NICE National Institute for Health and Care Excellence

NICE guidance

Guselkumab for treating moderate to severe plaque psoriasis

Technology appraisal guidance

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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 are 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.

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.

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1 Recommendations

1.1 Guselkumab is recommended as an option for treating plaque psoriasis in adults, only if:

- the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and
- the disease has not responded to other systemic therapies, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or these options are contraindicated or not tolerated and
- the company provides the drug according to the commercial arrangement.

1.2 Stop guselkumab treatment at 16 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 or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

1.3 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.

1.4 When using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties, that could affect the responses to the DLQI and make any adjustments they consider appropriate.

1.5 If patients and their clinicians consider guselkumab to be one of a range of suitable treatments, including ixekizumab and secukinumab, the least costly (taking into account administration costs and commercial arrangements) should be chosen.

1.6 This recommendation is not intended to affect treatment with guselkumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published,

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until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Guselkumab is proposed as an alternative to other biological therapies already recommended by NICE for treating severe plaque psoriasis in adults. Evidence from clinical trials and indirect comparisons show that guselkumab is more effective than TNF-alpha inhibitors (that is, adalimumab, etanercept and infliximab) and ustekinumab. It also suggests that guselkumab is likely to provide similar health benefits to ixekizumab and secukinumab.

For the cost comparison, it is appropriate to compare guselkumab with ixekizumab and secukinumab. Taking into account how many people continue treatment (which affects the cost to the NHS), guselkumab provides similar health benefits to ixekizumab and secukinumab at a similar or lower cost. It is therefore recommended as an option for treating plaque psoriasis in the NHS.

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2 Information about guselkumab

Marketing authorisation	Guselkumab (Tremfya, Janssen) is indicated for 'the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy'.
Dosage in the marketing authorisation	The recommended dosage of guselkumab is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a 100 mg maintenance dose every 8 weeks. Consideration should be given to stopping treatment in people whose disease has shown no response after 16 weeks of treatment.
Price	The list price of guselkumab is £2,250 per prefilled syringe (excluding VAT; British national formulary online; accessed March 2018). The company has a commercial arrangement. This makes guselkumab 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.

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3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Janssen and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence. The company proposed that this technology be considered in a fast track appraisal using cost-comparison methodology.

Decision problem

The company's decision problem is relevant to clinical practice

3.1 The company proposed that guselkumab should be considered as an alternative to other biological therapies for psoriasis in adults when non-biological systemic treatment or phototherapy is inadequately effective, not tolerated or contraindicated. The committee understood that the company's proposed decision problem was narrower than guselkumab's marketing authorisation. However, it agreed that the proposed population was consistent with previous NICE recommendations for biologicals for psoriasis, and with their use in clinical practice. The committee noted that the company presented comparisons with NICE-recommended biologicals, and considered that this was consistent with the criteria for a cost-comparison appraisal (the appropriateness of specific comparators is discussed in section 3.7). The committee recalled that previous technology appraisal guidance recommendations specified that treatment should stop if there is an inadequate response after induction. An adequate response is defined as:

- a 75% reduction in the Psoriasis Area and Severity Index score (PASI 75) from when treatment started or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in Dermatology Life Quality Index (DLQI) from when treatment started.

The committee considered that it would be reasonable to consider a similar approach for this appraisal. It accepted that the company's positioning reflected the likely place of guselkumab in clinical practice, and concluded that the company's decision problem was relevant to clinical practice.

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Clinical effectiveness

Guselkumab is more effective than adalimumab

3.2 Guselkumab has been studied in 3 randomised controlled trials including a total of 2,096 adults with plaque psoriasis. It was directly compared with adalimumab in 2 trials, VOYAGE-1 and VOYAGE-2. In these trials, guselkumab was associated with statistically significant improvements compared with adalimumab in primary and secondary outcomes, including PASI response rates. The committee noted, in particular, that patients randomised to guselkumab were statistically significantly more likely to have a PASI 75 response after induction (that is, at week 16) compared with adalimumab (VOYAGE-1: PASI 75 response rates 91.2% and 73.1% respectively, $p<0.001$). The committee accepted that the results of the VOYAGE trials showed that guselkumab was more effective than adalimumab.

The company's network meta-analysis is suitable for decision-making

3.3 The company's network meta-analysis compared guselkumab with adalimumab, etanercept, infliximab, ixekizumab, secukinumab and ustekinumab, using data from 45 trials. It understood that the ERG preferred the analyses based only on comparators specified in the decision problem (termed the 'restricted analyses') because these matched the scope. The committee accepted the ERG's view and concluded that the network meta-analysis provided by the company was suitable for decision-making.

