# Nemolizumab (atopic dermatitis)

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

**EXTRACT**

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**Medical and scientific advice**

No advisor on medical and scientific questions was available for the present dossier assessment.

**Patient and family involvement**

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 |
| EASI | Eczema Area and Severity Index |
| 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 |
| SAE | serious adverse event |
| SGB | Sozialgesetzbuch (Social Code Book) |
| SmPC | summary of product characteristics |
| TCI | topical calcineurin inhibitors |
| TCS | topical corticosteroids |

## 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 adults and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis 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 and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy | Dupilumab (in combination with TCS and/or TCI as appropriate) |
| a. Presented is the ACT specified by the G-BA.<br>ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids | |

In Module 3 A of the dossier, the company specified an individualized treatment choosing from dupilumab, abrocitinib and upadacitinib, in combination with topical corticosteroids (TCS) and/or topical calcineurin inhibitors (TCI) as appropriate, which deviated from the ACT as defined in Table 2. This was of no consequence for the benefit assessment, however, as the company's information retrieval included the ACT specified by the G-BA, and the company did not provide any data for comparison versus the ACT it had specified. This assessment was based on the ACT specified by the G-BA.

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 adults and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy.

***Evidence presented by the company – studies ARCADIA 1 and ARCADIA 2***

In Module 4 A of the dossier, the company presented results of the RCTs ARCADIA 1 and ARCADIA 2, were planned and conducted analogously. The studies ARCADIA 1 and ARCADIA 2 are double-blind RCTs comparing nemolizumab versus placebo in the given therapeutic indication.

Adults and adolescents aged 12 years and older with chronic atopic dermatitis with a disease duration of at least 2 years were enrolled.

In the ARCADIA 1 study, a total of 941 patients were randomized in a 2:1 ratio, with 620 patients assigned to the nemolizumab arm and 321 to the placebo arm. The ARCADIA 2 study included 787 patients; 522 were assigned to the nemolizumab arm and 265 to the placebo arm.

During the 16-week treatment phase, patients were either treated with nemolizumab in compliance with the summary of product characteristics (SmPC), or received a placebo. Treatment with dupilumab was prohibited during the 10 weeks before study entry as well as during the study. After the 16-week treatment phase, only the patients with a clinical response in the study were treated for a further 32 weeks, with patients in the placebo arm continuing placebo treatment. Thus, results for a comparison versus placebo for all randomized patients in ARCADIA 1 and ARCADIA 2 were only available for a treatment duration of 16 weeks.

***Studies ARCADIA 1 and ARCADIA 2 unsuitable for the benefit assessment***

The treatment in the comparator arms of ARCADIA 1 and ARCADIA 2 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. In addition, the comparative treatment duration of 16 weeks was too short to address the research question for this benefit assessment.

**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 and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy | Dupilumab (in combination with TCS and/or TCI as appropriate) | Added benefit not proven |
| a. Presented is the ACT specified by the G-BA.<br>ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids | | |

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 adults and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis 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 and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy | Dupilumab (in combination with TCS and/or TCI as appropriate) |
| a. Presented is the ACT specified by the G-BA.<br>ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids | |

In Module 3 A of the dossier, the company specified an individualized treatment choosing from dupilumab, abrocitinib and upadacitinib, in combination with TCS and/or TCI as appropriate, which deviated from the ACT as defined in Table 4. This was of no consequence for the benefit assessment, however, as the company's information retrieval included the ACT specified by the G-BA, and the company did not provide any data for comparison versus the ACT it had specified. This assessment was based on the ACT specified by the G-BA.

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 – studies ARCADIA 1 and ARCADIA 2**

Irrespective of the results of its information retrieval, the company presented results from 2 RCTs conducted in the therapeutic indication, ARCADIA 1 und ARCADIA 2 [3], in Module 4 A of the dossier. The studies ARCADIA 1 and ARCADIA 2 are double-blind RCTs comparing nemolizumab versus placebo. The 2 studies were planned and conducted analogously. The inclusion and exclusion criteria of both studies were identical, as were the definitions of the concomitant therapies permitted and prohibited by the study protocol.

Adults and adolescents aged 12 years and older with chronic atopic dermatitis with a disease duration of at least 2 years were enrolled. The following additional criteria had to be met at screening and baseline: body surface area involvement ≥ 10%, Investigator Global Assessment (IGA) score ≥ 3, Eczema Area and Severity Index (EASI) ≥ 16, and itching with a score of ≥ 4 on the Peak Pruritus Numerical Rating Scale (PP-NRS).

In the ARCADIA 1 study, a total of 941 patients were randomized in a 2:1 ratio, with 620 patients assigned to the nemolizumab arm and 321 to the placebo arm. The ARCADIA 2 study included 787 patients; 522 were assigned to the nemolizumab arm and 265 to the placebo arm. Randomization was stratified by baseline disease severity according to the IGA score (3 [moderate] versus 4 [severe]) and pruritus severity according to the PP-NRS score (< 7 versus ≥ 7).

During the 16-week treatment phase, patients were either treated with nemolizumab in compliance with the SmPC [4], or received a placebo. Patients in both treatment arms were allowed to receive additional low-to-moderate-potency TCS or low-potency TCI. Treatment with dupilumab was prohibited during the 10 weeks before study entry as well as during the study. After the 16-week treatment phase, only patients with a clinical response, defined as an IGA score of 0 (clear) or 1 (almost clear) or EASI-75 (≥ 75% improvement from baseline), continued treatment in the study. Patients in the intervention arm were randomized in a 1:1:1 ratio to 2 verum arms (30 mg nemolizumab every 4 weeks or 30 mg nemolizumab every 8 weeks) or 1 placebo arm, and received another 32 weeks of treatment. Patients in the placebo arm continued receiving placebo. The 32-week treatment in this maintenance phase was followed by an 8-week follow-up phase. Patients without a clinical response at Week 16 and all patients who had completed the maintenance phase were eligible to participate in the RD.06.SPR.118163 extension study [5], where they continued treatment with nemolizumab. Thus, results for a comparison versus placebo for all randomized patients in ARCADIA 1 and ARCADIA 2 were only available for a treatment duration of 16 weeks.

The co-primary outcomes were the proportion of patients with an IGA success (IGA of 0 or 1 and a ≥ 2-point improvement from baseline), and the proportion of patients with EASI-75, each at Week 16. Secondary outcomes were recorded in the categories morbidity, health-related quality of life and adverse events (AEs).

**Studies ARCADIA 1 and ARCADIA 2 unsuitable for the benefit assessment**

The treatment in the comparator arms of ARCADIA 1 and ARCADIA 2 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. In addition, the comparative treatment duration of 16 weeks was too short to address the research question for this benefit assessment.

## 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 adults and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy. There is no hint of an added benefit of abrocitinib 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 and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy | Dupilumab (in combination with TCS and/or TCI as appropriate) | Added benefit not proven |
| a. Presented is the ACT specified by the G-BA.<br>ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids | | |

The assessment described above deviates from that by the company, which derived a hint of a non-quantifiable added benefit of nemolizumab in adults and adolescents aged 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy, in comparison with dupilumab.

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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*The full report (German version) is published under https://www.iqwig.de/en/projects/a25-32.html.*