# Nemolizumab (prurigo nodularis)

## Benefit assessment according to §35a SGB V[1]

**EXTRACT**

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No feedback was received in the framework of the present dossier assessment.

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# Part I: Benefit assessment

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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

# I List of abbreviations

| Abbreviation | Meaning |
|---|---|
| ACT | appropriate comparator therapy |
| AE | adverse event |
| COPD | chronic obstructive pulmonary disease |
| G-BA | Gemeinsamer Bundesausschuss (Federal Joint Committee) |
| IGA | Investigator Global Assessment |
| IQWiG | Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care) |
| PP-NRS | Peak Pruritus Numerical Rating Scale |
| RCT | randomized controlled trial |
| SGB | Sozialgesetzbuch (Social Code Book) |
| SPC | Summary of Product Characteristics |

## I 1 Executive summary of the benefit assessment

### Background

In accordance with §35a Social Code Book V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug nemolizumab. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 17 February 2025.

### Research question

The aim of this report is to assess the added benefit of nemolizumab in comparison with dupilumab as the appropriate comparator therapy (ACT) in patients with moderate-to-severe prurigo nodularis who are candidates for systemic therapy.

The research question shown in Table 2 was defined in accordance with the ACT specified by the G-BA.

Table 2: Research question for the benefit assessment of nemolizumab

| **Therapeutic indication** | **ACT**[a] |
|---|---|
| Adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy | Dupilumab[b] |
| a. Presented is the ACT specified by the G-BA.<br>b. According to the G-BA, topical corticosteroids may be indicated in both treatment arms of a clinical study for the short-term treatment of inflammatory skin diseases. The use of UV phototherapy in the study is seen as a possible but not mandatory treatment option. In addition, the use of a topical basic therapy for skin care is an option for all patients (emollients).<br>ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; UV: ultraviolet radiation | |

The company followed the G-BA's specification of the ACT.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 24 weeks were used to derive the added benefit.

### Results

The review of the completeness of the study pool did not identify any RCTs for the direct comparison of nemolizumab with the ACT dupilumab in patients with moderate-to-severe prurigo nodularis who are candidates for systemic therapy.

#### *Evidence presented by the company – OLYMPIA 1 study*

In Module 4 B of the dossier, the company presented results of the double-blind RCT OLYMPIA 1 comparing nemolizumab versus placebo.

Adult patients diagnosed with prurigo nodularis at least 6 months prior were included.

Overall, 286 patients were enrolled in the OLYMPIA 1 study and allocated in a 2:1 ratio either to treatment with nemolizumab (N = 190) or to placebo (N = 96).

During the 24-week treatment phase, patients were either treated with nemolizumab in compliance with the Summary of Product Characteristics (SPC), or received a placebo. Treatment with dupilumab was prohibited up to 10 weeks before study entry as well as during the study.

***OLYMPIA 1 study unsuitable for the benefit assessment***

The treatment in the comparator arm of the OLYMPIA 1 study did not concur with the ACT, so no data were available on the comparison of nemolizumab with the comparator therapy specified by the G-BA.

The company presented data from the RCTs PRIME and PRIME2 in its reasoning, which compared dupilumab with placebo. The company did not consider these studies to be suitable for conducting an indirect comparison with the OLYMPIA 1 study in the given research question. It justified this with the insufficient similarity of the studies with regard to study population and background therapy as well as the high risk of bias of the results of the PRIME studies, and therefore did not present an indirect comparison.

Overall, there were no suitable data for deriving an added benefit of nemolizumab in comparison with the ACT.

**Results on added benefit**

Since no relevant study was available for the benefit assessment, there was no hint of an added benefit of nemolizumab in comparison with the ACT; an added benefit is therefore not proven.

## Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 presents a summary of the probability and extent of the added benefit of nemolizumab.

Table 3: Nemolizumab – extent and probability of added benefit

| Therapeutic indication | ACT[a] | Probability and extent of added benefit |
|---|---|---|
| Adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy | Dupilumab[b] | Added benefit not proven |

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, topical corticosteroids may be indicated in both treatment arms of a clinical study for the short-term treatment of inflammatory skin diseases. The use of UV phototherapy in the study is seen as a possible but not mandatory treatment option. In addition, the use of a topical basic therapy for skin care is an option for all patients (emollients).

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; UV: ultraviolet radiation

The G-BA decides on the added benefit.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) “proof”, (2) “indication”, (3) “hint”, or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

## I 2 Research question

The aim of this report is to assess the added benefit of nemolizumab in comparison with dupilumab as the ACT in patients with moderate-to-severe prurigo nodularis who are candidates for systemic therapy.

The research question shown in Table 4 was defined in accordance with the ACT specified by the G-BA.

Table 4: Research question for the benefit assessment of nemolizumab

| **Therapeutic indication** | **ACT**[a] |
|---|---|
| Adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy | Dupilumab[b] |
| a. Presented is the ACT specified by the G-BA.<br>b. According to the G-BA, topical corticosteroids may be indicated in both treatment arms of a clinical study for the short-term treatment of inflammatory skin diseases. The use of UV phototherapy in the study is seen as a possible but not mandatory treatment option. In addition, the use of a topical basic therapy for skin care is an option for all patients (emollients).<br>ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; UV: ultraviolet radiation | |

The company followed the G-BA's specification of the ACT.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs with a minimum duration of 24 weeks were used to derive the added benefit. This concurs with the company's inclusion criteria.

