NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Risankizumab for treating active psoriatic arthritis after inadequate response to DMARDs

1 Recommendations

1.1 Risankizumab, alone or with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults whose disease has not responded well enough to disease-modifying antirheumatic drugs (DMARDs) or who cannot tolerate them. It is recommended only if they have:

- peripheral arthritis with 3 or more tender joints and 3 or more swollen joints
- moderate to severe psoriasis (a body surface area of at least 3% affected by plaque psoriasis and a Psoriasis Area and Severity Index [PASI] score greater than 10)
- had 2 conventional DMARDs and at least 1 biological DMARD.

Risankizumab is recommended only if the company provides it according to the commercial arrangement (see section 2).

1.2 Assess the response to risankizumab from 16 weeks. Stop risankizumab if psoriatic arthritis has not responded adequately using the Psoriatic Arthritis Response Criteria (PsARC; an adequate response is an improvement in at least 2 of the 4 criteria, 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria). If PsARC response does not support continuing treatment but there is a

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PASI 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response.

1.3 If risankizumab is one of a range of suitable treatments, including guselkumab, choose the least expensive (taking into account administration costs, dosage, price per dose and commercial arrangements).

1.4 Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the PsARC, and make any adjustments needed.

1.5 Take into account how skin colour could affect the PASI score and make any adjustments needed.

1.6 These recommendations are not intended to affect treatment with risankizumab 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

People with psoriatic arthritis that is not controlled well enough with 2 conventional DMARDs are usually offered biological DMARDs. People whose disease has not responded to a biological DMARD and who also have moderate to severe psoriasis may be offered guselkumab, an IL-23 modulator already recommended by NICE. Risankizumab is also an IL-23 modulator.

Clinical evidence shows that risankizumab is effective for active psoriatic arthritis compared with placebo. Risankizumab has not been compared directly with other biological DMARDs for psoriatic arthritis. But the results of an indirect comparison suggest that it is as effective as guselkumab, particularly for skin and joint symptoms, and likely has similar safety.

Risankizumab has similar costs to guselkumab for people with moderate to severe psoriasis who have had 2 conventional DMARDs and at least 1 biological DMARD. So, risankizumab is recommended as an option for treating active psoriatic arthritis in this group.

2 Information about risankizumab

Marketing authorisation indication

2.1 Risankizumab (Skyrizi, AbbVie) 'alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs)'.

Dosage in the marketing authorisation

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

Price

2.3 The cost of a 150 mg pre-filled disposable injection of risankizumab is £3,326.09 (excluding VAT; BNF online, accessed May 2022). The company has a commercial arrangement (simple discount patient access scheme). This makes risankizumb 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

The company's decision problem is relevant to clinical practice

3.1 Risankizumab is licensed for treating active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to 1 or more disease-modifying antirheumatic drugs (DMARDs). The company's decision problem was narrower than risankizumab's marketing authorisation. It positioned risankizumab for people who also have moderate to severe psoriasis and have previously had 2 conventional and at least 1 biological DMARD. The proposed population was consistent with NICE's technology appraisal guidance on guselkumab. Risankizumab and guselkumab are both IL-23 modulators. The company presented a comparison with guselkumab, which the committee considered was consistent with the criteria for a cost-comparison appraisal (see section 3.6). The committee noted that NICE has recommended many treatments other than guselkumab for psoriatic arthritis. But, because guselkumab is the only treatment recommended for this specific subgroup it is an appropriate comparator for a cost-comparison appraisal. The committee concluded that the company's decision problem was relevant to clinical practice.

Clinical effectiveness

Risankizumab is more effective than placebo

3.2 Risankizumab has been studied in 3 randomised controlled trials including a total of 1,592 adults with active psoriatic arthritis. These trials compared risankizumab with placebo. The KEEPsAKE-2 trial (n=443) is the focus of the company's evidence submission because 46.5% of participants had previously had a biological DMARD. In the KEEPsAKE-2 trial, risankizumab showed statistically significant improvements in primary and secondary endpoints compared with placebo: a higher proportion had an American College of Rheumatology (ACR) 20 response at 16 weeks and 24 weeks, and a higher proportion had a Psoriasis Area and Severity

Index (PASI) 90 response at 24 weeks. The committee concluded that risankizumab was more effective than placebo.

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

3.3 The company did a series of network meta-analyses (NMAs) on PASI response rates, ACR response rates and safety outcomes. These compared risankizumab with guselkumab. The ERG was satisfied with the search strategy, the methodological quality of the included trials and the methodology used for the NMAs. The committee accepted the ERG's view, concluding that the NMAs provided by the company were suitable for decision making.

