NICE National Institute for Health and Care Excellence

NICE guidance

Tofacitinib for treating juvenile idiopathic arthritis

Technology appraisal guidance
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www.nice.org.uk/guidance/ta735

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 Tofacitinib is recommended as an option for treating active polyarticular juvenile idiopathic arthritis (JIA; rheumatoid factor positive or negative polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis in people 2 years and older. This is if their condition has responded inadequately to previous treatment with disease-modifying antirheumatic drugs (DMARDs), and only if:

- a tumour necrosis factor (TNF)-alpha inhibitor is not suitable or does not control the condition well enough, and
- the company provides tofacitinib according to the commercial arrangement.

1.2 Tofacitinib can be used with methotrexate, or as monotherapy when methotrexate is not tolerated or if continued treatment with methotrexate is inappropriate.

1.3 If tofacitinib is one of a range of treatments considered suitable by patients, or their parents or carers, and their clinicians, choose the least expensive (taking into account administration costs and commercial arrangements).

1.4 This recommendation is not intended to affect treatment with tofacitinib that was started in the NHS before this guidance was published. Children and young 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. This decision should be made jointly by the clinician, the child or young person, and their parents or carers.

Why the committee made these recommendations

Treatments for JIA that has not responded well enough to DMARDs include adalimumab, etanercept and tocilizumab.

Clinical trial evidence shows that tofacitinib is effective compared with placebo. There are

no trials directly comparing tofacitinib with current treatments. But an indirect comparison suggests that tofacitinib has similar effects to adalimumab and tocilizumab. There is no evidence for tofacitinib compared with etanercept.

Tofacitinib has similar costs to tocilizumab. But it costs more than adalimumab and is likely to cost more than etanercept.

Most people with the 2 kinds of JIA being considered have adalimumab or etanercept, which are TNF-alpha inhibitors. So tofacitinib is only recommended when a TNF-alpha inhibitor is unsuitable or has not worked well enough.

2 Information about tofacitinib

Marketing authorisation indication

2.1 Tofacitinib (Xeljanz, Pfizer) is indicated for: 'the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive or negative polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs'.

2.2 Tofacitinib can be used with methotrexate, or as monotherapy when methotrexate is not tolerated or if continued treatment with methotrexate is inappropriate.

Dosage in the marketing authorisation

2.3 The dosage schedule is available in the summary of product characteristics.

Price

2.4 The list price of a 56-tablet pack of 5 mg tofacitinib is £690.03 (excluding VAT; BNF online accessed August 2021). Tofacitinib is also available as an oral 1 mg/ml solution in 240 ml bottles.

2.5 The company has a commercial arrangement. This makes tofacitinib 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 Pfizer and 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.

Polyarticular juvenile idiopathic arthritis

Adalimumab and tocilizumab are appropriate comparators

3.1 The company positions tofacitinib for people with polyarticular juvenile idiopathic arthritis (JIA) whose disease has responded inadequately to or who are intolerant of, one or more disease-modifying antirheumatic drugs (DMARDs). This corresponds with how biological DMARDs are used in the NHS. The company also positions tofacitinib when biological DMARDs have not controlled disease well enough. The company's cost-comparison case proposes that tofacitinib has similar effects to adalimumab and tocilizumab, which are both recommended in NICE's technology appraisal guidance on abatacept, adalimumab, etanercept and tocilizumab for JIA. The company explained that it selected these comparators because adalimumab is the most frequently used biological DMARD, and tocilizumab represents an alternative mode of action. The ERG's clinical advisers suggested that 50% to 60% of people with JIA currently have adalimumab, 30% to 40% have tocilizumab and around 10% have etanercept. The company's estimates suggested a higher proportion having adalimumab. The committee agreed that adalimumab and tocilizumab are appropriate comparators.

Tofacitinib is likely to have similar clinical effectiveness to adalimumab and tocilizumab

3.2 Tofacitinib has been compared with placebo in a phase 3, randomised, double-blind trial, study A3921104. This showed that tofacitinib was superior to placebo for a range of outcomes at 44 weeks. To compare tofacitinib with adalimumab and tocilizumab, the company carried out

indirect comparisons. These suggested that, for the outcomes of disease flare, disease activity (measured by the American College of Rheumatology [ACR] 30, 50 and 70), tofacitinib is similar to the comparators (the exact results are considered confidential by the company and cannot be reported here). The ERG considered it was plausible that tofacitinib is non-inferior to the comparators. However, it noted that tofacitinib follow-up data was only for 44 weeks, while there is longer follow-up data for tocilizumab and adalimumab. The committee concluded that tofacitinib is likely to have similar clinical effectiveness to adalimumab and tocilizumab, although the long-term effectiveness is uncertain.

