National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Tofacitinib for treating active psoriatic arthritis following disease-modifying anti-rheumatic drugs

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	British Society for Rheumatology	Yes entirely appropriate.	Thank you for your comment. No changes to the scope are needed.
	Novartis Pharmaceuticals UK Ltd.	We consider the proposed appraisal appropriate.	Thank you for your comment. No changes to the scope are needed.
	Pfizer Ltd	It is appropriate for this topic to be referred to NICE.	Thank you for your comment. No changes to the scope are needed.

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	Psoriasis Association	Yes – this treatment offers a new approach in treating psoriatic arthritis	Thank you for your comment. No changes to the scope are needed.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	'It is important that appropriate topics are referred to NICE to ensure that NICE guidance is relevant, timely and addresses priority issues, which will help improve the health of the population. Would it be appropriate to refer this topic to NICE for appraisal?' - Yes	Thank you for your comment. No changes to the scope are needed.
Wording	British Society for Rheumatology	The wording underestimates the significant impact that Psoriatic Arthritis can have on an individual's life. PsA is associated with significant co-morbidities (hypertension, uveitis, inflammatory bowel disease, metabolic syndrome), fatigue and depression, loss of work, pain and impacts greatly on an individual's quality of life	Thank you for your comment. The remit should include a one sentence description of the draft remit or appraisal objective.
	MSD	'Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.' - Yes	Thank you for your comment.
	Novartis Pharmaceuticals UK Ltd.	Previous appraisals in psoriatic arthritis have not specified patients with intolerance or contraindication to DMARDs within their remit or final recommendations (e.g. TA199, TA220, TA340, TA445).[1-4] We suggest that this wording be omitted for consistency with the remit of previous appraisals.	Thank you for your comment. The remit of the scope has been amended to 'within its marketing authorisation for treating active psoriatic arthritis'.

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	Pfizer Ltd	The wording is appropriate.	Thank you for your comment.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	'Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.' - Yes	Thank you for your comment.
Timing Issues	British Society for Rheumatology	It is not urgent but does offer another agent for the treatment of PsA in a limited field of effective non-biological DMARDs.	Thank you for your comment. No changes to the scope are needed.
	Novartis Pharmaceuticals UK Ltd.	No comment.	Comment noted.
	Pfizer Ltd	It is important that clinicians in England and Wales are provided with timely NICE Guidance on the use of Tofacitinib in Psoriatic Arthritis (PsA) as this is a condition with a high unmet need.	Thank you for your comment. NICE aims to provide draft guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted. No changes to the scope are needed.
	Psoriasis	Not urgent	Thank you for your comment. No changes

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	Association		to the scope are needed.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Not particularly urgent. Other agents are available. Although, for those where all current treatments have failed, further options are urgently needed to avoid potential joint damage.	Thank you for your comment. NICE aims to provide draft guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted. No changes to the scope are needed.
Additional comments on the draft remit	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	No	Comment noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	British Society for Rheumatology	As above the impact of PsA and its associated comorbidities has been under-stated and does not reflect the significant impact on an individual's life. It would be important to note that psoriasis can also have a significant impact on an individual's quality of life with significant psychosocial implications eg depression and social isolation as well as associated co-morbidities.	Thank you for your comments. The background section is intended to provide a brief overview of the disease and its

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		The spondyloarthritis subgroup which can occur with or without peripheral joint or entheseal involvement has not been mentioned. This occurs in up to 30% of people with PsA. Peripheral arthritis can be a polyarthritis (>5 joints) or an oligoarthritis (4 or less joints). Some patients with oligoarthritis may have involvement of high impact joints e.g. knees and ankles but do not qualify for biological DMARDs as they do not have >3 tender and >3 swollen joints. Having a medication as a step up from non-biological DMARDs for this group would be particularly beneficial.	associated management. No changes to the scope are needed.
	Novartis Pharmaceuticals UK Ltd.	We request that the description of the secukinumab recommendation be more closely aligned to the wording of TA445 i.e. “secukinumab alone, or in combination with methotrexate, is also recommended when patients have had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks or TNF-alpha inhibitors are contraindicated.”[4]	Thank you for your comments. The scope has been amended for clarity.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Overall yes, but prevalence data appear a little low and based on 2013 publication, perhaps needs a further check?	Thank you for your comments. The background information in the scope refers to the most up-to-date prevalence data identified. No changes to the scope are needed.
	Pfizer Ltd	No comments.	Comment noted.
The technology/	British Society for	‘Is the description of the technology or technologies accurate?’ - Yes	Thank you for your comment. No changes

