# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## Tofacitinib for treating active ankylosing spondylitis

## Draft scope

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tofacitinib within its marketing authorisation for treating active ankylosing spondylitis.

### Background

Axial spondyloarthritis belongs to a clinically heterogeneous group of inflammatory rheumatologic diseases which share common genetic, histological and clinical features (also including psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated spondyloarthritis). Axial spondyloarthritis involves inflammation of the sacroiliac joints and spine. If inflammation is visible on x-ray (as erosions, thickening of the bone, or fusion of joints), the disease is classified as radiographic axial spondyloarthritis (also known as ankylosing spondylitis). If x-rays of the sacroiliac joints and spine are normal, but there are other objective signs of inflammation (elevated C-reactive protein or evidence on magnetic resonance imaging) the disease is classified as non-radiographic axial spondyloarthritis.

The clinical symptoms of axial spondyloarthritis can vary from person to person, but usually develop slowly over several months or years. The main symptoms can include back pain, usually inflammatory in nature, arthritis (inflammation of the joints in other parts of the body), enthesitis (inflammation where a bone is joined to a tendon), and fatigue. Extra-articular manifestations include uveitis, inflammatory bowel disease and psoriasis. The onset of symptoms typically occurs in the third decade of life, but it can be 7–10 years before a diagnosis is made. Many patients with mild disease may remain undiagnosed.

Around 200,000 people have been diagnosed as having ankylosing spondylitis in the UK. The prevalence is thought to range from 0.05% to 0.23%, representing approximately 2,300 new diagnoses each year in England and Wales. Ankylosing spondylitis is about 3 times more common in men than in women.[1,2]

Conventional therapy for radiographic axial spondyloarthritis includes anti-inflammatory treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. Tumour necrosis factor-alpha (TNF-alpha) inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab and infliximab) are typically used when the disease has not responded adequately to conventional therapy. NICE technology appraisal TA383 recommends

adalimumab, certolizumab pegol, etanercept, golimumab and infliximab as treatment options for adults with severe active ankylosing spondylitis in adults whose disease has responded inadequately to, or who cannot tolerate NSAIDs. Biosimilar versions of adalimumab, etanercept and infliximab are available. Infliximab is only recommended if the least expensive infliximab product is used. NICE technology appraisal 407 recommends the interleukin-17A (IL-17A) inhibitor secukinumab as an alternative to, or after inadequate response to TNF-alpha inhibitors.

## The technology

Tofacitinib (Xeljanz, Pfizer) is a Janus kinase (JAK) inhibitor, and is a targeted synthetic small molecule. Janus kinases are intracellular enzymes that transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of creating new blood cells in the body (hematopoiesis) and immune cell function. It is administered orally.

Tofacitinib does not have a marketing authorisation in the UK for axial spondyloarthritis. It has been studied in a clinical trial compared with placebo in adults with active ankylosing spondylitis whose disease had responded inadequately to or who are intolerant to non-steroidal anti-inflammatory drugs.

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| **Intervention(s)** | Tofacitinib |
| **Population(s)** | People with radiographic ankylosing spondylitis for whom nonsteroidal anti-inflammatory drugs have been inadequately effective or not tolerated |
| **Comparators** | TNF-alpha inhibitors including:<br>• Adalimumab<br>• Certolizumab pegol<br>• Etanercept<br>• Golimumab<br>• Infliximab<br>• Secukinumab<br>• Established clinical management without biologics |

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| **Outcomes** | The outcome measures to be considered include:<br>• disease activity for example, Assessment of SpondyloArthritis International Society (ASAS)<br>• functional capacity<br>• disease progression<br>• peripheral symptoms (including enthesitis, peripheral arthritis and dactylitis)<br>• symptoms of extra-articular manifestations (including uveitis, inflammatory bowel disease and psoriasis)<br>• adverse effects of treatment<br>• 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.<br>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. |
| **Other considerations** | The availability and cost of biosimilar products should be taken into account.<br>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** | **Related Technology Appraisals:**<br>'TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis' (2016) NICE |

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| **Pathways** | technology appraisal 383. Review date June 2021.<br>'Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors' (2016) NICE technology appraisal 407. Review date October 2020.<br>**Appraisals in development:**<br>'Ixekizumab for treating axial spondyloarthritis after NSAIDs' Publication expected May 2021<br>**Related Guidelines:**<br>Spondyloarthritis in over 16s: diagnosis and management (2017) NICE guideline 65. Review date to be confirmed.<br>**Related Quality Standards:**<br>Spondyloarthritis (2018) NICE quality standard 170.<br>**Related NICE Pathways:**<br>Managing spondyloarthritis in adults (2020) NICE pathway |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018) Manual for prescribed specialised services 2018/19.<br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,2,4 and 5.<br>https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 |

**Questions for consultation**

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

Which treatments are considered to be established clinical practice in the NHS for active ankylosing spondylitis?

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?

Where do you consider tofacitinib will fit into the existing NICE pathway, 'Managing spondyloarthritis in adults'?

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 National Ankylosing Spondyloarthritis Society: Facts & Figures. Available at https://nass.co.uk/about-as/as-facts-and-figures/ Accessed December 2020

2 Department of Health (2006) The musculoskeletal services framework. Accessed December 2020