Tofacitinib costs about the same as tocilizumab but more than adalimumab

3.3 Adalimumab biosimilars are available in the NHS at a considerable discount to the list price of the originator product (exact prices are confidential and cannot be reported here). There is also a confidential discount for tocilizumab. When this is applied, tofacitinib has similar overall costs to tocilizumab in both the company and the ERG's modelling. However, tofacitinib has higher costs than adalimumab in both the company and the ERG's modelling. The exact results are confidential and cannot be reported here.

Juvenile psoriatic arthritis

The evidence for tofacitinib in juvenile psoriatic arthritis is very limited

3.4 Although the A3921104 study included a small number of people with juvenile psoriatic arthritis (n=7 tofacitinib, n=8 placebo), this population was not included in the primary end point analysis. Results for people with juvenile psoriatic arthritis favoured tofacitinib for disease flare and ACR response and were similar to those for the polyarticular JIA cohort (exact results are considered confidential by the company and cannot be reported here). The results also favoured tofacitinib for the outcome of body surface area affected by psoriasis. The committee concluded that

the results suggest tofacitinib is clinically effective compared with placebo, but the evidence is very limited.

Etanercept is the relevant comparator for juvenile psoriatic arthritis

3.5 The only drug with a marketing authorisation for juvenile psoriatic arthritis is etanercept. Etanercept is recommended in NICE's technology appraisal guidance on abatacept, adalimumab, etanercept and tocilizumab (TA373) for juvenile psoriatic arthritis (referred to as psoriatic JIA). In that appraisal the only evidence available for etanercept came from a single-arm open label trial, CLIPPER. Also in the appraisal:

- The committee heard from the clinical experts that it was possible to generalise results for the effectiveness of etanercept for treating adult psoriatic JIA because the immunological effect is expected to be the same in adults and children. (Tofacitinib is recommended in NICE's technology appraisal guidance on tofacitinib for treating active psoriatic arthritis after inadequate response to DMARDs.)
- A clinical expert also said that in their experience there was no evidence to suggest that etanercept would be any less effective in reducing disease activity in people with psoriatic JIA than when using these drugs for polyarticular JIA.
- The assessment group was unable to separately model psoriatic JIA.
- The committee considered that the results of the model for polyarticular JIA were generalisable to people with psoriatic JIA.

  The committee concluded that etanercept was the relevant comparator for juvenile psoriatic arthritis and that it would consider the conclusions of TA373 in its decision making.

There is no evidence compared with etanercept

3.6 The company did not present any clinical evidence comparing tofacitinib with etanercept. The committee appreciated that this would have been difficult to do, and any analysis would have been very uncertain. This is

because of the small number of patients in the A3921104 study and because the CLIPPER trial was single arm. The company also did not provide a cost-comparison analysis comparing tofacitinib with etanercept. However, the committee was aware that etanercept biosimilars are available in the NHS at a considerable discount to the list price of the originator (exact prices are confidential and cannot be reported here).

Conclusion

Tofacitinib is recommended only if a TNF-alpha inhibitor is not suitable or does not control the condition well enough

3.7 The committee noted that a substantial proportion of people have adalimumab for polyarticular JIA (for more about appropriate comparators, see section 3.1). Although tofacitinib is similarly effective, it costs more than adalimumab. The committee recognised that patients and clinicians would welcome an additional treatment option with an alternative route of administration and mode of action. It noted that if people have already had adalimumab, or it is unsuitable, then tocilizumab may be used. Tofacitinib has similar costs and similar benefits to tocilizumab. Therefore, the committee considered that the cost-comparison case was demonstrated, but only if adalimumab is unsuitable or the condition has not responded well enough to it. The committee considered that the evidence relating to juvenile psoriatic arthritis was limited. But as in TA373 this could be generalised from polyarticular JIA and also from tofacitinib's use in adult psoriatic arthritis. However, the main comparator is etanercept for this population, for which there are low-cost biosimilars. This means tofacitinib is likely to have higher costs than etanercept. So the committee concluded that it could recommend tofacitinib for both polyarticular JIA and juvenile psoriatic arthritis, but only if a tumour necrosis factor (TNF)-alpha inhibitor (such as adalimumab and etanercept) is not suitable or does not control the condition well enough.

Other factors

3.8 No equality issues were identified.

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 tofacitinib 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 juvenile idiopathic arthritis and the doctor responsible for their care thinks that tofacitinib 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 C.

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

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Accreditation