NICE National Institute for Health and Care Excellence

NICE guidance

Nemolizumab for treating moderate to severe atopic dermatitis in people 12 years and over

Technology appraisal guidance
Published: 2 July 2025

www.nice.org.uk/guidance/ta1077

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 Nemolizumab with topical corticosteroids or calcineurin inhibitors, or both, can be used as an option to treat moderate to severe atopic dermatitis. It can be used in people 12 years and over with a body weight of 30 kg or more when systemic treatment is suitable, only if:

- the atopic dermatitis has not responded to at least 1 systemic immunosuppressant, or these treatments are not suitable, and
- a biological medicine would otherwise be offered, and
- the company provides nemolizumab according to the commercial arrangement.

1.2 Stop nemolizumab after 16 weeks if there has not been an adequate response, defined as a reduction from starting treatment of at least:

- 50% in the Eczema Area and Severity Index score (EASI 50)
- 4 points in the Dermatology Life Quality Index (DLQI).

1.3 Consider how skin colour could affect the EASI score and make any clinical adjustments needed.

1.4 Consider any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI, and make any clinical adjustments needed.

1.5 This recommendation is not intended to affect treatment with nemolizumab 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, until they and their NHS healthcare professional consider it appropriate to stop. For young people, this decision should be made jointly by the healthcare professional, the young person, and their parents or carers.

What this means in practice

Nemolizumab must be funded in the NHS in England for the condition and population in the recommendations, if it considered the most suitable treatment option. Nemolizumab must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that nemolizumab provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has produced tools and resources to support the implementation of this guidance.

Why the committee made these recommendations

Usual treatment for moderate to severe atopic dermatitis (eczema) includes emollients, corticosteroids and calcineurin inhibitors applied to the skin. If these treatments are not effective, systemic immunosuppressants can be added. If these are also not effective, or are unsuitable, a Janus kinase (JAK) inhibitor or a biological medicine can be used.

For this evaluation, the company asked for nemolizumab to be considered only for people who have had at least 1 systemic immunosuppressant treatment or when these are not suitable. This does not include everyone who it is licensed for.

Clinical trial evidence shows that nemolizumab is more effective than placebo at improving the symptoms of atopic dermatitis. Indirect comparisons with JAK inhibitors and with other biological medicines suggest that nemolizumab may work as well as most of these treatments.

The cost-effectiveness estimates for nemolizumab are within the range that NICE considers an acceptable use of NHS resources when compared with biological medicines, but not when compared with JAK inhibitors. So, nemolizumab can be used when a biological medicine would otherwise be offered.

2 Information about nemolizumab

Marketing authorisation indication

2.1 Nemolizumab (Nemluvio, Galderma) is indicated for 'the treatment of moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors in adults and adolescents 12 years and older with a body weight of at least 30 kg, who are candidates for systemic therapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of nemolizumab is £2,257 per 30-mg unit (company submission).

2.4 The company has a commercial arrangement. This makes nemolizumab available to the NHS with a discount. The size of the discount is commercial in confidence.

Carbon Reduction Plan

2.5 For information, the Carbon Reduction Plan for UK carbon emissions is published on Galderma's webpage on sustainability.

3 Committee discussion

The evaluation committee considered evidence submitted by Galderma, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of condition and patient perspectives

3.1 Atopic dermatitis (eczema) is a common, chronic and flaring inflammatory skin condition. The exact cause is unknown but involves genetic susceptibility and environmental triggers. Symptoms include dry, flaky and inflamed skin, which can be intensely itchy, and painful lesions typically affecting the hands, eyelids and skin folds. Patient experts explained that atopic dermatitis is often thought to be a minor condition, but moderate to severe atopic dermatitis can take over all aspects of life. Physical symptoms such as the inability to regulate temperature, weeping sores, pain and constant itch substantially impact quality of life. Another patient expert highlighted the substantial impact on sleep, education and the ability to form relationships. These all substantially impact mental health, leading to anxiety, depression and suicidal thoughts. They added that the effects of the condition can be particularly hard for younger people. This is because of a lack of acceptance among peers and the false expectation that they may 'grow out' of the condition after childhood. There is also a huge sense of responsibility and burden for parents of younger people with the condition. Patient expert submissions described the frustrating, and often unsuccessful, process of 'trial and error' to find a treatment that works. They added that even if a treatment works initially, the effects often wear off over time, resulting in an unmet need for new and effective treatments. A patient expert noted that some current treatments can have troubling side effects (such as eye problems) that could be avoided with nemolizumab. Patient experts added that the reduced frequency of injections with nemolizumab is also a notable advantage compared with current treatments. The committee concluded that there is an unmet need for additional effective treatments for atopic dermatitis and that nemolizumab has a reduced administration frequency compared with current treatments.

