

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Upadacitinib for treating active ankylosing spondylitis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

Background

Ankylosing spondylitis 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). People with these diseases often have the genetic marker human leukocyte antigen (HLA)-B27.

The clinical symptoms 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.

In the early stages of disease, radiographs of the sacroiliac joints and spines can be normal (so-called 'non-radiographic' disease) although sacroiliitis (inflammation of the sacroiliac joints) or inflammation of the spine may be visible on MRI before structural damage occurs. If definite radiographic sacroiliitis (abnormalities are seen in plain x-rays of the sacroiliac joints, such as erosions, sclerosis, and partial or total ankylosis) is present, the disease can be classified as ankylosing spondylitis. Radiographic changes to the spine are not part of the classification criteria, but new bone formation (such as syndesmophytes and ankylosis of the vertebral column) is characteristic of ankylosing spondylitis.

The prevalence of ankylosing spondylitis in the UK is thought to range from 0.05% to 0.23%. Based on population estimations in 2020, there are between 33,398 and 153,632 adults with ankylosing spondylitis in the UK.¹ Ankylosing spondylitis is about three times more common in men than in women, but men are more likely to develop radiographically evidence disease. The onset of symptoms typically occurs in the third decade of life.

Conventional therapy for ankylosing spondylitis includes non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. Tumour necrosis factor-alpha (TNF-alpha) inhibitors 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 for people who have active spinal disease as assessed on two separate occasions 12 weeks apart and have tried at least two NSAIDs but they have not worked. 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 secukinumab for treating active ankylosing spondylitis in adult whose disease has responded inadequately to conventional therapy (NSAIDs or TNF-alpha inhibitors).

The technology

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

Upadacitinib does not currently have a marketing authorisation in the UK for ankylosing spondylitis. Upadacitinib received positive opinion from the Committee for Medicinal Products for Human Use (CHMP) in December 2020 for the treatment active ankylosing spondylitis in adult patients who have responded inadequately to conventional therapy.

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| Intervention(s) | Upadacitinib |
| Population(s) | Treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy |
| Comparators | TNF-alpha inhibitors including: <ul style="list-style-type: none"> • Adalimumab • Certolizumab pegol • Etanercept • Golimumab • Infliximab • Secukinumab |
| Outcomes | The outcome measures to be considered include: <ul style="list-style-type: none"> • 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. |

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| <p>Economic analysis</p> | <p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>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.</p> |
| <p>Other considerations</p> | <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>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.</p> |
| <p>Related NICE recommendations and NICE Pathways</p> | <p>Related Technology Appraisals:</p> <p>‘TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis’ (2016). NICE Technology Appraisal 383. Review date June 2021.</p> <p>‘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.</p> <p>Ongoing appraisals:</p> <p>‘Secukinumab for treating non-radiographic axial spondyloarthritis’ Proposed NICE technology appraisal [ID 1419]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>‘Spondyloarthritis in over 16s: diagnosis and management’ (2017). NICE guideline 65.</p> <p>Related Quality Standards:</p> <p>‘Spondyloarthritis’ (2018) NICE quality standard 170.</p> |

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| | <p>Related NICE Pathways:</p> <p>‘Musculoskeletal-conditions’ (updated 2020). NICE pathway</p> <p>‘Managing spondyloarthritis in adults’ (updated June 2020) NICE pathway</p> |
| Related National Policy | <p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 5. Adult highly specialised rheumatology services</p> <p>NHS England (2018) NHS England Funding and Resource 2018/19: Supporting ‘Next Steps for the NHS Five Year Forward View’</p> <p>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</p> |

Questions for consultation

Have all relevant comparators for upadacitinib 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 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 ‘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 NIHR (2020) Health Technology Briefing: Tofacitinib for Ankylosing Spondylitis