National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Upadacitinib for previously treated moderately to severely active Crohn's disease [ID4027]

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Crohn's & Colitis UK	No comment	-
	UKCPA		Thank you for your comment. No changes to the scope needed
	AbbVie	Yes	Thank you for your comment. No changes to the scope needed
Wording	Crohn's & Colitis UK	Yes. Currently, there are limited treatment options available in treating moderate to severe Crohn's disease. 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 for your comment. No changes to the scope needed.
	UKCPA	The scope is appropriate, however upadacitinib does not have marketing authorisation in the UK for Crohn's disease	Thank you for your comment. No changes to the scope needed.

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	AbbVie	Yes	Thank you for your comment. No changes to the scope needed.
Timing Issues	Crohn's & Colitis UK	The timing of this appraisal is appropriate.	Thank you for your comment. No changes to the scope needed.
	UKCPA	Treatment options for Crohn's disease are limited. This would be the first oral biologic agent for the treatment of Crohn's disease. Therefore, this would be of significant urgency.	Thank you for your comment. No changes to the scope needed.
	AbbVie	The scope is appropriate, however upadacitinib does not have marketing authorisation in the UK for Crohn's disease	Thank you for your comment. The technology section notes that upadacitinib does not currently have a marketing authorisation in the UK for treating Crohn's disease.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Crohn's & Colitis UK	We would ask the Committee to revisit the description of the following sentences: "Less common symptoms include fever, nausea, vomiting, arthritis, inflammation and irritation of the eyes, mouth ulcers and areas of painful, red and swollen skin."	Thank you for your comment. The scope has been updated to reflect the comments made around the

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		- Remove less common - Refer to extra intestinal manifestations People with IBD are affected by more than just their bowel symptoms. Up to 50% will experience extraintestinal manifestations, involving different parts of their body, commonly joints, skin, bones, eyes, kidneys and liver. We would also strongly advocate for recognition within this section of the debilitating impact of the condition on the daily lives and quality of life of those affected, including its impact on mental health and wellbeing, education, employment and relationships. The symptoms of urgent diarrhoea, pain and fatigue, and associated stigma, can lead to people becoming depressed, anxious and isolated. Crohn's care has moved towards delivering personalised care and support, and not just remission, with a greater focus on the holistic needs of people with Crohn's disease. We would point out that the current guideline for Crohn's is not aligned with the IBD Standards or the most up-to-date British Society of Gastroenterology IBD guideline.	impact of the condition and to include suggested amendments.
	UKCPA	The 'number of patients living with Crohn's disease' reference source link does not work and the value on the Crohn's and Colitis website is significantly different to that quoted. The rest is accurate	Thank you for your comment. The non-functional link has been removed and the scope updated with the reference to the NICE guideline 129 which reports the relevant statistic.

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	AbbVie	No comments	-
Population	Crohn's & Colitis UK	No comments	Thank you for your comment. No changes to the scope needed.
	UKCPA	Does not specify if this will cover adults and children. Comparator NICE TA's have stated adult patients.	Thank you for your comment. The population has been left broad to include potentially both adults and children as the marketing authorisation has not yet been received.
	AbbVie	The population is defined appropriately	Thank you for your comment. No changes to the scope needed.
Subgroups	Crohn's & Colitis UK	No comments	Thank you for your comment. No changes to the scope needed.
	UKCPA	Children Those with fistulating/stricturing disease – would be useful to have more information on the use of upadacitinib in these patients Those who have failed multiple biologic agents Post-surgery prophylaxis for recurrence Those on immunosuppressant medicines for non-IBD indications	Thank you for your comment. Where relevant evidence allows, the committee will consider whether further subgroups as such shall be

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			considered during the appraisal. No changes to the scope needed.
	AbbVie	No comments	Thank you for your comment. No changes to the scope needed.
Comparators	Crohn's & Colitis UK	We would ask the Committee to remove steroids. Steroids are not recommended for maintenance of remission and are associated with a range of side effects.[1] [2]	Thank you for your comment. Conventional care (steroids) has been removed as a comparator.
	UKCPA	The listed comparators are appropriate	Thank you for your comment. No changes to the scope needed.
	AbbVie	A comparison with conventional care is not required in the conventional care failure population.	Thank you for your comment. Conventional therapy has been removed from the scope because it is anticipated that upadacitinib will be indicated after at least 1 previous therapy. Best supportive care has been added as a

