NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Nemolizumab for treating moderate to severe prurigo nodularis

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using nemolizumab in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: March 2025

Note that this document is not NICE's final guidance on nemolizumab. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using nemolizumab in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 24 April 2025
- Second evaluation committee meeting: TBC
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Nemolizumab should not be used to treat moderate to severe prurigo nodularis in adults when systemic treatments are suitable.

1.2 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.

What this means in practice

Nemolizumab is not required to be funded in the NHS in England to treat moderate to severe prurigo nodularis in adults when systemic treatments are suitable. It should not be used routinely in the NHS in England.

This is because the available evidence does not suggest that nemolizumab is value for money.

Why the committee made these recommendations

Usual treatment for moderate to severe prurigo nodularis is best supportive care. This includes systemic treatments (treatments that work throughout the body), such as corticosteroids and immunosuppressants.

Clinical trial evidence shows nemolizumab relieves itch and reduces the number of nodules compared with placebo.

There are uncertainties in the economic model. This is because of how it defines treatment response and how it reflects quality of life. Also, it does not appropriately consider what happens if the condition only partially responds to treatment.

Because of the uncertainties in the economic model, it is not possible to determine the most likely cost-effectiveness estimates for nemolizumab. So, it should not be used.

2 Information about nemolizumab

Marketing authorisation indication

2.1 Nemolizumab (Nemluvio, Galderma) is indicated for 'the treatment of adults with moderate-to-severe prurigo nodularis 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 (excluding VAT; company submission).

2.4 The company has a commercial arrangement, which would have applied if nemolizumab had been recommended.

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 current treatment options

3.1 Prurigo nodularis is a rare, chronic condition that affects the skin. It is characterised by firm, thick nodules (or bumps) on the surface of the skin. The cause of prurigo nodularis is unknown but it is associated with unusual levels of nerve fibres, neuropeptides and cytokine-producing

immune cells. Prurigo nodularis causes an intense and constant itch. The itch often disturbs sleep and can substantially affect quality of life. The appearance of the nodules can also be distressing for people with prurigo nodularis. The patient experts explained that prurigo nodularis has a large impact on all aspects of life. They highlighted its sustained and detrimental effect on their physical, mental and social health.

There is no established standard care for prurigo nodularis. The clinical experts explained that treatment usually follows a stepped approach, where the first treatments are emollients, topical corticosteroids, topical calcineurin inhibitors and antihistamines. After these, other treatments include phototherapy, topical capsaicin, and intralesional and oral corticosteroids. Immunosuppressants, antidepressants, pregabalin and gabapentin may also be considered. Finally, in the most severe cases, neurokinin-1 receptor antagonists, mu-opioid antagonists and thalidomide may be considered. None of these treatments has a marketing authorisation in the UK for treating prurigo nodularis. The patient experts explained that many people find these treatments ineffective, and systemic treatments in particular can have damaging side effects. This means that, in practice, for some people these treatments may not be suitable and they may have no other treatment options. The committee concluded that there is an unmet need for targeted treatment options for people with moderate to severe prurigo nodularis.

Clinical management

Comparators

3.2 The comparator in the company's submission was best supportive care, which included topical emollients, topical corticosteroids, topical calcineurin inhibitors, antihistamines, systemic corticosteroids and immunosuppressants. The EAG noted that in NHS practice people might have more treatments. For example, the company did not include phototherapy or antidepressants as comparators. The company stated that the treatments considered to constitute best supportive care were

informed by clinical experts. The company's clinical experts did not consider phototherapy or antidepressants to be commonly used to treat prurigo nodularis. The committee noted that neurokinin-1 receptor antagonists, mu-opioid antagonists and thalidomide were not included as comparators. But it recognised that there is no standard treatment pathway for moderate to severe prurigo nodularis in NHS practice. The clinical experts agreed that the company's comparators and the positioning of nemolizumab were appropriate. They stated that they would prefer to offer nemolizumab to anyone who required systemic therapy, rather than restrict its use to people who have already tried other systemic therapies. The committee noted that the population that would be eligible for nemolizumab in practice, based on the population included in the marketing authorisation, was fairly broad and did not restrict use of nemolizumab based on previous systemic treatments. The committee concluded that best supportive care was the appropriate comparator and the company's definition of best supportive care was acceptable.