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intervention	Rheumatology		to the scope are needed.
	MSD	'Is the description of the technology or technologies accurate?' - Yes	Thank you for your comment. No changes to the scope are needed.
	Pfizer Ltd	Please can the technology be described as follows: Tofacitinib (Xeljanz, Pfizer) is a Janus kinase (JAK) inhibitor and is a targeted synthetic small molecule that is taken orally. Please change the text included in the intervention to "Tofacitinib in combination with non-biological DMARD" (i.e. remove the words "alone or")	Thank you for your comments. The intervention description has been amended for clarity. The text in the table has not been changed. NICE will only appraise drugs within their marketing authorisation. If treatment with tofacitinib is restricted to only in combination with non-biological DMARDs by the marketing authorisation, the submission will be restricted to this treatment. Currently the marketing authorisation is not available so both options will remain in

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			the scope.
	Novartis Pharmaceuticals UK Ltd.	No comment.	Comment noted.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	No comments.	Comment noted.
Population	AbbVie	Since tofacitinib will be licensed for psoriatic arthritis but not for moderate to severe plaque psoriasis, the wording for the population should read: • Adults with active psoriatic arthritis whose disease has not responded adequately to previous DMARD therapy or for whom DMARDs are not tolerated or contraindicated and for whom a biological DMARD is not needed to treat moderate to severe plaque psoriasis Note in this regard that the following comparators listed in the draft scope in contrast are licensed both for psoriatic arthritis and moderate to severe plaque psoriasis: • Biological DMARDs (etanercept, adalimumab, infliximab, secukinumab and ustekinumab) • Apremilast Also in this regard the following two comparators listed in the draft scope are similarly licensed only for psoriatic arthritis and are not licensed for moderate to severe plaque psoriasis:	Thank you for your comments. The scope states that the relevant population is adults with active psoriatic arthritis which reflects the remit. It is not necessary to list all variations of psoriasis that are not included. No changes to the scope are needed.

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		• Certolizumab • Golimumab	
	British Society for Rheumatology	See above. The subgroups / clinical phenotypes of disease need to be accounted for in terms of appropriate outcome measures for the different facets of disease. There will be some individuals who have varying severities of psoriasis and some who have no psoriasis at all. The relative efficacies of tofacitinib on the different aspects of the psoriatic disease spectrum can therefore inform a clinician on choice of medication for that individual. No mention is made of Nail psoriasis which can be psychologically very intrusive.	Thank you for your comments. The population section is intended to provide an overview of the population. The presence and severity of concomitant psoriasis is included in 'other considerations. Scoping workshop attendees from recent PSA topics agreed that nail involvement was related to psoriasis rather than psoriatic arthritis so it was suggested this to be removed from the scope.
	MSD	'Is the population defined appropriately? Are there groups within this population that should be considered separately?' - Yes	Thank you for your comment. No changes to the scope are needed.
	Novartis	Previous appraisals in psoriatic arthritis have not specified patients with	Thank you for your

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	Pharmaceuticals UK Ltd.	intolerance or contraindication to DMARDs within their remit or final recommendations (e.g. TA199, TA220, TA340, TA445).[1-4] We suggest that this wording be omitted for consistency with the population included in previous appraisals.	comment. The remit of the scope has been amended to 'within its marketing authorisation for treating active psoriatic arthritis'.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Therefore, this is likely to be third line after DMARDs, which would put it in the same position as biologics, which sounds reasonable. Exploration of sequencing and whether used first or as second agent would be useful too.	Thank you for your comment. No changes to the scope are needed.
	Pfizer Ltd	No comments.	Comment noted
Comparators	AbbVie	Since both ustekinumab and secukinumab are biological DMARDs they should not be listed as comparators "for people in whom biological DMARDs are contraindicated or not tolerated" as is the case in the draft scope	Thank you for your comment. The comparator section has been amended.
	British Society for Rheumatology	It is unclear why best supportive care is not a comparator for all groups including 1 or 2 non-biological DMARDs. It should be mentioned that DMARDs are used not only to limit damage to joints but also for symptom control – some have proven efficacy for several aspects of the disease eg skin and joints, enthuses and spinal symptoms whereas others have efficacy only for the joints eg Sulphasalazime. It should be noted that the clinical trial data for the non-biological DMARDs is	Thank you for your comment. At this stage in the treatment pathway there are many treatments options available. In the absence of tofacitinib, patients would be likely to receive another active treatment rather than no treatment.

