulcerative Colitis.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 for your comment. Mirikizumab will be appraised independently of the NICE guideline on Ulcerative Colitis and the quality standard on Inflammatory Bowel Disease. No action required.
	Eli Lilly	Yes, this topic is appropriate to refer to NICE for appraisal.	Comment noted. No action required.
	Janssen	The proposed appraisal is appropriate.	Comment noted. No action required.

Section	Stakeholder	Comments [sic]	Action
Wording	Eli Lilly	Yes, the wording of the remit is appropriate.	Comment noted. No action required.
	Janssen	No comment.	Comment noted. No action required.
Timing issues	CCUK	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.	Comment noted. No action required.
	Eli Lilly	There remains a high unmet clinical need for new treatment options in this indication, with efficacy-related concerns representing the most commonly reported reason for treatment switching amongst a Europe-based cohort of patients with moderate-to-severe UC.1 In addition, patients who are contraindicated to TNF-alpha inhibitors face a greatly reduced armamentarium of treatment options. As mirikizumab provides effective and tolerable management of moderate-to-severe UC with a novel mechanism of action, Lilly considers that timely NICE guidance for its use in this indication would be valuable to patients and to the NHS.	Comment noted. No action required.
	Janssen	No comment.	Comment noted. No action required.

Comment 2: the final scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	CCUK	New research commissioned by Crohn's & Colitis UK estimates that over 500,000 or 1 in 123 people are living with Inflammatory Bowel Disease in the UK.[1] The aim of treatment is for people to live their best-possible lives, not just achieve remission. We would welcome further consideration about whether there may be circumstances in which a person with severe Ulcerative Colitis requiring intensive inpatient treatment may benefit from this treatment, in conjunction with other interventions. As currently written the background does not capture the significant unmet need for treatments within this patient cohort.	Thank you for your comments. The background section of the scope provides a brief overview of the disease. More detailed information will be provided at the submission stage. The remit of this appraisal is to evaluate mirikizumab within it's marketing authorisation. The background was updated to reflect that treatment is also to improve quality of life.
	Eli Lilly	As per its administration in the pivotal LUCENT clinical trials and anticipated posology, please amend the description of the administration route of mirikizumab as follows:	Thank you for your comment, the technology section of

[1] Crohn's & Colitis UK (2022). *Incidence and Prevalence of IBD in the United Kingdom.* epidemiology-summary-final.pdf (crohnsandcolitis.org.uk)

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		"Mirikizumab induction treatment is administered intravenously, with the maintenance treatment administered subcutaneously." In addition, we would recommend the current treatment options are updated to include the recently published NICE TA for filgotinib (TA792).2 Otherwise, Lilly considers the background information included to be appropriate.	the scope has been updated.
	Janssen	Under the background section, the list of current treatments for moderately to severely active ulcerative colitis should include filgotinib, which has now been appraised by NICE and the Technology Appraisal Guidance (TA792) was published on 1st July 2022[1]. [1] https://www.nice.org.uk/guidance/ta792	Thank you for your comment, the scope has been updated.
Population	Eli Lilly	The anticipated label for mirikizumab is as follows: *"Mirikizumab is indicated for the treatment of* [redacted]*".* In addition, it is anticipated that all patients with moderate-to-severe UC would receive conventional therapies such as oral corticosteroids or immunomodulators upfront in the treatment pathway, before mirikizumab is considered.	Thank you for your comment, the proposed marketing authorisation has been marked confidential and therefore will not be used in the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
		Therefore, Lilly suggests amending the wording of the proposed population to: *"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 previous systemic therapy."*	
	Janssen	No comment	Comment noted. No action required.
Subgroups	Eli Lilly	The proposed subgroups are defined appropriately	Comment noted. No action required.
	Janssen	No comment	Comment noted. No action required.
Comparators	CCUK	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 effects. Approximately 50% of patients experience short-term corticosteroid-related adverse events such as acne, oedema, sleep and mood disturbance, glucose intolerance and dyspepsia.	Thank you for your comment. Conventional therapies without biological treatments has been removed as a comparator from the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
	Eli Lilly	All comparators listed are appropriate for this appraisal. However, as per the anticipated label and as described in the "Population" section above, it is anticipated that mirikizumab will be positioned after conventional therapy, which is typically prescribed as a first-line treatment for moderate to severely active UC. Therefore, Lilly do not consider that conventional therapy without biological treatments will be a relevant comparator at the anticipated positioning.	Thank you for your comment. Conventional therapies without biological treatments has been removed from the scope.
	Janssen	We would like to bring attention to NICE that the Technology Appraisal Guidance of filgotinib for moderately to severely active ulcerative colitis was published on 1st July 2022 (TA792)[1,] [1] https://www.nice.org.uk/guidance/ta792	Thank you for your comment. The background of the scope has been amended.
Outcomes	CCUK	Improved medicine adherence and self-management.	Comment noted. Adherence is not considered a direct clinical outcome, however it should be considered as part of any economic analysis.
	Eli Lilly	Bowel urgency, defined as the sudden or immediate need for a bowel movement, is a common and burdensome symptom of UC, with over a quarter of UC patients reporting moderate to severe urgency and associated reductions in wellbeing.3 As such, urgency is an important clinical outcome measure to capture within this appraisal. In the pivotal Phase III clinical trials of mirikizumab in UC (LUCENT-1 and -2), urgency was assessed using the Urgency Numeric Rating Scale (NRS). Please amend the outcomes section to include "bowel urgency" as an outcome. All other outcomes listed are appropriate.	Comment noted. The scope has been updated to include bowel urgency as an outcome