## I 3 Information retrieval and study pool

The study pool for the assessment was compiled on the basis of the following information:

Sources used by the company in the dossier:

- Study list on nemolizumab (status: 2 January 2025)
- Bibliographical literature search on nemolizumab (last search on 2 January 2025)
- Search of trial registries/trial results databases for studies on nemolizumab (last search on 2 January 2025)
- Search on the G-BA website for nemolizumab (last search on 2 January 2025)

To check the completeness of the study pool:

- Search of trial registries for studies on nemolizumab (last search on 7 March 2025); for search strategies, see I Appendix A of the full dossier assessment

The review did not identify any relevant studies. This concurs with the company's assessment.

**Evidence presented by the company – OLYMPIA 1 study**

Irrespective of the result of its information retrieval, the company presented results of the OLYMPIA 1 study [3] in Module 4 B of the dossier. The OLYMPIA 1 study is a double-blind RCT comparing nemolizumab versus placebo.

Adult patients diagnosed with prurigo nodularis at least 6 months prior were included. This diagnosis had to include at least 20 prurigo nodularis lesions, with a bilateral distribution, on upper or lower limbs and/or trunk, as well as an Investigator Global Assessment (IGA) score of at least 3 (moderate). Patients also had to have reported a Peak Pruritus Numerical Rating Scale (PP-NRS) score of at least 7 at the first visit (screening) for the 24 hours preceding the visit, and a mean PP-NRS score of at least 7 at the second visit (start of treatment) for the previous 7 days. The exclusion criteria included uncontrolled asthma, chronic obstructive pulmonary disease (COPD) and active atopic dermatitis.

Overall, 286 patients were enrolled in the OLYMPIA 1 study and allocated in a 2:1 ratio either to treatment with nemolizumab (N = 190) or to placebo (N = 96). Randomization was stratified by study centre and body weight at baseline (< 90 kg versus ≥ 90 kg).

During the 24-week treatment phase, patients were either treated with nemolizumab in compliance with the SPC [4], or received a placebo. Treatment with dupilumab was prohibited up to 10 weeks before study entry as well as during the study. Similarly, the use of corticosteroids and topical calcineurin inhibitors in the OLYMPIA 1 study was only permitted

as part of rescue therapy. The continuation of background therapy using emollients as well as stable doses of sedatives and antidepressants was permitted in both study arms. Patients in the OLYMPIA 1 study were able to switch to the extension study RD.06.SPR.202699 [5] directly after the 24-week treatment phase; otherwise the 24-week treatment phase was followed by an 8-week follow-up phase.

The coprimary outcomes of the study were the proportion of patients with at least 4 points of improvement in PP-NRS at Week 16, and the proportion of patients with treatment success on the IGA, defined as an IGA score of 0 or 1 and an improvement of at least 2 points from baseline. Secondary outcomes were recorded in the categories morbidity, health-related quality of life and adverse events (AEs).

**OLYMPIA 1 study unsuitable for the benefit assessment**

The treatment in the comparator arm of the OLYMPIA 1 study did not concur with the ACT, so no data were available on the comparison of nemolizumab with the comparator therapy specified by the G-BA.

Although the company did not conduct a systematic information retrieval on the ACT, it presented data from the RCTs PRIME [6] and PRIME2 [7] in its reasoning, which compared dupilumab with placebo (for details, see benefit assessment A23-24 [8] and Addendum A23-82 [9]). However, the company did not consider these studies to be suitable for conducting an indirect comparison with the OLYMPIA 1 study in the given research question. It justified this with the insufficient similarity of the studies with regard to study population and background therapy as well as the high risk of bias of the results of the PRIME studies, and therefore did not present an indirect comparison. Thus, neither results from studies of direct comparisons nor from indirect comparisons were available for the present assessment.

Overall, there were no suitable data for deriving an added benefit of nemolizumab in comparison with the ACT.

## I 4 Results on added benefit

In its dossier, the company presented no suitable data to assess the added benefit of nemolizumab in comparison with the ACT dupilumab in patients with moderate-to-severe prurigo nodularis who are candidates for systemic therapy. There was no hint of an added benefit of nemolizumab in comparison with the ACT dupilumab; an added benefit is therefore not proven.

## I 5 Probability and extent of added benefit

Table 5 summarizes the result of the assessment of the added benefit of nemolizumab in comparison with the ACT.

Table 5: Nemolizumab – extent and probability of added benefit

| **Therapeutic indication** | **ACT[a]** | **Probability and extent of added benefit** |
|---|---|---|
| Adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy | Dupilumab[b] | Added benefit not proven |

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, topical corticosteroids may be indicated in both treatment arms of a clinical study for the short-term treatment of inflammatory skin diseases. The use of UV phototherapy in the study is seen as a possible but not mandatory treatment option. In addition, the use of a topical basic therapy for skin care is an option for all patients (emollients).

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; UV: ultraviolet radiation

The assessment described above deviates from that by the company, which derived a hint of a non-quantifiable added benefit based on the results of the OLYMPIA 1 study.

The G-BA decides on the added benefit.

## I 6 References for English extract

Please see full dossier assessment for full reference list.

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