Clinical effectiveness

Data sources

3.3 The clinical evidence came from 2 phase 3 randomised, multicentre, double-blind, placebo-controlled trials (OLYMPIA 1 [n=286] and OLYMPIA 2 [n=274]) and a long-term extension study (n=508). The trials measured itch using the Peak Pruritis Numerical Rating Scale (PP NRS) and number of nodules using the Investigator Global Assessment (IGA) scale. In OLYMPIA 1 at week 16, 58.4% of people having nemolizumab improved from baseline by at least 4 points on the PP NRS, compared with 16.7% of people having placebo. 26.3% of people having nemolizumab scored 0 or 1 on the IGA scale and reduced by more than 2 points from baseline, compared with 7.3% of people having placebo. In OLYMPIA 2 at week 16, 56.3% of people having nemolizumab improved from baseline by at least 4 points on the PP NRS, compared with 20.9% of people having placebo. 37.7% of people having nemolizumab scored 0

or 1 on the IGA scale and reduced by more than 2 points from baseline, compared with 11.0% of people having placebo. There were also results from OLYMPIA 1 at 24 weeks, but the company considers these confidential so they are not reported here. The committee concluded that nemolizumab was effective in relieving itch and decreasing the number of nodules.

Generalisability

3.4 The inclusion criteria for OLYMPIA 1 and 2 required people to have at least 20 nodules, an IGA score of at least 3 and a PP NRS score of at least 7. The marketing authorisation for nemolizumab is for moderate to severe disease. The clinical experts noted that, in practice, they may not strictly use the trial inclusion criteria, such as IGA score, to classify the disease as moderate or severe. The patient experts agreed that itch is the most important measure of disease severity. So, in practice, the population eligible for treatment with nemolizumab is likely to be broader than the trial population. This would mean that, in practice, best supportive care would include more treatments than used in the trial. The committee agreed that it would consider the generalisability of the trial results to the broader population in its decision making.

Economic model

Company's modelling approach

3.5 The company's model had 2 stages: a decision tree for 16 weeks, followed by a Markov model with a lifetime horizon. At the end of the decision tree at 16 weeks, people were assigned a response status, depending on whether their condition did or did not respond to treatment (from here, referred to respectively as 'responder' and 'non-responder'). Response to treatment was assessed by a composite measure of itch relief and nodule reduction. People then transitioned into the appropriate health state in the Markov model. The Markov model had 3 health states: responder, non-responder (a tunnel state for up to 3 cycles) and death.

People could transition from the responder to the non-responder state, but could not transition from the non-responder to responder state. In the model, treatment with nemolizumab was stopped when the composite response (see section 3.6) was not reached after 16 weeks of treatment or when a response was lost. The summary of product characteristics for nemolizumab states that 'consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment for prurigo nodularis'. The clinical experts said that if someone was having some benefit from treatment but not to the level of the composite response, they would want to continue treatment beyond 16 weeks. The committee decided that the stopping rule in the company's model did not reflect how nemolizumab would be used in practice. The EAG said that its preferred model structure would include a partial response state, where people could still have treatment with some quality-of-life benefits even if the full composite response was not reached. The committee agreed that it would prefer a model that could account for some people whose condition didn't reach the full response definition continuing to have nemolizumab and having some benefit from it, to better reflect how nemolizumab would be used in clinical practice.