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		poor (especially Sulphasalazine and methotrexate) although leflunomide data is stronger. There is no evidence for any enhanced efficacy of biological DMARDs with concurrent methotrexate but it is associated with longer drug 'survival'. Ustekinumab is used if an individual has failed one TNFi (the text says only if they have been treated with one TNFi)	Furthermore, ustekinumab is recommended as an option, alone or in combination with methotrexate, for treating active psoriatic arthritis in adults only when: • treatment with tumour necrosis factor (TNF) alpha inhibitors is contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis and golimumab for the treatment

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			of psoriatic arthritis) or • the person has had treatment with 1 or more TNF–alpha inhibitors.
	MSD	'Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be described as 'best alternative care'?' - Yes	Thank you for your comment. No changes to the scope are needed.
	Novartis Pharmaceuticals UK Ltd.	We propose some wording amendments in relation to the third population, "people whose disease has not responded adequately to non-biological and biological DMARDs". Since access to biological DMARDs is restricted to patients with inadequate response to prior non-biological DMARDs, we consider that "non-biological" does not need to be specified for this population. In addition, TA340 and TA445 specify inadequate response specifically to prior TNF-alpha inhibitors, rather than "biological DMARDs".[3,4] We therefore propose the following amended wording: "people whose disease has not responded adequately to TNF-alpha inhibitors". In addition, we suggest that clarification be added that certolizumab pegol is only a comparator amongst the subpopulation with inadequate response to prior TNF-alpha inhibitors after 12 weeks of treatment.[4]	Thank you for your comment. The scope has been amended for clarity.
	Psoriasis and Psoriatic	Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be	Thank you for your comment. No changes

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	Arthritis Alliance (PAPAA)	described as 'best alternative care'? - Yes	to the scope are needed.
	Pfizer Ltd	No comments.	Comment noted.
Outcomes	British Society for Rheumatology	It is not stipulated what measure of disease activity will be utilised eg PsARC, MDA (minimal disease activity). There is no measure of spinal outcomes eg BASDAI or back pain score. It would also be helpful to measure work productivity and fatigue – 2 outcomes very important to patients.	Thank you for your comment. During the scoping stage of previous PSA topics, scoping workshop attendees agreed that pain and fatigue were important outcomes and agreed that they were covered by the existing, broader outcomes. No action required. Work productivity has been already captured under 'functional capacity'. The list of outcome measures is not exhaustive and the company can provide information on additional outcomes.

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	MSD	'Will these outcome measures capture the most important health related benefits (and harms) of the technology?' - Yes	Thank you for your comment. No changes to the scope are needed.
	Psoriasis Association	The health-related quality of life measures should include measures of fatigue and pain. These are areas of great concern for people with psoriatic arthritis	Thank you for your comment. During the scoping stage of previous PSA topics, scoping workshop attendees agreed that pain and fatigue were important outcomes and agreed that they were covered by the existing, broader outcomes. The list of outcome measures is not exhaustive and the company can provide information on additional outcomes. No changes to the scope are needed.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Impact on psoriasis and nail involvement would be helpful, given other agents improve these elements too.	Thank you for your comment. Scoping workshop attendees from recent PSA topics

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			agreed that nail involvement was related to psoriasis rather than psoriatic arthritis so it was suggested this outcome be removed. The presence and severity of concomitant psoriasis is included in 'other considerations. No action required.
	Novartis Pharmaceuticals UK Ltd.	No comment.	Comment noted.
	Pfizer Ltd	No comments.	Comment noted.
Economic analysis	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Chronic disease with onset often in early 20s. So sufficient length to include loss of efficacy over time, and the need for other interventions. Hence a need for sequencing guidance.	Thank you for your comment. No changes to the scope are needed.
	British Society for Rheumatology	No comments.	Comment noted.

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	Novartis Pharmaceuticals UK Ltd.	No comment.	Comment noted.
	Pfizer Ltd	No comments.	Comment noted.
Equality and Diversity	British Society for Rheumatology	No equality issues are apparent	Thank you for your comment. No changes to the scope are needed.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	None that would be seen under the laws.	Thank you for your comment. No changes to the scope are needed.
	Novartis Pharmaceuticals UK Ltd.	No comment.	Comment noted.
	Pfizer Ltd	No comments.	Comment noted.
Other considerations	Novartis Pharmaceuticals UK Ltd.	We suggest a wording amendment to the first bullet point, as follows; “the reason for previous treatment failure…” “Moderate psoriasis” occurs in two of the potential subgroups defined by presence or severity of concomitant psoriasis. We consider that the following description would be clearer: “no psoriasis, mild psoriasis, moderate to severe psoriasis”.	Thank you for your comment. The scope has been amended for clarity.

