NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

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

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tofacitinib within its marketing authorisation for treating active psoriatic arthritis in adults whose disease has not responded adequately to previous disease-modifying anti-rheumatic drug (DMARD) therapy, or for whom DMARDs are not tolerated or contraindicated.

Background

Psoriatic arthritis (also called psoriatic arthropathy) is an inflammatory arthritis closely associated with psoriasis. It is estimated that around 1 in 5 people with psoriasis develop psoriatic arthritis[1], although this figure may be higher in people who have severe psoriasis[1]. In around 70% of people psoriasis precedes psoriatic arthritis[1]. The prevalence of psoriatic arthritis in England in 2016 was estimated to be around 105,010 adults[2,3]. Men and women are equally likely to develop psoriatic arthritis with the peak onset being between the ages of 30 and 50 years[1].

Although psoriatic arthritis is a chronic condition that progresses in the joints, its course may be erratic, with flare-ups and remissions. Arthritis symptoms can range from inflammation of the synovial membrane surrounding a joint (synovitis), ligaments and tendons (enthesitis and tendonitis), and inflammation of digits (dactylitis) to severe progressive erosion of the joints. Skin symptoms include the presence of patchy, raised, red areas of skin inflammation with scaling, which can affect any part of the body but is most commonly found on the extensor surfaces of the elbows and knees, the scalp and ears, the navel, and around the genital areas or anus.

The aim of treatment is to suppress joint, tendon and ligament inflammation, and to manage the skin symptoms of the disease. Current practice involves early diagnosis and early use of non-biological disease modifying anti-rheumatic drugs (DMARDs), including methotrexate, sulfasalazine and leflunomide, in order to minimise damage to joints. Non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy and intra-articular corticosteroid injections may also be used.

Biological tumour necrosis factor (TNF)-alpha inhibitors may be used for treating people with active psoriatic arthritis. NICE technology appraisal guidance 199 and 220 recommend etanercept, infliximab, adalimumab or

golimumab when a person has peripheral arthritis with 3 or more tender joints and 3 or more swollen joints, and the psoriatic arthritis has not responded to at least 2 non-biological DMARDs, given on their own or together. Ustekinumab is recommended in NICE technology appraisal guidance 340 when treatment with TNF-alpha inhibitors are contraindicated but would otherwise be considered or the person has had treatment with 1 or more TNF-alpha inhibitors. Apremilast, certolizumab pegol and secukinumab are recommended in NICE technology appraisal guidance 433 and 445, respectively; for people whose disease has not responded to at least 2 non-biological DMARDs. Certolizumab pegol is also recommended when a tumour necrosis TNF-alpha inhibitor stopped responding after the first 12 weeks and secukinumab is also recommended when TNF-alpha inhibitor has not responded within the first 12 weeks or has stopped responding after 12 weeks or contraindicated. Biosimilar products for some of the biological therapies are available for use in the NHS.

The technology

Tofacitinib (Xeljanz, Pfizer) is a novel oral janus kinase (JAK) inhibitor that inhibits JAK1, 2 and 3 in vitro, with functional specificity for JAK1 and 3. It is administered orally.

Tofacitinib does not currently have a marketing authorisation in the UK for treating psoriatic arthritis. It has been studied in clinical trials compared with placebo and adalimumab in adults with active psoriatic arthritis whose disease has not responded adequately to previous non-biological DMARDs or whose disease has not responded adequately or could not tolerate TNF-alfa inhibitor therapies.

Intervention(s)	Tofacitinib (alone or in combination with non-biological DMARD)
Population(s)	Adults with active psoriatic arthritis whose disease has not responded adequately to previous DMARD therapy or for whom DMARDs are not tolerated or contraindicated

Comparators	For people whose disease has not responded adequately to 1 non-biological DMARD • Non-biological DMARDs For people whose disease has not responded adequately to at least 2 non-biological DMARDs: • Biological DMARDs (with or without methotrexate, including etanercept, adalimumab, infliximab, golimumab, certolizumab pegol, secukinumab) • Apremilast For people whose disease has not responded adequately to non-biological and biological DMARDs: • Ustekinumab • Certolizumab pegol • Secukinumab • Best supportive care For people in whom biological DMARDs are contraindicated or not tolerated: • Ustekinumab • Secukinumab • Best supportive care
Outcomes	The outcome measures to be considered include: • disease activity • functional capacity • disease progression • periarticular disease (for example enthesitis, tendonitis, dactylitis) • mortality • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account. For the comparators the availability and cost of biosimilars should be taken into consideration.
Other considerations	If evidence allows the following subgroups will be considered: • the reason for treatment failure (for example due to lack of efficacy, intolerance or adverse events). • presence or severity of concomitant psoriasis (no psoriasis, mild to moderate psoriasis, moderate to severe psoriasis) Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (review of technology appraisal guidance 104 and 125)' (2010). NICE Technology Appraisal 199 (moved to the static list). 'Golimumab for the treatment of psoriatic arthritis' (2011). NICE Technology Appraisal 220 (moved to the static list). 'Ustekinumab for treating active psoriatic arthritis' (2015). NICE Technology Appraisal 340 (moved to the static list). 'Certolizumab pegol and secukinumab for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs' (2017) NICE

	Technology Appraisals 445. Review date: May 2020 `Apremilast for treating active psoriatic arthritis` (2017) NICE Technology Appraisal 433 Review date: February 2020 **Related Guidelines:** 'Psoriasis: assessment and management' (2012). NICE clinical guideline 153. Last updated: April 2017. `Spondyloarthritis in over 16s: diagnosis and management` (NG65) Published in February 2017 **Related Quality Standards:** 'Psoriasis' (2013). Quality Standard 40. Last updated: April 2017. **Related NICE Pathways:** NICE Pathway: musculoskeletal conditions, Pathway last updated March 2017.
Related National Policy	NHS England (2016) 'Manual for Prescribed Specialised Services'. Chapter 5, Adult highly specialist rheumatology services Department of Health, NHS Outcomes Framework 2016-2017, April 2016. Domains 2 to 5. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf

Questions for consultation

Where do you consider tofacitinib will fit into the existing musculoskeletal conditions NICE pathway, after how many previous lines of DMARDs?

Have all relevant comparators for tofacitinib been included in the scope?

Are the outcomes listed appropriate?

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?

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 tofacitinib 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.

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)?

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?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which 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?

- 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?

References

[1]Psoriasis Association (2014) 'Psoriasis Arthritis' Accessed March 2017

[2] Ogdie, A., Langan, S., Love, T., Haynes, K., Shin, S., Seminara, N., Mehta, N., Troxel, A., Choi, H., Gelfand, J. (2013) 'Prevalence and treatment patterns of psoriatic arthritis in the UK'. Rheumatology (Oxford) Mar 52(3): 568-75

[3] Office for National Statistics (2017) Population estimates mid-year 2016