Lanadelumab
(hereditary angioedema, 2 to 11 years)

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

EXTRACT

Project: A23-135 Version: 1.0 Status: 6 Mar 2024 DOI: 10.60584/A23-135_en

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Lanadelumab (hereditäres Angioödem, 2 bis 11 Jahre)– Nutzenbewertung gemäß § 35a SGB V*. 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.

Publishing details

Publisher

Institute for Quality and Efficiency in Health Care

Topic

Lanadelumab (hereditary angioedema, 2 to 11 years) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

14 December 2023

Internal Project No.

A23-135

DOI-URL

https://doi.org/10.60584/A23-135_en

Address of publisher

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No advisor on medical and scientific questions was involved in the present dossier assessment.

Patient and family involvement

No patients or their families were involved in the present dossier assessment.

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Keywords

Lanadelumab, Angioedemas – Hereditary, Child - Preschool, Child, Benefit Assessment

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
CTCAE	Common Terminology Criteria for Adverse Events
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HAE	hereditary angioedema
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug lanadelumab. 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 December 2023.

Research question

The aim of the present report is the assessment of the added benefit of lanadelumab in comparison with the appropriate comparator therapy (ACT) in children aged 2 to 11 years for routine prevention of recurrent attacks of hereditary angioedema (HAE).

The research question presented in Table 2 results from the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of lanadelumab

Therapeutic indication	**ACT**[a]
Children aged 2 to 11 years for routine prevention of recurrent attacks of HAE[b, c]	Routine prevention with C1 esterase inhibitor[d]
a. Presented is the ACT specified by the G-BA. b. The therapeutic indication of lanadelumab is assumed to comprise only patients with type I or type II AEs. c. Both study arms should offer the possibility of acute treatment of HAE attacks. d. C1-esterase inhibitor is only approved for use in patients aged 6 years and older. According to G-BA, the off-label use based on the generally accepted state of medical knowledge is considered the therapy standard in the therapeutic indication under evaluation and is generally preferred over the drugs approved in the therapeutic indication so far. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HAE: hereditary angioedema	

The company deviates from the specifications of the G-BA and refers to a treatment of physician's choice as ACT, referring to an outdated definition of the G-BA. The present benefit assessment is carried out in comparison with the G-BA's current ACT. The deviation of the company is of no consequence for the present assessment, as the company did not provide comparative data for the benefit assessment.

The assessment is 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 for deriving any added benefit.

Results

Concurring with the company, the check of the information retrieval identified no relevant study.

The company mentioned the results of the SPRING approval study when deriving the added benefit, but did not refer to this study when deriving the added benefit. The company's approach is appropriate as the single-arm study SPRING does not allow for comparison with the ACT.

Results on added benefit

No suitable data are available to assess the added benefit of lanadelumab compared with the ACT in children aged 2 to 11 years for routine prevention of recurrent attacks of HAE. There is no hint of an added benefit of lanadelumab 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 lanadelumab.

Table 3: Lanadelumab – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Children aged 2 to 11 years for routine prevention of recurrent attacks of HAE[b, c]	Routine prevention with C1 esterase inhibitor[d]	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. The therapeutic indication of lanadelumab is assumed to comprise only patients with type I or type II AEs.
c. Both study arms should offer the possibility of acute treatment of HAE attacks.
d. C1-esterase inhibitor is only approved for use in patients aged 6 years and older. According to G-BA, the off-label use based on the generally accepted state of medical knowledge is considered the therapy standard in the therapeutic indication under evaluation and is generally preferred over the drugs approved in the therapeutic indication so far.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HAE: hereditary angioedema

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 the present report is the assessment of the added benefit of lanadelumab in comparison with the ACT in children aged 2 to 11 years for routine prevention of recurrent attacks of HAE.

The research question presented in Table 4 results from the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of lanadelumab

Therapeutic indication	**ACT**[a]
Children aged 2 to 11 years for routine prevention of recurrent attacks of HAE[b, c]	Routine prevention with C1 esterase inhibitor[d]
a. Presented is the ACT specified by the G-BA. b. The therapeutic indication of lanadelumab is assumed to comprise only patients with type I or type II AEs. c. Both study arms should offer the possibility of acute treatment of HAE attacks. d. C1-esterase inhibitor is only approved for use in patients aged 6 years and older. According to G-BA, the off-label use based on the generally accepted state of medical knowledge is considered the therapy standard in the therapeutic indication under evaluation and is generally preferred over the drugs approved in the therapeutic indication so far. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HAE: hereditary angioedema	

The company deviates from the specifications of the G-BA and refers to a therapy according to medical discretion as ACT, referring to an outdated definition of the G-BA. The present benefit assessment is carried out in comparison with the G-BA's current ACT. The deviation of the company is of no consequence for the present assessment, as the company did not provide comparative data for the benefit assessment (see Section I 3).

The assessment is 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 for deriving any added benefit. This concurs with the company’s inclusion criteria.

I 3 Information retrieval and study pool

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

Sources of the company in the dossier:

- study lists on lanadelumab (status: 9 October 2023)
- bibliographical literature search on lanadelumab (last search on 9 October 2023)
- search in trial registries/trial results databases for studies on lanadelumab (last search on 9 October 2023)
- search on the G-BA website for lanadelumab (last search on 20 October 2023)

To check the completeness of the study pool:

- search in trial registries for studies on lanadelumab (last search on 19 December 2023); for search strategies, see Appendix A of the full dossier assessment

Concurring with the company, the check identified no relevant study.

The company mentioned the results of the SPRING approval study when deriving the added benefit (Module 4B, Section 4.4.2), but did not refer to this study when deriving the added benefit. The company's approach is appropriate.

SPRING study

The single-arm SPRING study included children aged 2 to 11 years with a documented diagnosis of HAE (type I or II). A total of 24 patients were observed in the first phase of the study. In this phase, all patients had to discontinue their previous long-term prophylaxis and the HAE attack rate at baseline was determined over a period of up to 12 weeks. 21 patients who reported ≥ 1 HAE attack in these 3 months entered the 52-week treatment period with lanadelumab. After the end of the 52-week treatment period, the patients were followed up for an additional 2 or 4 weeks depending on the dosage. The primary aim of the study was to evaluate the safety and pharmacokinetics of lanadelumab.

The SPRING study offers no comparison with the ACT and is therefore unsuitable for the assessment of added benefit.

I 4 Results on added benefit

No suitable data are available to assess the added benefit of lanadelumab compared with the ACT in children aged 2 to 11 years for routine prevention of recurrent attacks of HAE. There is no hint of an added benefit of lanadelumab in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

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

Table 5: Lanadelumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Children aged 2 to 11 years for routine prevention of recurrent attacks of HAE[b, c]	Routine prevention with C1 esterase inhibitor[d]	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. The therapeutic indication of lanadelumab is assumed to comprise only patients with type I or type II AEs.
c. Both study arms should offer the possibility of acute treatment of HAE attacks.
d. C1-esterase inhibitor is only approved for use in patients aged 6 years and older. According to G-BA, the off-label use based on the generally accepted state of medical knowledge is considered the therapy standard in the therapeutic indication under evaluation and is generally preferred over the drugs approved in the therapeutic indication so far.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HAE: hereditary angioedema

The assessment described above concurs with that of the company.

The G-BA decides on the added benefit.

I 6 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.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 06.10.2023]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

2. Skipka G, Wieseler B, Kaiser T et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2016; 58(1): 43-58. https://doi.org/10.1002/bimj.201300274.

The full report (German version) is published under https://www.iqwig.de/en/projects/a23-135.html.