NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Secukinumab for treating moderate to severe plaque psoriasis in children and young people

1 Recommendations

1.1 Secukinumab is recommended as an option for treating plaque psoriasis in children and young people aged 6 to 17 years, only if:

- the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and
- the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and
- the company provides the drug according to the commercial arrangement (see section 2).

1.2 Stop secukinumab treatment at 12 weeks if the psoriasis has not responded adequately. An adequate response is defined as a 75% reduction in the PASI score (PASI 75) from when treatment started.

1.3 Choose the least expensive treatment if patients (or their parents or carers) and their clinicians consider secukinumab to be one of a range of suitable treatments. Take into account availability of biosimilar products, administration costs, dosage, price per dose and commercial arrangements.

1.4 Take into account how skin colour could affect the PASI score and make any appropriate clinical adjustments.

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1.5 These recommendations are not intended to affect treatment with secukinumab 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. 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

Secukinumab is a possible alternative to other biological treatments (adalimumab, etanercept and ustekinumab) already recommended by NICE for treating severe plaque psoriasis in children and young people.

Evidence from clinical trials shows that secukinumab is more effective than etanercept. Evidence from an indirect comparison suggests that it is similarly effective to ustekinumab. How its effectiveness compares with that of adalimumab is uncertain because of a lack of evidence, but adalimumab is thought to be similarly effective to ustekinumab.

Comparing the costs of secukinumab with those of adalimumab, etanercept and ustekinumab is appropriate because they work in a similar way and are all options for plaque psoriasis. The cost of secukinumab are similar to or lower than those of adalimumab, etanercept and ustekinumab. Therefore, secukinumab is recommended.

2 Information about secukinumab

Marketing authorisation indication

2.1 Secukinumab (Cosentyx, Novartis) has a marketing authorisation for 'the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of secukinumab is £609.39 for a 150 mg/ml prefilled syringe (excluding VAT; BNF online, accessed August 2021).

2.4 The company has a commercial arrangement (simple discount patient access scheme). This makes secukinumab 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 (section 6) considered evidence submitted by Novartis and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

It is valuable to have a range of biological treatment options for children and young people with psoriasis

3.1 The committee was aware that the aim of treatment for psoriasis is to reduce the area of skin covered with psoriatic lesions and improve symptoms such as redness, flaking and itching. It noted that children and young people have topical treatments first line. Then, if there is an inadequate response to treatment or if it is contraindicated or not tolerated, they can have systemic non-biological therapies second line. These therapies include methotrexate, ciclosporin and phototherapy. Clinicians then offer children and young people biological therapies such as adalimumab, etanercept and ustekinumab. The committee noted that, if the condition no longer responds to a biological treatment, people are offered another biological therapy. It concluded that it is valuable to have

a range of biological treatment options for plaque psoriasis that have different mechanisms of action.

Decision problem

The company's proposed population is consistent with previous NICE recommendations for biological treatments for psoriasis

3.2 The company's proposed population for this appraisal was narrower than secukinumab's marketing authorisation. This was because it excluded people who had not had systemic non-biological therapy or phototherapy. The company considered that secukinumab would be used to treat psoriasis in children and young people as an alternative to other biological therapies for psoriasis. That is, it would be used for people whose condition has not responded adequately to non-biological systemic treatment or phototherapy, or if these treatments are contraindicated or not tolerated. The committee concluded that the proposed population was consistent with previous NICE recommendations for biological treatments for psoriasis, and in line with the expected use of secukinumab in clinical practice.

Ustekinumab, etanercept and adalimumab are relevant comparators

3.3 The company provided a comparison with 2 of the biological treatments (etanercept and ustekinumab) recommended in NICE's technology appraisal guidance on adalimumab, etanercept and ustekinumab for treating plaque psoriasis in children and young people. The committee was aware that, similar to secukinumab, which is a monoclonal antibody antihuman interleukin (IL) 17 inhibitor, ustekinumab is an IL-12 and -23 inhibitor. It also noted that etanercept is a tumour necrosis factor (TNF)-inhibitor. The company did not provide a comparison with the other biological treatment in its original submission and recommended in the NICE guidance, that is, adalimumab (also a TNF inhibitor). It explained that it was not possible to connect adalimumab to the network meta-analysis because of a lack of overlap in comparators in paediatric studies.

The committee was aware that adalimumab is licensed for children and young people 4 years and older but that ustekinumab is only licensed for young people 12 years and older. So, adalimumab may be an important comparator for the 6 to 17 years age range. The committee also noted that there are several biosimilar adalimumab products available and that it represents a substantial proportion of the market share. However, it recognised that, in a chronic condition that can relapse and remit, people are likely to cycle through multiple treatments options. It was aware that cost-comparison recommendations include a statement to note that if patients and their clinicians consider the intervention to be one of a range of suitable treatments, the least expensive should be chosen. The committee concluded that ustekinumab, etanercept and adalimumab are all relevant comparators.

The definition of response is consistent with NICE's technology appraisal guidance on adalimumab, etanercept and ustekinumab

3.4 The committee recalled that, in NICE's technology appraisal guidance on adalimumab, etanercept and ustekinumab for treating plaque psoriasis in children and young people, treatment should stop if there is an inadequate disease response after an initial treatment period (etanercept at 12 weeks, and adalimumab and ustekinumab at 16 weeks). An adequate response is defined as a 75% reduction in the Psoriasis Area and Severity Index (PASI) score from the start of treatment. The committee further noted that the definition of response to secukinumab proposed by the company is in line with these criteria. It concluded that the definition of response is consistent with the other NICE technology appraisal guidance, although timing of this assessment varies slightly between different biological treatments.

