NICE National Institute for Health and Care Excellence

NICE guidance

Upadacitinib for treating active ankylosing spondylitis

Technology appraisal guidance
Published: 30 September 2022

www.nice.org.uk/guidance/ta829

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 ankylosing spondylitis that is not controlled well enough with conventional treatments in adults, only if:

- the condition has a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of 4 units or more and a spinal visual analogue scale (VAS) of 4 cm or more
- tumour necrosis factor (TNF)-alpha inhibitors are not suitable or have not controlled the condition well enough, and
- the company provides upadacitinib according to the commercial arrangement.

1.2 If patients and their clinicians consider upadacitinib to be one of a range of suitable treatments (including secukinumab and ixekizumab), choose the least expensive treatment, taking into account administration costs, dosage, price per dose and commercial arrangements.

1.3 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 BASDAI score to 50% of the pre-treatment value or by 2 or more units and
- a reduction in the spinal pain VAS by 2 cm or more.

1.4 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.

1.5 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 ankylosing spondylitis in adults 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, is secukinumab or ixekizumab. Upadacitinib is another treatment that works in a similar way.

Evidence from clinical trials shows that upadacitinib is more effective than placebo. Indirect comparisons of upadacitinib with secukinumab and ixekizumab suggest they have similar clinical effectiveness.

A cost comparison suggests upadacitinib has similar costs and overall health benefits as secukinumab and ixekizumab. So upadacitinib is recommended for treating active ankylosing spondylitis in adults if it is used in the same population as secukinumab and ixekizumab.

2 Information about upadacitinib

Marketing authorisation indication

2.1 Upadacitinib (Rinvoq, AbbVie) is 'indicated for the treatment of active ankylosing spondylitis in adult patients who have responded inadequately to conventional therapy'.

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 June 2022). The annual cost of treatment with one 15-mg tablet per day is £10,501.05 (excluding VAT; BNF online, accessed June 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 appraisal committee considered evidence submitted by AbbVie, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

Decision problem

A cost-comparison analysis with secukinumab as the comparator was the most appropriate decision problem

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 ankylosing spondylitis that is not controlled well enough with conventional therapy and when tumour necrosis factor (TNF)-alpha inhibitors are not suitable (biological-naive population) or do not control the condition well enough (biological-experienced population). The company's proposed decision problem was narrower than upadacitinib's marketing authorisation because it excluded people who had had TNF-alpha inhibitors. However, the committee agreed that the proposed population was consistent with previous NICE recommendations for IL-17 inhibitors for ankylosing spondylitis, 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 active ankylosing spondylitis and ixekizumab for treating axial spondyloarthritis). The committee agreed that this was consistent with the criteria for a cost-comparison appraisal (see section 3.7). The clinical expert explained that secukinumab was likely to be chosen over ixekizumab by clinicians. The committee was aware that secukinumab was recommended for ankylosing spondylitis in 2016, while ixekizumab was recommended in 2021. It considered both comparators relevant but reasoned that secukinumab is more established in NHS clinical practice than ixekizumab. The committee recalled that NICE's technology appraisal guidance on secukinumab and ixekizumab recommend that treatment should stop if there is an inadequate response at 16 weeks or after 16 to 20 weeks, respectively. An

adequate response is defined as:

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

The committee considered that it would be reasonable to apply the same approach for this appraisal. It concluded that secukinumab was the more relevant comparator and represented the decision problem that had the most validity to NHS clinical practice.

Clinical effectiveness

Upadacitinib is more clinically effective at reducing symptom burden than placebo

3.2 Upadacitinib has been compared with placebo in 2 randomised controlled trials in ankylosing spondylitis: SELECT-AXIS 1, which included 187 people who had not previously had biological disease-modifying antirheumatic drugs (DMARDs), and study 1 of SELECT-AXIS 2, which included 420 adults with active ankylosing spondylitis who had had previous treatment with biological DMARDs. In both trials, upadacitinib was associated with statistically significant improvements compared with placebo in primary and secondary outcomes, including the Assessment in Spondyloarthritis International Society 40% (ASAS40) response and BASDAI 50 score. The clinical expert explained that the ASAS40 score is mostly used in clinical trials as a measure of treatment effect. In clinical practice, the BASDAI 50 or back pain score are used to assess treatment response (see section 3.1). In study 1 of SELECT-AXIS 2, 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 at reducing symptom burden than placebo.