Guselkumab provides greater benefits than TNF-alpha inhibitors and ustekinumab, and similar benefits to secukinumab and ixekizumab

3.4 The committee noted that the results of the network meta-analysis suggested that guselkumab was statistically significantly more effective, in terms of PASI 75 response, than the TNF-alpha inhibitors (that is, adalimumab, etanercept and infliximab) and ustekinumab. It considered that guselkumab would provide substantial clinical benefits over adalimumab, etanercept, infliximab and ustekinumab in practice. It also considered that, although guselkumab appeared to be statistically significantly better than secukinumab in terms of PASI 75 response in the network meta-analysis, the difference might not be clinically meaningful. The committee also noted that guselkumab was similarly effective to ixekizumab in this outcome, and that no statistically

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significant difference was seen. It therefore considered that guselkumab was likely to provide similar benefits to secukinumab and ixekizumab in clinical practice. The committee acknowledged that PASI 75 is a key outcome for informing treatment continuation after induction. However, it also understood that patients are interested in having complete clearance of their psoriasis symptoms so it considered that PASI 100 is also a relevant outcome. The committee appreciated that the company analyses also covered a range of outcomes, and that the results for PASI 100 were broadly consistent with those for PASI 75. The committee noted the safety and tolerability outcomes in the company's network meta-analysis and considered that guselkumab had a similar safety profile to other biologicals, regardless of treatment class. It concluded that guselkumab provides substantially greater clinical benefits compared with adalimumab, etanercept, infliximab and ustekinumab, and is likely to provide similar benefits to secukinumab and ixekizumab.

Cost comparison

The committee prefers the cost-comparison analysis provided by the ERG

3.5 The company presented a cost-comparison analysis that modelled the total costs of guselkumab, adalimumab and ustekinumab treatment over 5 years. It took into account stopping treatment after induction (based on PASI 75 response rates, which was consistent with the stopping rules specified in NICE technology appraisal guidance for the comparators), using an assumption that guselkumab and the comparators were similarly effective (that is, it assumed clinical similarity between treatments). The analysis also took into account the long-term stopping of treatment during maintenance therapy. The committee noted the ERG's view that assuming similar effectiveness was inappropriate because of the statistically significant differences between treatments in clinical effectiveness. Therefore, the ERG presented exploratory analyses either using the company's assumption of clinical similarity, or using different treatment continuation rates for each treatment based on PASI 75 response rates from the network meta-analysis (see section 3.4). These exploratory analyses included all biologicals and used a 10-year time horizon. The committee appreciated that guselkumab is statistically significantly more effective than some other subcutaneous biological treatments (see section 3.4). It was aware that differences in effectiveness led to differences in the number of people stopping treatment after induction, resulting in differences in treatment duration

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between therapies and hence differences in costs to the NHS. It considered that treatment duration should be taken into account in a cost-comparison analysis when it is directly affected by clinical effectiveness, and that when there is a difference in effectiveness between guselkumab and a comparator, different continuation rates should be used. The committee therefore concluded that the ERG's cost-comparison analysis was preferable for decision-making.

Secukinumab and ixekizumab are the relevant comparators for cost comparison

3.6 For comparators in its base case, the company focused on adalimumab and ustekinumab. The committee understood that the company chose these because they are the most frequently used biologicals for psoriasis, and accepted this rationale. However, it recalled the statistically and clinically significant increased benefits for guselkumab compared with adalimumab and ustekinumab (see section 3.2), and that such increased benefits affected the cost comparison (see section 3.5). It noted that, in the ERG's analysis, guselkumab was more expensive than adalimumab and ustekinumab. The committee also noted that, when a technology provides greater benefits than a comparator but at a greater cost, it is not possible to reach a conclusion using cost-comparison methods. It therefore concluded that adalimumab and ustekinumab were not acceptable comparators to focus on in a cost-comparison context. Conversely, the committee recognised that, because guselkumab, ixekizumab and secukinumab are likely to provide similar clinical benefits (see section 3.4), it was possible to reach a recommendation using cost-comparison methods by considering the comparison of guselkumab with secukinumab and ixekizumab. It noted that secukinumab has a rapidly growing market share, and that ixekizumab is expected to be used more frequently over time. The committee concluded that ixekizumab and secukinumab, not adalimumab and ustekinumab, were the relevant comparators for the cost-comparison analysis.

Guselkumab meets the criteria to be recommended using cost comparison

3.7 The committee focused on the cost comparison with ixekizumab and secukinumab using the ERG's exploratory analyses (see section 3.5) and taking into account all confidential patient access schemes. In these analyses, the total costs associated with guselkumab were similar to or lower than those associated with ixekizumab and secukinumab (the exact results cannot be reported here because the discounts are confidential). The committee concluded that the criteria for a positive cost comparison were met because:

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

The committee therefore recommended guselkumab as an option for treating plaque psoriasis in adults. It concluded that the recommendations for guselkumab should be consistent with the company's proposal and the NICE recommendations for ixekizumab and secukinumab, that is:

- for people with severe disease (a PASI of 10 or more and a DLQI of more than 10) and
- when the disease has not responded to standard systemic therapies or when these treatments are unsuitable
- and with consideration given to stopping treatment after induction if the disease does not respond adequately.

The PASI and DLQI may not be appropriate for all people with psoriasis

3.8 The committee noted, as in previous NICE technology appraisals on psoriasis, potential equality issues:

- the PASI might underestimate disease severity in people with darker skin
- the DLQI has limited validity in some people, and may miss anxiety and depression.

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. Also, it concluded that, when using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties, that could affect the responses to the DLQI and make any adjustments they consider appropriate.

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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 guselkumab 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 determination.

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

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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.

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