NICE National Institute for Health and Care Excellence

NICE guidance

Upadacitinib for treating active non-radiographic axial spondyloarthritis

Technology appraisal guidance
Published: 1 February 2023

www.nice.org.uk/guidance/ta861

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Upadacitinib is recommended as an option 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) in adults. It is recommended only if:

- tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough and
- the company provides upadacitinib according to the commercial arrangement.

1.2 Assess response to upadacitinib after 16 weeks of treatment. Continue treatment only if there is clear evidence of response, defined as a reduction in:

- the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pretreatment value or by 2 or more units and
- the spinal pain visual analogue scale (VAS) by 2 cm or more.

1.3 Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the BASDAI and spinal pain VAS and make any adjustments needed.

1.4 If patients and their clinicians consider upadacitinib to be 1 of a range of suitable treatments (including secukinumab and ixekizumab), discuss the advantages and disadvantages of the available treatments. After that discussion, if more than 1 treatment is suitable, choose the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

1.5 These recommendations are not intended to affect treatment with upadacitinib that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician

consider it appropriate to stop.

Why the committee made these recommendations

Usual treatment for active non-radiographic axial spondyloarthritis in adults that is not controlled well enough with NSAIDs, and when TNF-alpha inhibitors are not suitable or do not control the condition well enough, is secukinumab or ixekizumab. These are biological treatments. Upadacitinib is another biological treatment.

Evidence from clinical trials shows that upadacitinib reduces symptoms and improves quality of life better than placebo. Indirect comparisons suggest that upadacitinib works as well as secukinumab and ixekizumab.

A cost comparison suggests upadacitinib has similar costs and overall health benefits as secukinumab and ixekizumab. So upadacitinib is recommended.

2 Information about upadacitinib

Marketing authorisation indication

2.1 Upadacitinib (RINVOQ, AbbVie) is indicated for 'the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs)'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for upadacitinib.

Price

2.3 The list price is £805.56 per 28-tablet pack, with each tablet containing 15 mg of upadacitinib (excluding VAT; BNF online, accessed November 2022). The annual cost of treatment with one 15-mg tablet per day is £10,501.05 (excluding VAT; BNF online, accessed November 2022).

2.4 The company has a commercial arrangement. This makes upadacitinib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The evaluation committee considered evidence submitted by AbbVie, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

Decision problem

Cost comparison

3.1 The company proposed that upadacitinib should be considered in adults as an alternative to the currently NICE-recommended interleukin (IL)-17 inhibitors secukinumab and ixekizumab for active non-radiographic axial spondyloarthritis that is not controlled well enough with conventional therapy and when TNF-alpha inhibitors are not suitable or do not control the condition well enough. The committee agreed that the proposed population was consistent with previous recommendations for IL-17 inhibitors for active non-radiographic axial spondyloarthritis, and with their use in clinical practice. The company presented a comparison with 2 NICE-recommended IL-17 inhibitors (NICE technology appraisal guidance on secukinumab for treating non-radiographic axial spondyloarthritis and ixekizumab for treating axial spondyloarthritis). The committee agreed that this was consistent with the criteria for a cost-comparison evaluation.

Comparators

3.2 Secukinumab and ixekizumab are anti-IL-17 injections recommended by NICE for treating non-radiographic axial spondyloarthritis. Upadacitinib is an oral JAK inhibitor. The clinical and patient experts highlighted the convenience of upadacitinib over IL-17 inhibitors owing to its oral administration. They also suggested that upadacitinib would be especially helpful for people with needle phobias or dexterity issues that make self-injecting difficult. Clinical advice to the EAG suggested that secukinumab is chosen more often than ixekizumab for treating active

non-radiographic axial spondyloarthritis. Secukinumab has been available for ankylosing spondylitis since 2016, suggesting that secukinumab is more established in NHS clinical practice than ixekizumab, which became available in 2021. The committee concluded that secukinumab and ixekizumab are appropriate comparators for upadacitinib, but that secukinumab was the more relevant comparator.