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	Janssen	No comment.	Comment noted. No action required.
Equality	CCUK	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.	Thank you for this comment. This barrier to access has been noted in the equality impact assessment form.
	Eli Lilly	No equality issues have been identified.	Comment noted. No action required.
	Janssen	No comment.	Comment noted. No action required.
Other considerations	Eli Lilly	No additional comments	Comment noted. No action required.
	Janssen	No comment.	Comment noted. No action required.
Questions for consultation	Eli Lilly	**1. Where do you consider mirikizumab will fit into the existing care pathway for ulcerative colitis?** As per the proposed label, mirikizumab is anticipated to be a treatment option for "[redacted]"	Comments noted. Thank you for your responses to these questions. We look forward to receiving further information at the submission stage.

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		[redacted]." In addition, as noted in the "Population" section above, it is anticipated that patients with moderate-to-severe UC would receive conventional therapies first-line in the treatment pathway. As such, mirikizumab is anticipated to be positioned within the care pathway after conventional therapies for: Biologic-naïve patients who are contraindicated to, or otherwise unsuitable to receive, currently available systemic treatment options Biologic-experienced patients for whom the systemic therapy has failed to control disease adequately **2. Are all relevant comparators included in the scope?** As discussed above, all relevant comparators have been included in the draft scope. **3. Would mirikizumab be a candidate for managed access?** No, Lilly does not believe mirikizumab would be a suitable candidate for managed access. **4. Do you consider mirikizumab 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)? The introduction of a licensed therapy with a unique mechanism of action would be of significant benefit to patients with UC, particularly since cycling through treatments is a common feature of the treatment pathway. **5. Do you consider that the use of mirikizumab can result in any potential 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 committee to take account of these benefits.** No health-related benefits that are not captured within the QALY calculation have been identified. **6. Would it be appropriate to use the cost-comparison methodology for this topic? Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?** It is anticipated that mirikizumab will offer improved clinical outcomes and similar resource use compared with existing treatments. As such, a cost-comparison methodology would not be appropriate for this appraisal. Lilly believes a single technology appraisal is the most appropriate assessment route for mirikizumab in moderate to severely active UC. **7. Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?** The primary outcome in the LUCENT clinical trials, which additionally represents the key efficacy input for the cost-effectiveness model, was clinical	

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		remission of UC as per the modified Mayo score (MMS). The MMS a composite outcome that comprises patient-reported outcomes (stool frequency and rectal bleeding), endoscopic appearance of the mucosa, and the physician-reported outcome Patient's Global Assessment. As such, the MMS represents a comprehensive and clinically relevant instrument for the assessment of UC, and its use is in alignment with previous NICE Technology Appraisals in this disease area.[2, 4, 5] **8. Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?** Lilly is not aware of any substantial new evidence for comparator technologies that has not already been considered, or of any important ongoing trials are due to report in the next year	
	Janssen	No comment.	Comment noted. No action required.

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

None