National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Ustekinumab for treating moderately to severely active ulcerative colitis [ID1511]

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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	MSD	Yes	Thank you for your comment.
	Napp Pharmaceuticals Limited	Yes	Thank you for your comment.
	Janssen	Yes, this topic is appropriate to refer to NICE for appraisal.	Thank you for your comment.
Wording	Napp Pharmaceuticals Limited	Yes	Thank you for your comment.
	Janssen	Yes, the wording of the remit is appropriate.	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
Timing Issues	Napp Pharmaceuticals Limited	There are a number of medicines available for first, second and third line treatments in UC. This product brings an additional approach and may offer patients an alternative at the most appropriate point in the treatment pathway following the publication of NICE guidance in line with the product licensing timelines.	Thank you for your comment.
	Janssen	The timing of this appraisal is appropriate.	Thank you for your comment.
Additional comments on the draft remit	Janssen	No additional comments.	Noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD	It is accurate	Thank you for your comment.
	Pfizer Ltd	NICE has now completed the appraisal on tofacitinib in ulcerative colitis and the guidance has been published as TA547. Please delete NICE is also currently appraising tofacitinib for treating moderately to severely active ulcerative colitis (NICE technology appraisal guidance ID1218) And replace with: NICE technology appraisal 547 recommends tofacitinib for moderately to severely active ulcerative colitis.	Thank you for your comment. This section has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
	Janssen	Appropriate.	Thank you for your comment.
The technology/ intervention	Napp Pharmaceuticals Limited	Yes	Thank you for your comment.
	Janssen	1. The wording does not reflect the current indications for ustekinumab and only includes Crohn's disease. Please include the following sentence to accurately reflect the current indications for ustekinumab: "Additionally, ustekinumab has marketing authorisations for the treatment of Plaque Psoriasis, Paediatric Plaque Psoriasis and Psoriatic Arthritis." 2. The wording does not appropriately reflect the administration of ustekinumab. It is given via IV injection for induction and SC infusion in maintenance. Please replace the existing sentence, "It is available for administration by intravenous infusion or subcutaneously", with the following sentence to provide certainty on the administration: "It is available for administration by intravenous infusion for induction and subcutaneous injection for maintenance."	Thank you for your comment. Although we recognise that ustekinumab is licensed in other disease areas, scopes do not include details of marketing authorisations in unrelated disease areas.
Population	MSD	Yes it is	Thank you for your comment.
	Napp Pharmaceuticals Limited	No	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
	Janssen	The population is not defined appropriately and does not accurately reflect the expected marketing authorisation and the likely place in therapy. Additionally, the population described is not consistent with previous appraisals TA342 (vedolizumab) and TA547 (tofacitinib). Please include the additional wording 'or loss of response' and 'or a JAK inhibitor (tofacitinib)' in the following sentence: "People 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 biologic therapy (a TNF-alpha inhibitor or vedolizumab) or a JAK inhibitor (tofacitinib), or conventional therapy (oral corticosteroids and/or immunomodulators)."	Thank you for your comment. The population in the scope has been aligned to the trial and has been updated.
Comparators	Napp Pharmaceuticals Limited	All treatments described have a place to play depending on severity of disease.	Thank you for your comment.
	Pfizer Ltd	NICE has now completed the appraisal on tofacitinib in ulcerative colitis and the guidance has been published as TA547. Please delete: • *Tofacitinib (subject to ongoing NICE appraisal)* And replace with • *Tofacitinib*	Thank you for your comment. This section has been updated.
	Janssen	Tofacitinib is no longer subject to ongoing NICE appraisal. Please remove the wording 'subject to ongoing NICE appraisal'.	Thank you for your comment. This section has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
Outcomes	Napp Pharmaceuticals Limited	Yes	Thank you for your comment.
	AbbVie	Steroid- free remission should be included as an outcome Induction period and maintenance data should be represented separately	Thank you for your comment. Corticosteroid- free remission has been included as an outcome. In order to maintain flexibility, the scope does not set out how data should be presented.
	Janssen	In ulcerative colitis (UC), endoscopic healing and mucosal healing are used interchangeably. In the ustekinumab UNIFI study protocol, mucosal healing is defined as a combination of endoscopic healing with histological healing, which refers to a deeper healing outcome. For the avoidance of doubt, please remove the wording 'achieving mucosal healing' and replace with the following outcomes: • Endoscopic healing • Combined endoscopic healing and histological healing	Thank you for your comment. The outcomes have been updated.
Economic analysis	Napp Pharmaceuticals Limited	We are pleased to see that NICE has recommended that biosimilars should be included alongside the originator medicines. We would like to remind NICE that biosimilars are subject to price tendering and therefore a highly competitive number of discounts are available. The price of biosimilar	Thank you for your comment. If the appraisal proceeds, the availability of any