The company's network meta-analyses are suitable for decision making

3.3 The company did a series of network meta-analyses comparing upadacitinib with secukinumab on measures of efficacy, including ASAS40 and BASDAI 50 response rates. It provided results with fixed effect and random effects models for people with ankylosing spondylitis that has not been treated with biological therapies (biological-naive population). The company did scenario analyses comparing upadacitinib with secukinumab for people with ankylosing spondylitis that has been treated with 1 or more biological DMARD (biological-experienced population). It acknowledged the lack of robust data for secukinumab in people who have had biological treatments. The company highlighted that the published secukinumab trials included few people with ankylosing spondylitis who had had biological DMARDs. Also, it indicated that the inclusion criteria and patient populations in the secukinumab trials were different from the study 1 of the SELECT-AXIS 2 trial. The network meta-analyses for the biological-naive population did not find any significant differences between upadacitinib and secukinumab for any of the outcomes analysed. However, the ERG indicated that the results were uncertain and that this could favour upadacitinib. The company extrapolated the results of the biological-naive population analyses to the biological-experienced population based on clinician opinion that upadacitinib would have similar efficacy in both populations. The clinical expert confirmed that they would expect upadacitinib to have similar efficacy in both populations. The committee concluded that the network meta-analyses estimates were uncertain, but they supported the company's position that upadacitinib is likely to have similar clinical effectiveness to secukinumab.

It is plausible that the long-term efficacy of upadacitinib is equivalent to that of secukinumab, but this is uncertain

3.4 The methods guide states that a cost-comparison analysis requires that the technology have similar health benefits to the comparator over the average time on treatment. The company network meta-analyses compared upadacitinib with secukinumab for outcomes measured between 12 and 16 weeks and found no significant differences (see section 3.3). The ERG indicated that there is limited long-term data available for upadacitinib's efficacy, which adds uncertainty to the

assumption of clinical equivalence between upadacitinib and secukinumab. The ERG also noted that in previous appraisals in ankylosing spondylitis, companies presented trial data for 2 to 5 years of follow up which showed that drug responses were maintained in the long term. The company stated that there is evidence available for upadacitinib's efficacy in the long term (up to 2 years) which shows maintenance of response, but only for biological-naive populations. The clinical expert stated that long-term efficacy of upadacitinib (a small molecule drug) was expected to be similar or greater than that of biological drugs such as secukinumab. This is because biological drugs can cause an immune response that can lead to their gradual destruction and loss of efficacy over time. However, this is less likely to happen with small molecules such as upadacitinib. The committee considered this explanation biologically plausible. However, it concluded that there was still substantial uncertainty around long-term efficacy because of potential safety concerns and whether people will take upadacitinib as intended (see section 3.5 and section 3.6).

The company's economic model

There is uncertainty about whether upadacitinib has an equivalent discontinuation rate to secukinumab

3.5 Differences in treatment discontinuation can lead to differences in efficacy and costs between the technology and comparators. The company assumed upadacitinib has an annual discontinuation rate of 11%, based on the rate used in the appraisal of secukinumab. However, it presented limited data on discontinuation rates. The ERG indicated there may be differences in adherence between upadacitinib and secukinumab because upadacitinib is taken daily and this may affect adherence. The company stated that there is no evidence to support the assumption of worse adherence with upadacitinib compared with secukinumab. The clinical expert added that, in their experience, if a drug is working then adherence is likely to be high. The patient expert confirmed this and stated it is unlikely for someone to forget to take the drug because the effect of the disease on all parts of life was so substantial. They also explained that the effect of injectable biologicals wears off in the days before the next dose and symptoms worsen as a result. The committee concluded that, although there was

no evidence to suggest that discontinuation rates would be different between upadacitinib and secukinumab, there was uncertainty that could favour either technology.