Clinical management

Treatment pathway

3.2 Moderate to severe atopic dermatitis is initially treated with emollients, topical corticosteroids and topical calcineurin inhibitors. When the condition has not responded adequately to topical treatment, first-line systemic immunosuppressants may be offered. These include azathioprine, ciclosporin, methotrexate and mycophenolate mofetil. If the condition does not respond to first-line systemic immunosuppressants, or if these are not tolerated or not suitable, then a biological medicine (dupilumab, lebrikizumab or tralokinumab) or a Janus kinase (JAK) inhibitor (abrocitinib, baricitinib or upadacitinib) can be offered. The company positioned nemolizumab after first-line systemic treatments or if these treatments are not suitable. The clinical experts agreed with the company's positioning. The committee concluded that nemolizumab was appropriately positioned. The committee added that, in practice, adults would likely have biological medicines such as nemolizumab as a second-line systemic treatment after first-line systemic immunosuppressants, but young people would likely have these at first line. This is because typical first-line systemic options are not suitable for young people.

Comparators

3.3 Comparators for nemolizumab in the company's model included the JAK inhibitors abrocitinib, baricitinib or upadacitinib, and the biological medicines dupilumab, lebrikizumab or tralokinumab, but not first-line systemic treatments such as ciclosporin or methotrexate. In its submission, the company noted that the previous NICE technology appraisal recommendations for baricitinib, dupilumab and tralokinumab were for adults only. So, it did not initially include these treatments as comparators for young people. The EAG highlighted in its report that the marketing authorisations for dupilumab and tralokinumab have since been extended (to people 6 months and over for dupilumab and 12 years and over for tralokinumab). Clinical advice to the EAG was that both dupilumab and tralokinumab are used in young people so these should also be included as comparators. The company updated its model at clarification stage to include

dupilumab and tralokinumab for young people. At the committee meeting, a clinical expert explained that treatment choice is highly individual. Comorbidities, the safety profiles of treatments, individual preference for an injection or oral medicine, and how fast a response is needed all impact treatment choice. The clinical expert added that JAK inhibitors may be used by people who prefer an oral medicine. JAK inhibitors are also faster acting than biological medicines. But JAK inhibitors may not be suitable for everyone because they have a higher risk of venous thromboembolism and cardiovascular events. The committee concluded that both JAK inhibitors and biological medicines were relevant comparators and noted that this was in line with previous NICE technology appraisals of biological medicines for moderate to severe atopic dermatitis.

Clinical effectiveness

Clinical trials

3.4 The clinical evidence for nemolizumab came from the ARCADIA 1 (n=941), ARCADIA 2 (n=787) and ARCADIA-CYCLO (n=276) trials. ARCADIA 1 and ARCADIA 2 were phase 3, double-blind, randomised controlled trials comparing nemolizumab with placebo in adults and young people over 12 years with moderate to severe atopic dermatitis. ARCADIA-CYCLO was a phase 3b, double-blind, randomised controlled trial comparing nemolizumab with placebo in adults whose condition was not adequately controlled with ciclosporin or for whom ciclosporin was unsuitable. In all trials, best supportive care with treatments such as emollients, topical corticosteroids and topical calcineurin inhibitors was used alongside nemolizumab or placebo. The primary outcomes in ARCADIA 1 and ARCADIA 2 were assessed at week 16. These included EASI 75 response (a reduction of at least 75% from baseline Eczema Area and Severity Index [EASI] score) and Investigator's Global Assessment (IGA) success (defined as an IGA of 0 [clear] or 1 [almost clear], and at least a 2-point reduction from baseline). The primary outcomes in ARCADIA-CYCLO were EASI 75 and Peak Pruritus Numerical Rating Scale, a measure of itch intensity. In ARCADIA 1 and ARCADIA 2 there was a statistically significantly greater proportion of people with EASI 75 response for nemolizumab compared with placebo at week 16 (ARCADIA 1, 43.5% versus 29.0%; ARCADIA 2, 42.1% versus 30.2%). This response was continued in the

pooled maintenance period up to week 48. Similarly, there was a statistically significantly greater proportion of people with IGA success for nemolizumab compared with placebo at week 16 (ARCADIA 1, 35.6% versus 24.6%; ARCADIA 2, 37.7% versus 26.0%). This was continued in the pooled maintenance period up to week 48. Results of ARCADIA-CYCLO are considered confidential by the company so cannot be reported here. The committee concluded that nemolizumab was more effective than placebo.