Definition of response

3.6 The response criterion used in the model was a composite of an improvement in the itch score PP NRS by at least 4 points, and an IGA score of 0 or 1 with an improvement by 2 or more points, representing nodule reduction. The EAG thought this was a high standard to reach. The company stated that a composite response was accepted in NICE's evaluation of dupilumab for treating moderate to severe prurigo nodularis. The clinical experts agreed that the composite response definition was a high standard to reach, particularly within 16 weeks, and it was plausible that people could experience benefits of treatment while not meeting both the requirements of the composite response. They said an itch response would probably be seen within 16 weeks, but flattening or reduction of nodules would usually take longer. The company presented a scenario

analysis in which response was defined only by a reduction in PP NRS score by 4 or more points. This had a small effect on the cost-effectiveness results. The EAG said that, in this scenario, it was not clear whether all relevant parameters had been updated. The committee was mindful that a reduction in itch was a very important outcome for people with prurigo nodularis (see section 3.4). But it also noted that a more objective measure of improvement in the number or appearance of nodules would help standardise treatment availability across the NHS. The committee concluded that it would prefer to see alternative scenario analyses using different outcome measures and thresholds to define treatment response. The committee would welcome input from clinical experts and patients on the most appropriate definition of response but proposed the following suggestions:

- a reduction in PP NRS score by 4 or more points alone or with an IGA score of 0 or 1
- a reduction in PP NRS score by 4 or more points alone or with an IGA score of 0 or 1, or an improvement by 2 or more points.

The committee also noted that clinical and patient input would be helpful in defining partial response (see section 3.5).

Age and weight in the model

3.7 The population in the model was based on the population in the OLYMPIA trials. The mean age was 55.2 years and 40.4% were male. 30% of people in the model were 90 kg or more. The dose of nemolizumab was higher for people who are 90 kg or more than for people less than 90 kg. The EAG highlighted a 2023 study by Bahloul et al. that linked data from the Clinical Practice Research Datalink and Hospital Episode Statistics for people with moderate or severe prurigo nodularis. The cohort in this study was on average older (by about 6 years) and of higher weight (approximately 4 kg heavier) than the mean population in OLYMPIA. The committee noted that increasing the proportion of people in the model who

were 90 kg or more would affect the cost-effectiveness results, because the costs of nemolizumab treatment are higher in this subgroup. It thought it would be preferable to have a flat price across the different weight subgroups. The committee concluded that it would like to see a scenario analysis in which the mean age and weight from the study by Bahloul et al. was applied in the economic model.

Utility values

Baseline utility values in the non-responder health state

3.8 Health state utility values in the company's model were based on data from OLYMPIA 1 and 2. The company used the baseline utility value from the trials (0.579) to reflect utility in the non-responder health state (except in the first year of the nemolizumab arm; see section 3.9). The EAG noted that some treatments, such as immunosuppressants, topical calcineurin inhibitors and systemic corticosteroids, were prohibited in the weeks before the start of the trial. So, it thought the utility value at baseline may not be reflective of the population that would be eligible for nemolizumab in clinical practice. In its base case, the EAG preferred to use the utility value observed in the trial for non-response in both arms (0.734). The committee recalled the patient experts' testimonies about how detrimental prurigo nodularis is to their lives. It agreed that a utility value of 0.734 seemed too high to reflect lack of response to treatment. It also noted that, in the trial, this value was measured in a group of people who did have some benefit from nemolizumab. The committee agreed that a utility value of 0.579 was too low, because it reflected a group of people who had not been having treatments that would be available in NHS practice. The committee noted that the utility value observed in the trial for non-response in the best supportive care arm was 0.664. It noted that the difference between the baseline value of 0.579 and 0.664 could be because of regression to the mean. But the clinical experts noted that, unlike with other skin conditions, the severity of prurigo nodularis does not tend to fluctuate over time. It concluded that, with the current modelling

approach, it was more plausible to use a utility value of 0.664 for the non-responder health state, because it reflected people having some symptomatic treatment but not having had any benefit from nemolizumab.