Clinical effectiveness

Data sources

3.3 Upadacitinib has been studied in 1 randomised controlled trial including 313 adults with active non-radiographic axial spondyloarthritis (SELECT-AXIS 2, study 2). It was compared with placebo. In SELECT-AXIS 2, study 2, upadacitinib was associated with statistically significant improvements compared with placebo in the primary and secondary outcomes, including the Assessment in Spondyloarthritis international Society 40% (ASAS40) response, BASDAI 50 score and total back pain score. Upadacitinib was associated with higher ASAS40 and BASDAI 50 responses and total back pain score improvement at week 14 than placebo. People having upadacitinib also had statistically significantly higher scores in the Ankylosing Spondylitis Quality of Life (ASQoL) measure. The committee concluded that upadacitinib was more clinically effective than placebo.

Network meta-analysis

3.4 The company did a series of network meta-analyses comparing clinical-effectiveness data for upadacitinib (SELECT-AXIS 2, study 2) with data for secukinumab (PREVENT) and ixekizumab (COAST-X). The analyses investigated measures of efficacy, including binary outcomes (ASAS40, BASDAI 50) and continuous outcomes (BASDAI [change from baseline] and Bath Ankylosing Spondylitis Functional Index [change from baseline]). The EAG highlighted that although the median values favoured upadacitinib over ixekizumab (except for BASDAI 50 score) and secukinumab, the credible intervals were wide. It explained that the health benefits for all treatments could be similar, but could also differ.

The clinical experts stated in their submission that they would expect upadacitinib to provide clinically meaningful benefits compared with IL-17 inhibitors. The EAG also identified heterogeneity between the trials included in the network meta-analysis that may impact its validity, but acknowledged that there were no studies available that directly compared upadacitinib with either secukinumab or ixekizumab. The committee confirmed this and noted that uncertainties relating to heterogeneity were unlikely to be resolved by a more detailed cost–utility analysis. The committee concluded that the network meta-analysis was uncertain, but supported the company's position that upadacitinib has similar clinical effectiveness to secukinumab and ixekizumab.

Safety comparisons between trials

3.5 The company provided safety data comparing upadacitinib with placebo (SELECT-AXIS 2, study 2), secukinumab (PREVENT) and ixekizumab (COAST-X). The company and EAG agreed that the safety profiles of all treatments were broadly similar. However, the EAG highlighted that the company had only provided naive comparisons, and the differences between adverse event incidence between the trials was likely to be influenced by differences in trial design, length of follow up and differences in adverse event definitions in each trial. The committee agreed with the EAG. It concluded that it was difficult to draw definitive conclusions from the safety data, and formal modelling of the available safety data would have been helpful for decision making.

Cost comparison

Cost-comparison estimates

3.6 The company presented a base-case cost-comparison analysis that modelled the total costs of upadacitinib, secukinumab and ixekizumab over 5 years. It also provided a scenario analysis modelling the costs over 10 years. It considered that the clinical evidence available supported the assumption of clinical equivalence between upadacitinib, secukinumab and ixekizumab. The EAG was satisfied with the company's cost-comparison analysis methods, so did not provide its own cost-

comparison estimates. Taking into account the confidential patient access schemes for upadacitinib, secukinumab and ixekizumab, the committee concluded that the total costs associated with upadacitinib were similar to or lower than those associated with secukinumab and ixekizumab. The discounts for all treatments are confidential, so the incremental costs cannot be shared here.

Conclusion

Recommendation

3.7 The committee concluded that the criteria for a cost comparison were met because:

- upadacitinib provided similar overall health benefits to those of secukinumab or ixekizumab, and
- the total costs associated with upadacitinib were similar to or lower than the total costs associated with secukinumab or ixekizumab.

The committee therefore recommended upadacitinib as an option for treating active non-radiographic axial spondyloarthritis in adults.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication. Because upadacitinib has been recommended through the cost-comparison process, NHS England and commissioning groups have agreed to provide funding to implement this guidance 30 days after publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has active non-radiographic axial spondyloarthritis and the doctor responsible for their care thinks that upadacitinib is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Charles Crawley
Chair, technology appraisal committee B

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Emily Leckenby
Technical lead

Caron Jones
Technical adviser

Thomas Feist
Project manager

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Accreditation