There may be additional monitoring costs for upadacitinib that the company did not include in the cost-comparison model

3.6 The company base case in the cost-comparison model included only drug acquisition, administration and monitoring costs. The ERG raised the issue that the costs of adverse effects and some monitoring costs were excluded. The company did not include annual lipid monitoring in its base case but provided a scenario with these costs included. The ERG base case included these costs and also had slightly different drug acquisition costs, because of differences in the assumed duration of a trimester (13.04 weeks compared with 12 weeks assumed by the company). These differences meant that the calculated number of doses of secukinumab in a year were higher in the ERG base case. Also, the ERG excluded administration costs from its base case because people would receive training to self-administer subcutaneous injections when they first start treatment, but do not need training for later lines of subcutaneous treatment. The company stated that it agreed with the ERG base case. The committee considered that the changes proposed in the ERG base case did not have a large effect on the cost-comparison estimates. The ERG also considered that the exclusion of the costs of adverse events could bias the analysis in favour of upadacitinib if the adverse event profile was different to those of the comparators in the long term. The clinical expert explained that it was unlikely that adverse events with upadacitinib would be different from those of secukinumab. They highlighted that even if incidence of some viral infections was higher with upadacitinib, this would be made up by the lack of inflammatory bowel issues associated with IL-17 inhibitors such as secukinumab. The committee accepted this but questioned whether, in light of the Medicines and Healthcare products Regulatory Agency (MHRA) safety warning for tofacitinib, there may be additional monitoring costs for upadacitinib, such as electrocardiograms for cardiovascular monitoring or screening for malignancies, which could incur substantial additional costs. The clinical expert stated that they would take into account the MHRA safety warning, and the individual risk of each patient before deciding whether to use upadacitinib. So it is unlikely that

additional monitoring costs would be incurred. The committee noted this but concluded that it was still highly uncertain if upadacitinib would incur additional monitoring costs in the longer term as many of these costs were tied to long-term safety, which it also considered uncertain.

Cost comparison

The total costs associated with upadacitinib are similar to or lower than those associated with secukinumab and ixekizumab

3.7 The company presented a cost-comparison analysis that modelled the total costs of upadacitinib and secukinumab over 10 years. The committee considered that the comparison against secukinumab was the most important and represented the most valid decision problem. It considered that the clinical evidence available supported the assumption of clinical equivalence between upadacitinib and secukinumab. The committee preferred the ERG's base case model. Taking into account the confidential patient access schemes for upadacitinib and secukinumab, the committee concluded that the total costs associated with upadacitinib were similar to or lower than those associated with secukinumab (the exact results cannot be reported here because the discounts are confidential).

Upadacitinib is recommended as an option for treating active ankylosing spondylitis in adults

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

- upadacitinib provided similar overall health benefits to 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 ankylosing spondylitis in adults. It concluded that the recommendations for upadacitinib should be consistent with the company's proposal and NICE's technology appraisal guidance recommendations for secukinumab and ixekizumab, that is:

- when the condition has not responded to conventional therapy and
- when TNF-alpha inhibitors are not suitable or do not control the condition well enough and
- when treatment is stopped at 16 weeks if the condition has not responded adequately.

Other factors

Equality

3.9 No equality issues were identified that were not addressed in recommendation 1.4.

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 clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication. Because upadacitinib has been recommended through the fast track appraisal 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 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 appraisal document.

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 ankylosing spondylitis that is not controlled well enough with conventional therapy in adults, TNF-alpha inhibitors are not suitable or do not control the condition well enough 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 Appraisal committee members and NICE project team

Appraisal 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 to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

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

NICE project team

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

George Braileanu and Samuel Slayen
Technical leads

Adam Brooke
Technical adviser

Daniel Davies
Project manager

6 Update information

December 2025: We have made minor editorial changes to the wording in section 1.1 to align with the NICE guideline on spondyloarthritis in over 16s: diagnosis and management. This does not affect the meaning or intent of the guidance.

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