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		infliximab (Remsima®) has fallen considerably since the date (Feb 2015) of the last MTA for UC (TA329) making biosimilar infliximab even more cost effective. We suggest that the ERG should apply discounted prices for infliximab that are within the range of 75-90% of the NHS list price for the originator infliximab Remicade® at £419.62 for 100mg (ex. VAT)	commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
	Janssen	Appropriate.	Thank you for your comment.
Equality and Diversity	Napp Pharmaceuticals Limited	None	Thank you for your comment.
	Janssen	No comment.	Noted.
Other considerations	Janssen	The likely place in therapy is in two populations, that is, • patients that have not previously received biologics therapy (a TNF-alpha inhibitor or vedolizumab) or a JAK inhibitor (tofacitinib) • patients who have previously received one or more biologics therapy (a TNF-alpha inhibitor or vedolizumab) or a JAK inhibitor (tofacitinib)	Thank you for your comment. The scope specifies that if the evidence allows, the following subgroups will be considered: 'people who have been previously treated with one or more biologics; people who have not received prior biologics therapy.'

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Innovation	Napp Pharmaceuticals Limited	*[Do you consider the technology 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)?]* Yes *[Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?]* No	Thank you for your comment. If the topic proceeds, the appraisal committee will consider any innovative aspects of ustekinumab.
	Janssen	Ustekinumab offers a new mechanism of action in the treatment of UC. Among the different cytokines implicated in the pathogenesis of UC, IL-12 and IL-23 are known to be responsible for T cell activation processes and considered a key therapeutic target. Ustekinumab is expected to be the first IL12/IL-23 inhibitor licensed for the treatment of UC. Ustekinumab has been studied in the broadest UC trial population to date: the UNIFI study includes patients who have failed conventional therapies, and patients who have failed TNF-alpha inhibitors and/or vedolizumab. Ustekinumab represents an innovation in the management of UC as it offers a rapid onset of high remission and response rates in induction and importantly this efficacy is maintained over the long term. In addition, ustekinumab is the only treatment to demonstrate combined endoscopic and histological healing. Ustekinumab has a convenient dosing schedule with IV induction and SC dosing in maintenance (every 12 weeks), thereby reducing the treatment burden for patients. UC is associated with a significant burden and various indirect costs related to loss of productivity. These measures are not currently captured in the QALY calculation and therefore the full benefit of ustekinumab in inducing and maintaining remission and response cannot be fully captured.	Thank you for your comment. If the topic proceeds, the appraisal committee will consider any innovative aspects of ustekinumab or whether there are any benefits that are not adequately captured by the QALY estimate. The Guide to the methods of technology appraisal states that productivity costs are not included in either the reference-case or non-reference-case analyses.

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Questions for consultation	Janssen	Where do you consider ustekinumab will fit into the existing NICE pathway, Ulcerative colitis? Ustekinumab is anticipated to be an option in the treatment pathway for: • patients that have not previously received biologics therapy (a TNF-alpha inhibitor or vedolizumab) or a JAK inhibitor (tofacitinib) • patients who have previously received one or more biologics therapy (a TNF-alpha inhibitor or vedolizumab) or a JAK inhibitor (tofacitinib)	Thank you for your comment. The scope specifies that if the evidence allows, the following subgroups will be considered: 'people who have been previously treated with one or more biologics; people who have not received prior biologics therapy.'
Additional comments on the draft scope	Napp Pharmaceuticals Limited	None	Noted.
	Pfizer Ltd	NICE has now completed the appraisal on tofacitinib in ulcerative colitis and the guidance has been published as TA547. Please update the reference to the tofacitinib NICE appraisal in the "Related NICE recommendations and NICE pathway" section of the draft scope. Therefore, please delete; *Appraisals in development* *Tofacitinib for moderately to severely active ulcerative colitis. NICE technology appraisals guidance [ID1218]. Publication expected: January 2019* And add following reference link to the Related Technology Appraisal list;	Thank you for your comment. This section has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
		Tofacitinib for moderately to severely active ulcerative colitis (2018). Technology appraisal guidance TA547. Review date November 2021	
	Janssen	No additional comments.	Noted.

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

Amgen Ltd.