Network meta-analysis

3.5 There were no clinical trials directly comparing nemolizumab with the relevant comparators (see section 3.3). So, the company did a network meta-analysis (NMA) for a range of efficacy, quality-of-life and adverse-event outcomes. EASI 75 response at week 16 was the efficacy outcome used in the economic model (see section 3.7). Separate NMAs were done for:

- adults (18 years or over), second-line treatment (ciclosporin-experienced)
- young people (12 to 17 years), first-line treatment (ciclosporin-naive).

The company's NMA results for the second-line adult population did not show a statistically significant difference in the odds of EASI 75 response for nemolizumab compared with the biological medicines (dupilumab, lebrikizumab and tralokinumab) or JAK inhibitors (abrocitinib, baricitinib and 15 mg upadacitinib). But the results did show a statistically significant difference in favour of 30 mg upadacitinib. The company's NMA results for the first-line young-people population did not show a statistically significant difference in the odds of EASI 75 response for nemolizumab compared with abrocitinib, lebrikizumab or 15 mg upadacitinib. The company's NMA in the first-line young-people population showed a statistically significant difference in favour of 30 mg upadacitinib, but it was noted that this is not the recommended starting dose for adolescents. The exact odds ratios from the NMA are considered confidential by the company so cannot be reported here. The EAG did its own NMA to validate the company's NMA and to correct minor methodological issues. Results of the EAG's NMA were similar to the company's for both populations. The committee noted the uncertainty in the company's NMA results, as shown by wide credibility intervals around

odds ratios.

Clinical equivalence assumption

3.6 When results of the company's NMA did not show a statistically significant difference between nemolizumab and a comparator (see section 3.5), the company assumed clinical equivalence. That is, the company assumed that each comparator had the same efficacy as nemolizumab, by applying an odds ratio of 1 in its economic model. The EAG did not agree with the company's approach. It preferred to use point estimates for the odds ratios based on the EAG's own NMA. Clinical experts considered whether all the biological medicines could be assumed to have the same efficacy. One clinical expert explained that they each have different mechanisms of action, which is likely to result in them having different efficacy and tolerability profiles. But the expert explained that the current biological medicines target the same immune pathway. They also noted that nemolizumab may improve symptoms of itching more than other biological medicines because of its unique mechanism of action. The committee noted that point estimates from the NMA showed substantial differences between treatments (odds ratios not close to 1). It added that the wide credible intervals suggested high uncertainty around the relative benefits. The committee noted that not finding a statistically significant difference in efficacy between treatments is not the same as the treatments being clinically equivalent. The committee concluded that it could not assume equal efficacy across all the biological medicines in either adults or young people. The committee concluded that it preferred using the EAG's approach with point estimates of odds ratios from the EAG's NMA, rather than assuming clinical equivalence.

Economic model

Company's modelling approach

3.7 The company's economic model was a hybrid model that consisted of a short-term (1-year) decision tree followed by a long-term Markov model (year 2 onwards). At baseline, people in the model had nemolizumab or a comparator for

a 16-week induction period. People whose condition had responded to treatment at week 16 were described as 'responders' and were able to continue maintenance treatment with nemolizumab or a comparator up to week 52. 'Non-responders' were people who had an initial treatment response at week 16 that was then lost, or people who stopped treatment for any reason including side effects by week 52. After week 52, responders and non-responders entered different phases of the long-term Markov model. The long-term Markov model included 3 mutually exclusive health states: maintained response, no response, and dead. Transitions between health states were informed by probabilities of losing response, discontinuation and death. For the long-term Markov model, an annual cycle length with a half-cycle correction was applied. The model assumed a time horizon of 60 years and applied an annual discount rate of 3.5% for costs and quality-adjusted life years (QALYs). The company's base-case model assumed clinical equivalence between treatments when NMA results were not statistically significantly different (see section 3.6). This meant that the QALY gain for nemolizumab in the company's model was small and resulted from nemolizumab having a better side-effect profile and lower probability of flare-ups. The EAG corrected model programming errors and minor issues with the company's model, including increasing the time horizon to cover an entire lifetime. The committee concluded that the corrected model was suitable for decision making.