Utility values for the nemolizumab arm in the non-responder health state

3.9 For non-responders in the nemolizumab arm, the company increased the utility value from 0.579 for the first year to account for a potential partial response to treatment. It used a utility value of 0.751, which was the midpoint of the baseline and responder values in the trials. The company stated that this approach was in line with the model used in the evaluation of dupilumab for treating moderate to severe prurigo nodularis. The EAG thought there was a lack of robust evidence from the trials to support a treatment-specific benefit in nemolizumab non-responders in the long term. It also noted that this approach assumed that all non-responders had a partial response to nemolizumab. The committee noted the large difference between the baseline utility values of 0.579 and 0.751. It also noted that no additional costs of nemolizumab were included for this first year. The committee thought that if it were possible for some people to have this magnitude of benefit from nemolizumab without meeting the composite response threshold, it would suggest that the response threshold in the model was not appropriate. The committee decided that any potential partial response should be explicitly modelled to capture quality of life and costs in both treatment arms (see section 3.5). It concluded that it was not appropriate to include treatment-specific utility values in the non-response health state.

Utility values in the responder health state

3.10 For the first year in the model, the company based the utility value for the responder health state on the mean utility score at week 16 of all responders observed in the trials, independent of the treatment arm. This was a utility value of 0.922. After the first year, the company increased the utility value by 5% to 0.968. It said this was based on advice from a clinical expert who stated that initial improvement in quality of life would

be from itch relief, and that healing of nodules would take longer but provide further improvements in quality of life in the long term. The company cited data from a long-term extension study of nemolizumab in atopic dermatitis, which reported a 10% increase in utility between weeks 16 and 104. It stated that including a 5% increase in utility in the model for prurigo nodularis was a conservative estimate. The EAG was concerned that long-term data from a different disease area with different definitions of response was unlikely to be transferable to prurigo nodularis. It highlighted that the utility value in year 1 (0.922) was higher than age- and sex-adjusted general population utility values for the UK, so increasing it further in year 2 and beyond lacked face validity. The EAG also had some concerns about the regression model the company used to validate its assumptions. In its base case, the EAG preferred to remove the 5% utility increase for responders after year 1. The clinical experts said that it was clinically plausible for quality of life to improve further in the long term because reduction in nodules would take longer than itch relief. They also highlighted the mechanism of action of nemolizumab, and that the inflammatory response is plausibly a long-term effect. The patient experts highlighted that, because prurigo nodularis is so detrimental to all aspects of life, if symptoms improved with nemolizumab it was plausible that improvements to quality of life could still occur in year 2 and beyond, as a person continued to rebuild their life. The company said that it had presented a scenario analysis where health-state utility values were capped at general population values. The committee noted that this scenario made no difference to the cost-effectiveness results because the incremental utilities between the treatment arms had not changed. It agreed that inflating the utility value further above UK general population values was implausible. It noted that, although not reported by response status, the utility values based on the PRIME trials (trials of dupilumab for moderate to severe prurigo nodularis) in NICE's evaluation of dupilumab were lower than those in the model for nemolizumab. The committee concluded that utility values in the responder health state should not be

increased by 5% after the first year. It also agreed that it would like to see the scenario analysis in which the health-state utility values are capped at general population values updated to apply utility values multiplicatively against age- and sex-adjusted general population values.

Costs

Costs of best supportive care

3.11 In the company's model, once a response was lost, it could not be regained. In the non-responder state, people had a more intensive form of best supportive care than in the responder state, which included oral immunosuppressants and corticosteroids. They continued to have these treatments indefinitely, but there was no opportunity in the model to gain any benefit from them. The EAG thought that, in practice, it was unlikely that any treatment would be continued indefinitely without benefit. In the EAG's base case, it removed the costs of best supportive care to account for the lack of benefit modelled. The committee acknowledged that, although most people would get little or no benefit from best supportive care, a small number of people would, but this was not captured in the model. It concluded that it would prefer the model to reflect a benefit of treatment for some people having best supportive care. It noted that this could be accounted for by modelling partial response (see section 3.5).

Severity

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

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

3.13 The company's probabilistic base-case incremental cost-effectiveness ratio (ICER) for nemolizumab with best supportive care compared with best supportive care alone was £34,655 per QALY gained. The EAG

corrected errors in the company's base case and made several further changes to the model in its preferred base case, which included:

- removing best supportive care costs from the non-responder health state (see section 3.11)
- using a utility value of 0.734 for the non-responder health state (see section 3.8)
- removing the partial response utility for nemolizumab in the non-responder health state (see section 3.9)
- removing the 5% increase in utility value after year 1 in the responder health state (see section 3.10).

