IQWiG Reports – Commission No. A21-94

Tralokinumab (atopic dermatitis) –

Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Tralokinumab (atopische Dermatitis) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 13 October 2021). Please note: This document was translated by an external translator and is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

2 Benefit assessment

2.1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book (SGB) 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 tralokinumab. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 14 July 2021.

Research question

The aim of this report is to assess the added benefit of tralokinumab in comparison with the appropriate comparator therapy (ACT) of dupilumab for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy.

The G-BA's specification of the ACT results in the research question presented in Table 2.

Table 2: Research question of the benefit assessment of tralokinumab

Therapeutic indication	**ACT**[a]
Moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy[b]	Dupilumab (possibly combined with TCS and/or TCI)

a. Presented is the ACT specified by the G-BA.
b. As per approval, the therapeutic indication comprises patients who are candidates for systemic therapy. For the purposes of determining the ACT, the target population has been narrowed down to adult patients with moderate-to-severe atopic dermatitis who are indicated for long-term/continuous systemic therapy; this is because the drug tralokinumab is to be administered as continuous therapy and therefore represents an option only for patients indicated for long-term/continuous systemic therapy.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids

The company followed the G-BA's specification by identifying dupilumab as the ACT.

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

Results

Consistent with the company's assessment, the check of completeness did not identify any relevant RCT for assessing the added benefit of tralokinumab in comparison with the ACT. The company also did not present any other data for assessing added benefit.

No suitable data are available for assessing the added benefit of tralokinumab in comparison with the ACT for the treatment of moderate-to-severe atopic dermatitis in adult patients who

are candidates for systemic therapy. Consequently, there is no hint of added benefit of tralokinumab 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 added benefit of tralokinumab.

Table 3: Tralokinumab – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy[b]	Dupilumab (possibly combined with TCS and/or TCI)	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. As per approval, the therapeutic indication comprises patients who are candidates for systemic therapy. For the purposes of determining the ACT, the target population has been narrowed down to adult patients with moderate-to-severe atopic dermatitis who are indicated for long-term/continuous systemic therapy; this is because the drug tralokinumab is to be administered as continuous therapy and therefore represents an option only for patients indicated for long-term/continuous systemic therapy.

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].

2.2 Research question

The aim of this report is to assess the added benefit of tralokinumab in comparison with the ACT of dupilumab for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy.

The G-BA's specification of the ACT results in the research question presented in Table 4.

Table 4: Research question of the benefit assessment of tralokinumab

Therapeutic indication	**ACT**[a]
Moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy[b]	Dupilumab (possibly combined with TCS and/or TCI)

a. Presented is the ACT specified by the G-BA.
b. As per approval, the therapeutic indication comprises patients who are candidates for systemic therapy. For the purposes of determining the ACT, the target population has been narrowed down to adult patients with moderate-to-severe atopic dermatitis who are indicated for long-term/continuous systemic therapy; this is because the drug tralokinumab is to be administered as continuous therapy and therefore represents an option only for patients indicated for long-term/continuous systemic therapy.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids

The company followed the G-BA's specification by identifying dupilumab as the ACT.

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

2.3 Information retrieval and study pool

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

Sources cited by the company in the dossier:

- Study list on tralokinumab (as of 22 June 2021)
- Bibliographic literature search on tralokinumab (most recent search on 25 May 2021)
- Search in trial registries / study results databases on tralokinumab (most recent search on 25 May 2021)
- Search on the G-BA website on tralokinumab (most recent search on 25 May 2021)
- Bibliographic literature search on the ACT (most recent search on 27 May 2021)
- Search in trial registries or results databases on the ACT (most recent search on 26 May 2021)
- Search on the G-BA website for the ACT (most recent search on 25 May 2021)

To check the completeness of the study pool:

- Search in trial registries for studies on tralokinumab (most recent search on 23 July 2021); see Appendix A of the full dossier assessment for search strategies.

The check did not reveal any relevant RCTs for assessing the added benefit of tralokinumab in comparison with the ACT. This concurs with the company's assessment.

Evidence provided by the company

To assess the added benefit of tralokinumab versus the ACT, the company did not find any directly comparative RCTs. To nevertheless illustrate medical benefit, the company has submitted the 2 placebo-controlled studies conducted in the therapeutic indication, ECZTRA 3 [3] and ECZTRA 7 [4]. Reasoning consistently, the company did not derive any added benefit from them, however. The company reported that, in view of the two studies, it conducted a systematic search for an indirect comparison between tralokinumab and the ACT using placebo as the common comparator. The company reports initially finding 2 RCTs through this search (1 study with tralokinumab: ECZTRA 7; 1 study with dupilumab: CHRONOS [5]), but after evaluating the similarity of the patient population, concomitant medication, and available analysis time points (ECZTRA 7: 26 Weeks; CHRONOS: 52 Weeks), it now deems them unsuitable. The company reports that it did not present an indirect comparison for this reason. Overall, the company therefore sees no proof of added benefit of tralokinumab in comparison with the ACT.

The company's approach is plausible. The ECZTRA 3 and ECZTRA 7 studies are randomized, double-blind studies investigating tralokinumab for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy. Both studies used placebo as the ACT. Hence, the ACT of dupilumab has not been implemented. Concurring with the company, the studies are therefore deemed unsuitable for assessing the added benefit of tralokinumab in comparison with the ACT.

All in all, the company therefore has not submitted any directly or indirectly comparative evidence for the present research question, and it has not derived any added benefit in comparison with the ACT.

2.4 Results on added benefit

No suitable data are available for assessing the added benefit of tralokinumab in comparison with the ACT for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy. Consequently, there is no hint of added benefit of tralokinumab comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

Table 5 presents a summary of the results of the assessment of added benefit of tralokinumab in comparison with the ACT.

Table 5: Tralokinumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy[b]	Dupilumab (possibly combined with TCS and/or TCI)	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. As per approval, the therapeutic indication comprises patients who are candidates for systemic therapy. For the purposes of determining the ACT, the target population has been narrowed down to adult patients with moderate-to-severe atopic dermatitis who are indicated for long-term/continuous systemic therapy; this is because the drug tralokinumab is to be administered as continuous therapy and therefore represents an option only for patients indicated for long-term/continuous systemic therapy.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids

The above assessment concurs with that of the company.

The G-BA decides on the added benefit.

References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a21-94.html.