Clinical effectiveness

Secukinumab is more effective than etanercept

3.5 Secukinumab has been compared with etanercept and placebo in a randomised control trial (Paediatric Study A2310) including 84 children and young people with plaque psoriasis. The trial showed that people having secukinumab had a higher PASI response rate (PASI 75, that is, a 75% reduction in PASI score from baseline) compared with placebo and etanercept at week 12. The trial also showed that, at week 52, the higher response rates were sustained. The committee accepted the results of these trials and concluded that secukinumab was likely more effective than etanercept.

Secukinumab has a similar effectiveness to ustekinumab

3.6 To provide a comparison of effectiveness with ustekinumab, the company produced network meta-analyses using a fixed-effect model with data from 4 clinical trials. The model provided PASI response rates, Children's Dermatology Life Quality Index scores and safety outcomes comparing secukinumab with etanercept, ustekinumab and placebo, The committee accepted that the model was suitable for decision making. It further noted that the results showed that secukinumab has a similar efficacy to ustekinumab and is likely to be more effective than etanercept and placebo. The committee noted the safety and outcome results were similar to those for other biologicals used for psoriasis. It concluded that secukinumab has a similar effectiveness to ustekinumab.

In the absence of evidence, it is reasonable to assume adalimumab and ustekinumab are equally effective

3.7 The company's provided network meta-analysis did not include adalimumab as a comparator. It said that this was because there were no paediatric studies of adalimumab with overlapping comparators that would allow it to be connected to the network. The committee acknowledged that it had not been possible to include paediatric adalimumab data within the

network. The company presented a scenario that assumed adalimumab to be equal in effectiveness to ustekinumab. The ERG preferred a naive indirect comparison of adalimumab from the paediatric study (comparing methotrexate and adalimumab). This comparison resulted in a lower response rate for adalimumab than etanercept. The committee thought this to be unlikely and recalled conclusions from previous appraisals on treatments for plaque psoriasis in adults and children. It acknowledged that, in NICE's technology appraisal guidance on adalimumab, etanercept and ustekinumab, some potential biases in using data from adults had been noted. However, these had been considered to have been mitigated through adjustment. The committee further noted that the conclusion in that appraisal had been that ustekinumab and adalimumab are broadly similar in effectiveness. In the absence of evidence for adalimumab, the committee concluded that it would be reasonable to assume that adalimumab and ustekinumab are equally effective, but that this was likely to be a conservative estimate.

Cost comparison

The total costs for secukinumab are similar to or lower than those for ustekinumab, etanercept and adalimumab

3.8 The company presented a cost-comparison analysis that modelled the total costs of secukinumab, ustekinumab and etanercept over 5 years. To determine the proportion of people who continue treatment, it took into account stopping treatment based on PASI 75 response rates. This was consistent with the stopping rules specified in previous NICE's technology appraisal guidance on treatments for plaque psoriasis. The company's base-case analysis assumed similar monitoring, safety profile, treatment administration and subsequent therapies for all 3 treatments. So, these costs were excluded. That is, the base-case analysis considered only the acquisition costs of secukinumab, ustekinumab and etanercept. The committee agreed that it was reasonable to assume similar healthcare resource use across the 3 treatments. The ERG considered that a 12-year

time horizon was more appropriate. It also thought that the assumption of no further costs after stopping treatment was not reflective of clinical practice. The ERG produced a cost-comparison analysis over 12 years that included adalimumab as a comparator and a scenario that simplified further treatment costs. The committee preferred the 12-year time horizon. It considered the results that accounted for the confidential patient access schemes for secukinumab and the comparators. The committee concluded that the total costs for secukinumab were similar to or lower than those for ustekinumab, etanercept and adalimumab (the exact results cannot be reported here because the discounts are confidential).

Equality issues

The PASI may not be appropriate for all people with psoriasis

3.9 The committee noted, as in previous NICE technology appraisals on psoriasis, the potential equality issues with the PASI because it might underestimate disease severity in people with darker skin. It concluded that, when using the PASI, healthcare professionals should take into account skin colour and how this could affect PASI scores, and make the clinical adjustments they consider appropriate.

Conclusion

Secukinumab is recommended as an option for treating severe plaque psoriasis in children and young people

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

- secukinumab provides similar or greater overall health benefits than ustekinumab, etanercept and adalimumab, and
- the total costs of secukinumab are similar to or lower than the total costs of ustekinumab, etanercept and adalimumab.

The committee therefore recommended secukinumab as an option for

treating plaque psoriasis in children and young people. It concluded that the recommendations for secukinumab should be consistent with the company's proposal and NICE's recommendations for other biological therapies, that is:

- if the disease is severe (that is, a PASI of 10 or more) and
- when the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and
- when treatment is stopped at 12 weeks if the psoriasis has not responded adequately
- if patients and their clinicians consider secukinumab to be one of a range of suitable treatments (for example, ustekinumab, etanercept and adalimumab), choosing the least expensive (taking into account administration costs, dosage, price per dose and commercial arrangements).

4 Implementation

4.1 Section 7(6) 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 secukinumab 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. 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.

4.2 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 moderate of sever plaque psoriasis and the doctor responsible for their care thinks that secukinumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Review of guidance

5.1 The guidance on this technology will be considered for review 3 years after publication. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Sanjeev Patel
Vice - Chair, committee B
September 2021

6 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 a health technology assessment analyst (who acts as technical lead for the appraisal), a health technology assessment adviser and a project manager.

Henry Edwards
Associate director

George Millington
Associate technical analyst

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