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			comparator for people who may be taking upadacitinib after all other biologic treatment options.
Outcomes	Crohn's & Colitis UK	We would ask the Committee to consider additions of: • Avoidance of steroid therapy • Patient experience and outcomes. • Improved medicine adherence and self-management. • Hospitalisation, readmission and emergency admissions The ability to treat earlier with a personalised drug treatment regime judged to be more clinically effective has the potential to reduce the need for surgery.	Thank you for your comment. The list of outcomes is not intended to be exhaustive at this stage. Where relevant, the company is welcomed to provide the evidence on all outcomes that are important for people with the condition during the evaluation..
	UKCPA	Outcomes seem appropriate	Thank you for your comment. No changes to the scope needed.
	AbbVie	The outcomes listed are appropriate	Thank you for your comment. No changes to the scope needed.
Equality and Diversity	Crohn's & Colitis UK	The mode of administration is a benefit for those with disabilities and remote communities in terms of reducing the need for travel to hospital and could potentially improve adherence.	Thank you for your comment. Benefits with mode of administration will be considered by the NICE appraisal

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			committee during the appraisal process.
	UKCPA	Appropriate dose decrease for elderly patients Not suitable for Child Pugh C Under 12 years not reviewed Some commissioners do not fund beyond four biologics so needs to be option at any point to avoid postcode lottery Oral agent so of benefit for those who are needle phobic or needle exhausted Is there evidence to differentiate between responders and primary non-responders? i.e., if a patient is a non-responder to another JAK inhibitor will they also not respond to this? Enables at home treatment so travel to hospital outpatients not required, so cost effective for patients. Will require 'at home' blood tests and so links with Primary Care are paramount as patients will need to be furnished with appointments for example.	Thank you for your comment. Benefits with mode of administration and other aspects mentioned will be considered by the NICE appraisal committee during the appraisal process.
	AbbVie	No comments	Thank you for your comment. No changes to the scope needed.

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Other considerations	Crohn's & Colitis UK	No comments	Thank you for your comment. No changes to the scope needed
	UKCPA	Concomitant immunomodulator treatment (e.g. thiopurines)	Thank you for your comment. No changes to the scope needed
	AbbVie	Please update the technology section (paragraph 2) from: "*It has been studied in clinical trials compared with placebo in adults with moderate to severe Crohn's disease who have inadequately responded to/are intolerant to biologic therapy"* To read: "Upadacitinib ***has been studied in placebo-controlled clinical trials in adults with moderate-to-severe Crohn's disease who have inadequately responded to or are intolerant to conventional therapy and/or biologic therapy***"	Thank you for your comment. The scope has been updated to reflect the change requested.
Questions for consultation	AbbVie	**Q. Where do you consider upadacitinib will fit into the existing treatment pathway for previously treated moderately to severely active Crohn's disease? Would it be used as an alternative to:** • **Tumour necrosis factor-alpha inhibitors (infliximab and adalimumab); or** • **Vedolizumab and ustekinumab** **Or would upadacitinib be used after these treatments already available in the NHS?**	Thank you for your comment. No changes to the scope needed beyond those already actioned in responses to the above comments.

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		A. We would currently anticipate to consider both TNFalpha inhibitors as well as vedolizumab and ustekinumab relevant comparators – as per draft scope. **Q. Have all relevant comparators for upadacitinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for moderately to severe Crohn's disease?** A. Addressed above, conventional therapy would not be considered a comparator to upadacitinib considering its place in the treatment pathway **Q. Are the outcomes listed appropriate?** A. Yes **Q. Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom upadacitinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?** A. Addressed above, currently we consider these subgroups appropriate**.** **Q. Would upadacitinib be a candidate for managed access?** A. It would not likely be a candidate. **Q. Do you consider upadacitinib 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 upadacitinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?**	

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		Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. A. Upadacitinib will the first oral advanced treatment (alongside biologics) to be available for the treatment of CD. This could have a positive impact on patients' QoL as they will no longer be depending on IV infusions in hospitals or SC injections. **Q. 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 upadacitinib 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.** A. Not likely a concern for upadacitinib in CD **To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.**	

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		A. No barriers to adoption of upadacitinib as it is an oral treatment. **Q. NICE intends to evaluate this technology through its Single Technology Evaluation Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).** **NICE's unified manual states the methods to be used where a cost comparison case is made.** • **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?** • **Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?**	

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		• **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?** A. Currently we anticipate that the STA route is the most appropriate for upadacitinib in CD.	

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

Bladder and Bowel Community (not taking part)