The EAG preferred to include disutilities for adverse events in the model, which the committee noted had a very small impact on the ICER. The EAG also included a weight parameter in its probabilistic sensitivity analysis. The EAG's probabilistic base-case ICER was £89,990 per QALY gained. The committee noted that neither the company's nor the EAG's base-case ICERs were based on its preferred model structure, which would account for partial response. The committee was aware that if partial response were to be included in the model, it could affect the most appropriate parameters to use in other health states. The committee also noted that both the company's and the EAG's base-case ICERs were higher than the upper value of the range that NICE normally considers an acceptable use of NHS resources. The committee thought that a model that captured a partial response would be likely to increase the ICER further, because more people would have nemolizumab for longer, increasing costs. But it was unclear by how much the ICER might increase because there would also be some additional benefits. The committee concluded that it was not possible to determine the most likely cost-effectiveness estimates for nemolizumab, but it was unlikely that nemolizumab represented a cost-effective use of NHS resources.

Committee's preferred assumptions

3.14 The committee could not provide a preferred ICER because of its concerns about how response is defined in the model and how the model reflects quality of life. The committee would like to see:

- a model structure that can account for partial response to treatment (see section 3.5 and section 3.11)
- scenarios presenting different outcome measures and thresholds to define treatment response (see section 3.6)
- a scenario analysis in which the mean age and weight from the study by Bahloul et al. was applied in the economic model (see section 3.7)
- a baseline utility for the non-response state of 0.664 (see section 3.8)
- removal of treatment-specific utility values in the non-response state (see section 3.9)
- no 5% increase in utility values in the response health state after the first year (see section 3.10)
- a scenario analysis in which the health-state utility values are capped at general population values updated to apply utility values multiplicatively against age- and sex-adjusted general population values (see section 3.10).

Other factors

Equality

3.15 Stakeholders highlighted that prurigo nodularis may be more common in people from Black African, Black Caribbean, Hispanic, South Asian and East Asian groups, and in women. Race and sex are protected characteristics under the Equality Act 2010. Issues related to differences in prevalence or incidence of a disease cannot be addressed in a technology appraisal. Another stakeholder highlighted that assessment of itch severity, sleep quality and quality of life may be more difficult in people with visual, hearing or cognitive impairment or communication difficulties. The committee was aware that the challenges highlighted were not limited to this disease area. A professional organisation highlighted

that the Dermatology Life Quality Index (DLQI), which was used in the OLYMPIA trials to measure quality of life, may not adequately capture impact in older people or those not in a relationship, and may poorly capture anxiety and depression, which may be more common in people with prurigo nodularis. One stakeholder highlighted that people with skin of colour have a greater propensity for papulation, lichenification, prurigo nodularis, pigmentary changes and extensor surface involvement than people with white skin, and that erythema may be underestimated in people with darker skin tones. The committee noted that if it had recommended nemolizumab, it would have taken into account how skin colour could affect the measurement of severity of disease. Because the committee did not recommend nemolizumab, there was no need to reflect these potential issues in the preliminary recommendations.

Uncaptured benefits

3.16 The committee considered whether there were any uncaptured benefits of nemolizumab. It did not identify additional benefits of nemolizumab not captured in the economic modelling. So, the committee concluded that all additional benefits of nemolizumab had already been taken into account.

Conclusion

Nemolizumab is not recommended

3.17 The committee agreed that further analyses were needed to provide robust estimates of cost effectiveness for nemolizumab for treating prurigo nodularis. Given the uncertainty, the committee agreed there were no plausible cost-effective estimates. The committee also recalled that the existing estimates using incomplete analyses are above the range that NICE normally considers an acceptable use of NHS resources. So, nemolizumab is not recommended for moderate to severe prurigo nodularis.

4 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

Baljit Singh

Vice 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.

Kirsty Pitt

Technical lead

Caron Jones

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Jeremy Powell

Project manager

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