NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Upadacitinib for treating active non-radiographic axial spondyloarthritis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for treatment of active non-radiographic axial spondyloarthritis.

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 spondylarthritis). 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 joins 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 average age of onset of symptoms is 24 years, with an average of 8.5 years before a diagnosis is made, by which time damage to the spine which can be irreversible may have occurred.[1]

Around 220,000 adults have been diagnosed as having axial spondyloarthritis and an estimated 1 in 200 of the adult population in the UK is affected.[1]

Conventional therapy for non-radiographic axial spondyloarthritis includes anti-inflammatory treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. NICE technology appraisal guidance 383 and 497 recommend tumour necrosis factor-alpha inhibitors adalimumab, certolizumab pegol, etanercept and golimumab as treatment options in people with disease that does not respond adequately to or cannot tolerate NSAIDs. Biosimilar versions of adalimumab, etanercept and golimumab are now available.

NICE technology appraisals 719 and 718 recommend secukinumab and ixekizumab as options for treating active non-radiographic axial spondyloarthritis with objective signs of inflammation (shown by elevated C-reactive protein or MRI) that is not controlled well enough with non-steroidal anti-inflammatory drugs (NSAIDs) only if tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough.

The technology

Upadacitinib (Rinvoq, AbbVie) is a selective and reversible Janus kinase-1 (JAK-1) inhibitor, which is administered orally.

Upadacitinib does not currently have a marketing authorisation in the UK for treating non-radiographic axial spondyloarthritis. It has been studied in a clinical trial compared with placebo in adults with non-radiographic axial spondyloarthritis with objective signs of inflammation.

Upadacitinib has a marketing authorisation for treating active ankylosing spondylitis in adult patients who have responded inadequately to conventional therapy.

Intervention(s)	Upadacitinib
Population(s)	Adults with active non-radiographic axial spondyloarthritis

Comparators	• Secukinumab
	• Ixekizumab
	• TNF-alpha inhibitors including:
	  o Adalimumab
	  o Certolizumab pegol
	  o Etanercept
	  o Golimumab
	• Established clinical management without biological treatments

Outcomes	The outcome measures to be considered include: • disease activity • functional capacity • disease progression • pain • peripheral symptoms (including enthesitis, peripheral arthritis and dactylitis) • symptoms of extra-articular manifestations (including uveitis, inflammatory bowel disease and psoriasis) • 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. 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. 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	The availability and cost of biosimilar and generic products should be taken into account. 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:** 'Ixekizumab for treating axial spondyloarthritis' (2021) NICE technology appraisal 718 'Secukinumab for treating non-radiographic axial spondyloarthritis' (2021) NICE technology appraisal 719 'Golimumab for treating non-radiographic axial spondyloarthritis' (2018) NICE technology appraisal 497. Review date December 2020. 'TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis' (2016) NICE technology appraisal 383. Review date June 2021. 'Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors' (2016) NICE technology appraisal 407. Review date September 2019. **Related Guidelines:** 'Spondyloarthritis in over 16s: diagnosis and managment' (2017) NICE guideline 65. Review date to be confirmed.

	Related Quality Standards: 'Spondyloarthritis'. NICE quality standard 170. Review date August 2019. **Related NICE Pathways:** 'Musculoskeletal-conditions' (updated 2020). NICE pathway 'Managing spondyloarthritis in adults' (updated June 2020)
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 5. Adult highly specialised rheumatology services NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1, 2, 4 and 5 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Where is upadacitinib likely to be used in the treatment pathway? Is it expected that upadacitinib would be used after the condition has not responded to NSAIDs or biological disease modifying anti-rheumatic drugs? Which treatments had people previously received in the key clinical trial?

Have all relevant comparators for upadacitinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for treating active non-radiographic axial spondyloarthritis?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom upadacitinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider upadacitinib will fit into the existing NICE pathway 'musculoskeletal-conditions' and '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 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.

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 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 Axial Spondyloarthritis Society. *What are the issues in axial SpA (AS)?* Available from: https:// nass.co.uk/about-as/as-facts-and-figures/