Discontinuation probability

3.8 The company did not use the discontinuation probabilities obtained in ARCADIA 1 and 2 because it thought that these were likely to be different to those observed in current practice. Instead, the company assumed the same discontinuation probability for nemolizumab as other biological medicines. It used the discontinuation probabilities used in NICE's technology appraisal guidance on lebrikizumab (TA986), which were applied according to treatment class (3.9% for biological medicines and 10.0% for JAK inhibitors). These were based on clinical opinion rather than trial data and were substantially different to the discontinuation probabilities observed in ARCADIA 1 and 2. The company provided data to explain the difference between the discontinuation probabilities observed in the trials and the treatment-class-based discontinuation probabilities used in TA986. The data showed a large proportion of people stopped treatment

at their own request. The company believed that this had been affected by the COVID-19 pandemic, when the trials were done. The company also provided a naive comparison of discontinuation probabilities at 16 weeks of nemolizumab, dupilumab, lebrikizumab and tralokinumab. The EAG said that the naive comparisons were not useful for decision making. Instead, it did 3 NMAs comparing the discontinuation probabilities of nemolizumab in the trials with discontinuation probabilities of other treatments. These compared the:

- discontinuation probabilities of each comparator with nemolizumab
- discontinuation probabilities of each treatment class with nemolizumab
- placebo discontinuation probabilities in the first 16 weeks.

The results of the NMAs are confidential and cannot be reported here. The EAG explained that there were limitations to the NMAs. This is because data was only available from the first 16 weeks, and JAK inhibitors appear to have a much lower discontinuation rate than seen in current practice. The EAG used the discontinuation probabilities from TA986 in its base case and explored 4 scenario analyses. One scenario analysis used discontinuation probabilities from ARCADIA 1 and 2. The other 3 scenario analyses used different discontinuation probabilities obtained from its NMAs. The EAG's scenario analyses had a large impact on the cost-effectiveness results. Nemolizumab was cost effective against some but not all comparators. Which comparators were less cost effective than nemolizumab differed by scenario. Clinical experts could not explain why discontinuation probabilities for nemolizumab would be different from those for other biological medicines, because nemolizumab appeared to be better tolerated. Another clinical expert explained that the discontinuation probabilities in the trials may be different because the number of alternative treatment options has increased since biological medicines were first recommended by NICE. The EAG and clinical experts noted that the results of the NMAs should be interpreted with caution. The committee would have preferred to see the company produce a hierarchical Bayesian NMA to better assess the variability between the treatments. In the absence of this, the committee preferred to use the EAG's NMA results over the naive comparison provided by the company. It agreed that while trial-based data was preferred, the discontinuation probabilities from ARCADIA 1 and 2 may have been affected by the COVID pandemic. It

noted that nemolizumab is unlikely to have a largely different discontinuation probability compared to other biological medicines. So, it opted for the scenario analysis that used discontinuation probabilities taken from the EAG's NMA that assumed equal discontinuation rates for nemolizumab and all other biological medicines. This had a slightly higher class-based discontinuation probability than the one previously agreed in TA986.

Utility values

3.9 Health-state utility values in the company's and EAG's models for responders (in years 1 and 2) and non-responders were based on the EQ-5D-3L data from ARCADIA 1 and ARCADIA 2 (for both adults and young people) and ARCADIA-CYCLO (for adults only). The health-state utility value for responders (in year 3 and beyond) was based on a long-term extension study. The committee noted that some of the utility values seemed implausibly high compared with general population utility values, and also higher than those used in TA986. The committee preferred to cap health-state utility values in the model at general population levels. The company said that capping utility values would not accurately capture the difference in utility between responders and non-responders. It suggested that if a utility cap is applied, then an equal utility decrement should be applied to all health states to ensure this difference is retained. The EAG presented 2 base cases in which a utility cap was applied:

- at general population levels
- at general population levels and an equal utility decrement was applied to all health states.

The committee considered that utility values higher than the general population remained implausible and so preferred the EAG base case that included the utility cap and decrement.