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	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Oral administration so affect of dosing regime (twice daily?) versus injection (less frequent), whether this is likely to influence adherence or wastage, might be useful to consider.	Thank you for your comment. No changes to the scope are needed.
	British Society for Rheumatology	No comments.	Comment noted.
	Pfizer Ltd	No comments.	Comment noted.
Innovation	British Society for Rheumatology	This is a step change again in the field of PsA. This is an oral agent and will add to the increasing repertoire of agents now with proven efficacy for PsA. Where it will be placed depends on the relative efficacy, safety profile and cost.	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it, if the topic is referred for appraisal.
	Pfizer Ltd	Tofacitinib is innovative and is a step-change in the management of PsA. Tofacitinib is an oral therapy that has a different mode of action to currently available treatments, and provides an additional treatment option for patients. The benefits of an oral therapy cannot be captured fully in the QALY calculation. The benefits include ease of disease management for the patient, and also providing a solution to those patients who have difficulties with intravenous and subcutaneous administration.	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it, if the

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			topic is referred for appraisal.
	Psoriasis Association	It is innovative in that it is the first JAK inhibitor for psoriatic arthritis. We don't believe it offers a step-change in the management of the condition. However it provides greater flexibility for patients than some of the biological DMARDs in terms of being able to travel (does not require refrigeration nor courier delivery).	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it, if the topic is referred for appraisal.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Different target, oral, so potentially innovative. Although apremilast is available now, so maybe less innovative on delivery method third-line.	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it, if the topic is referred for appraisal.
	Novartis Pharmaceuticals UK Ltd.	No comment.	Comment noted.
Questions for	British Society	It is definitely recommended that this is considered for a TA as it offers	Thank you for your

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consultation	for Rheumatology	another mode of treatment in a disabling and devastating condition	comment. No changes to the scope are needed.
	Novartis Pharmaceuticals UK Ltd.	*Where do you consider tofacitinib will fit into the existing musculoskeletal conditions NICE pathway, after how many previous lines of DMARDs?* *Novartis: We would expect tofacitinib to be positioned alongside other treatments recommended by NICE for psoriatic arthritis i.e. for patients whose disease has not responded to adequate trials of at least 2 standard DMARDs.* *Have all relevant comparators for tofacitinib been included in the scope?* *Novartis: See comments above on "Comparators"* *Are the outcomes listed appropriate?* *Novartis: No comment.* *Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom tofacitinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?* *Novartis: See comments above under "Other considerations".* *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*	Thank you for your comment. No changes to the scope are needed.

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		proposed remit and scope may need changing in order to meet these aims. *Novartis: No comment.* *Do you consider tofacitinib 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)?* *Novartis: No comment.* *Do you consider that the use of tofacitinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* *Novartis: No comment.* *Do you consider that there will be any barriers to adoption of this technology into practice?* *Novartis: No comment.* *NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process.* *Novartis: We consider that the STA process is the appropriate route for this appraisal.* *Would it be appropriate to use the cost comparison methodology for this topic?*	

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		Novartis: Given the range of populations within the remit of the appraisal we consider the STA process will be more appropriate than a cost comparison. *Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?* *Novartis: No comment.* *Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?* *Novartis: No comment.* *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?* *Novartis: No comment.*	
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	Sequencing in pathway would be important and the effectiveness following other agents.	Thank you for your comment. No changes to the scope are needed.
	Pfizer Ltd	No comments.	Comment noted.
Additional comments on the draft scope	Novartis Pharmaceuticals UK Ltd.	The date of the last update to 'Psoriasis: assessment and management' (2012). NICE clinical guideline 153 should be corrected from April 2017 to September 2017.	Thank you for your comment. The scope has been amended for clarity.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Society for Rheumatology	None	Comment noted.
	Psoriasis and Psoriatic Arthritis Alliance (PAPAA)	No.	Comment noted.

References

1. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA199). Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (2010). Available at https://www.nice.org.uk/guidance/ta199. Last accessed 13th October 2017.
2. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA220). Golimumab for the treatment of psoriatic arthritis (2011). Available at https://www.nice.org.uk/guidance/ta220. Last accessed 13th October 2017.
3. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA340). Ustekinumab for treating active psoriatic arthritis (2015). Available at https://www.nice.org.uk/guidance/ta340. Last accessed 13th October 2017.

National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA445). Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs (2017). Available at https://www.nice.org.uk/guidance/ta445. Last accessed 13th October 2017.

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

Celgene
Jane Newton
British Association of Dermatologists