Risankizumab provides similar ACR and PASI response rates to guselkumab

3.4 The NMAs showed no significant differences between risankizumab and guselkumab for any of the ACR (20, 50, 70) and PASI (50, 75, 90, 100) outcomes. Also, there were no significant differences in adverse events rates. The ERG advised that the lack of significant differences does not imply clinical equivalence and that the wide confidence intervals around the point estimates suggest uncertainty. The committee noted this uncertainty. But, it agreed that their effectiveness is likely to be comparable. This is because the point estimates were close to 1 (or 0) for the main efficacy outcomes at 24 weeks and the drugs have the same mechanism of action.

The trial results are generalisable to the population in the company's decision problem

3.5 The ERG highlighted several limitations with the NMA. The company positioned risankizumab for also treating moderate to severe psoriasis in people who have had 2 conventional DMARDs and at least 1 biological DMARD. A pre-specified subgroup of the trial had all previously had a biological DMARD. However, in this subgroup only 51.0% had also had 2 conventional DMARDs. In addition, only a small proportion of the previous

biological DMARD subgroup had moderate to severe psoriasis (the exact figures are considered confidential by the company and cannot be reported here). However, the committee recalled that when appraising guselkumab it had accepted the assumption that efficacy specific to people who had a biological DMARD was generalisable to that of people who also had 2 conventional DMARDS. Also, that modelling was appropriate regardless of disease severity. The committee agreed that the trial results were generalisable to the population in the company's decision problem.

Cost comparison

It is appropriate to assess response to risankizumab at 16 weeks

3.6 NICE's technology appraisal guidance on guselkumab recommends that response to treatment should be assessed from 16 weeks and stopped at 24 weeks if there is an inadequate Psoriatic Arthritis Response Criteria (PsARC) response. The summary of product characteristics for guselkumab specifies considering stopping treatment if no response is shown at 24 weeks. In its base case, the company modelled assessing PsARC response at 24 weeks for both treatments, aligned with the recommendation for guselkumab. However, the summary of product characteristics for risankizumab states that 'consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment'. The company also submitted a scenario modelling response assessment at 16 weeks. The committee recalled that there was strong clinical support in the appraisal of guselkumab for assessing response at 16 weeks. Also, that this is more aligned with clinical practice of using other biologic therapies for this condition. The committee considered it was appropriate to assess response to risankizumab at 16 weeks, in line with the summary of product characteristics.

The total costs associated with risankizumab are similar to or lower than those associated with guselkumab

3.7 The company presented a cost-comparison analysis that modelled the total costs of risankizumab and guselkumab over 5 years. The base case assumes that the only difference between the 2 treatment options arises from costs associated with drug acquisition. Additional scenario analyses explored the impact of variable drug administration and monitoring costs. It also assumed clinical equivalence between the 2 treatment options, based on evidence from the NMA outlined above (see section 3.3). The base case assumed treatment response was assessed at 24 weeks and applied a 16.5% annual probability of discontinuing treatment after initial assessment of response, for both risankizumab and guselkumab. This was in line with the modelling for the guselkumab appraisal for this indication. A scenario explored the impact of assessing response at 16 weeks. Taking into account the patient access scheme discounts, the total costs associated with risankizumab were similar to or lower than those associated with guselkumab. This was whether response was assessed at 16 weeks or 24 weeks (the exact results cannot be reported here because the discounts are confidential).

Risankizumab is recommended as an option for treating active psoriatic arthritis

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

- risankizumab provided similar overall health benefits to guselkumab, and
- the total costs associated with risankizumab were similar or lower than the total costs associated with guselkumab.

The committee therefore recommended risankizumab as an option for treating active psoriatic arthritis in adults. It concluded that the recommendations for risankizumab should be consistent with the

company's proposal and NICE's technology appraisal guidance on guselkumab, that is, only if the person has:

- peripheral arthritis with 3 or more tender joints and 3 or more swollen joints
- moderate to severe psoriasis (a body surface area of at least 3% affected by plaque psoriasis and a PASI score greater than 10)
- had 2 conventional DMARDs and at least 1 biological DMARD.

The response to risankizumab should be assessed from 16 weeks. If psoriatic arthritis has not responded adequately using the PsARC (an adequate response is an improvement in at least 2 of the 4 criteria, 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria), risankizumab should be stopped. If PsARC response does not support continuing treatment but there is a PASI 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response.

Clinicians should take into account factors that may affect PsARC and PASI and make any clinical adjustments needed

3.9 The committee noted that some people may have physical, sensory or learning disabilities or communication difficulties that could affect their responses to components of the PsARC. It concluded that this should be taken into account when using the PsARC. The committee was also aware that the PASI might underestimate disease severity in people with darker skin. The committee concluded that, when using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score, and make the clinical adjustments they consider appropriate.

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 risankizumab 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 psoriatic arthritis and the doctor responsible for their care thinks that risankizumab 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. NICE will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Lindsay Smith
Vice-chair, appraisal committee D
May 2022

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 D.

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) and a project manager.

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