Severity

3.10 NICE's methods on conditions with a high degree of severity did not apply.

Cost-effectiveness estimates

Acceptable ICER

3.11 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty resulting from the company's NMA (see section 3.5). But it also recalled the potential benefit of nemolizumab's novel mechanism of action in reducing itching (see section 3.6). Clinical experts added that EASI scores are not very sensitive to improvements in itch symptoms and so this benefit has not been captured fully. A patient expert explained that symptoms can vary greatly by day, and so the EASI score at an appointment may not reflect the full extent of symptoms experienced at other times. The committee considered the psychological impact of the condition, particularly on young people (see section 3.1). But it noted that, on balance, elements of these were already factored into the QALY calculation. It also noted nemolizumab's reduced administration frequency compared with other biological medicines (see section 3.1). The committee concluded that an acceptable ICER would be around the middle of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

Company and EAG cost-effectiveness estimates

3.12 Because of confidential discounts for nemolizumab and the comparators, the company's and EAG's cost-effectiveness results are confidential and cannot be reported here. The EAG presented results using a fully incremental analysis for all comparators (JAK inhibitors and biological medicines) and also calculated pairwise net monetary benefit for each comparator individually. Net monetary benefit was presented because the cost-effectiveness results spanned all quadrants of the cost-effectiveness plane. The EAG corrected minor issues in the

company's base case and used point estimates for odds ratios (see section 3.6). The committee preferred the EAG's base case that applied a cap on health-state utility values at general population levels and applied an equal utility decrement to all health states (see section 3.9). The committee also preferred using:

- the discontinuation probability obtained from the EAG's NMAs that assumed equal discontinuation rates for nemolizumab and all other biological medicines (see section 3.8)
- stopping treatment after 16 weeks if there is not an adequate response (defined as EASI 50 and a reduction of 4 points or more in the Dermatology Life Quality Index [DLQI]). This is consistent with the recommendations for the comparator treatments and had a small impact on the cost-effectiveness results.

  The committee understood that nemolizumab would not be cost effective against JAK inhibitors but that it was cost effective against some biological medicines in both adults and young people. This is when using its preferred assumptions, and when assessing pairwise ICERs and incremental net monetary benefit.

Equality

3.13 Stakeholders highlighted that moderate to severe atopic dermatitis may be more common in people from Black or Asian ethnicities, or in people living in deprived or urban areas. The committee concluded that issues related to differences in prevalence or incidence of a disease cannot be addressed in a technology appraisal. Stakeholders also highlighted that measures such as EASI are part of the inclusion criteria for many clinical trials for atopic dermatitis, including the trials for nemolizumab. Because erythema (redness of the skin) is one of the clinical signs used to determine EASI score, severity can be underestimated in people with black or brown skin. This could lead to undertreatment or exclusion from clinical trials. They explained that inflammation may also have a greater impact on people with black or brown skin because it may result in long-term pigmentation changes. Race is a protected characteristic under the Equality Act 2010. The committee noted that healthcare professionals should consider how

skin colour could affect the EASI score and make any clinical adjustments needed. Stakeholders noted that some neurodiverse young people may struggle with using certain comparator treatments. They said that this is because of sensory issues and because a higher frequency of injections and primary or secondary care visits may be needed compared with nemolizumab. Stakeholders further highlighted that the DLQI may not adequately capture the impact of the condition in older people or those not in a relationship, and may capture anxiety and depression poorly. Furthermore, they said that lower socioeconomic groups may have difficulties accessing JAK inhibitors and that some treatments may not be suitable for people who are unable to store it in the right conditions. Age and disability are protected characteristics under the Equality Act 2010. The committee considered all the potential equality issues raised by stakeholders and concluded that its recommendation would not differentially impact anyone on the basis of any protected characteristic.

Conclusion

3.14 The committee concluded that the cost-effectiveness estimates for nemolizumab compared with some biological medicines were within the range that NICE considers a cost-effective use of NHS resources. So, it recommended nemolizumab for treating moderate to severe atopic dermatitis when a biological medicine would otherwise be offered.

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 integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of 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 guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

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 atopic dermatitis and the healthcare professional responsible for their care thinks that nemolizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation 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 being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

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

Chair

Charles Crawley
Chair, technology appraisal committee B.

NICE project team

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

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