Faricimab (neovascular age-related macular degeneration)

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

EXTRACT

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[1] Translation of Sections I 1 to I 6 of the dossier assessment *Faricimab (neovaskuläre altersabhängige Makuladegeneration) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This translation 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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IQWiG thanks the medical and scientific advisor for her contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by 4 people.

IQWiG thanks the respondents for participating in the written exchange about how they experienced the disease and its treatment and about the treatment goals. The respondents were not involved in the actual preparation of the 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
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)
SPC	Summary of Product Characteristics

I 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 faricimab. 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 October 2022.

Research question

The aim of this report is to assess the added benefit of faricimab in comparison with ranibizumab or aflibercept as the appropriate comparator therapy (ACT) in patients with neovascular (wet) age-related macular degeneration.

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

Table 2: Research question for the benefit assessment of faricimab

Therapeutic indication	**ACT**[a]
Adult patients with neovascular (wet) age-related macular degeneration	Ranibizumab or **aflibercept**
a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in **bold**. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification by choosing aflibercept as the ACT.

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 are used for the derivation of added benefit.

Results

Concurring with the company, the check of the study pool did not identify any relevant study which would allow a comparison of faricimab with aflibercept.

Approach of the company

In its information retrieval, the company did not identify any relevant data for the present research question, but presented the results of the studies TENAYA and LUCERNE as supplementary information in its dossier. The studies TENAYA and LUCERNE are double-blind, multicentre RCTs comparing faricimab and aflibercept in patients aged 50 years and older with neovascular age-related macular degeneration. In both studies, after initiation with 3 monthly

injections, aflibercept was administered on a fixed regimen every 8 weeks for a total study period of 2 years. In the intervention arms of both studies, however, in compliance with the Summary of Product Characteristics (SPC) of faricimab, a flexible dosing regimen with personalized treatment intervals of up to 16 weeks depending on disease activity was used starting at 20 or 24 weeks treatment initiation. According to the SPC of aflibercept, treatment should be initiated with one injection per month for 3 consecutive doses. The treatment interval should then be extended to 2 months. Based on the physician's judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at 2 months or further extended using a treat-and-extend dosing regimen, where injection intervals are increased in 2- or 4-weekly increments on a patient-specific basis. However, unlike the approach in the faricimab arm, the studies did not provide for flexibilization of the treatment regimen of aflibercept. The differences between the dosing regimens in the different study arms resulted in a disparity between the faricimab and aflibercept treatment arms. The lack of consideration of an individual treatment adjustment in the comparator arm as recommended in the SPC may have a relevant influence on the treatment result. The studies TENAYA and LUCERNE are therefore not suitable for the benefit assessment.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of faricimab 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 added benefit of faricimab.

Table 3: Faricimab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Adult patients with neovascular (wet) age-related macular degeneration	Ranibizumab or **aflibercept**	Added benefit not proven

a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.

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

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 faricimab in comparison with ranibizumab or aflibercept as the ACT in patients with neovascular (wet) age-related macular degeneration.

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

Table 4: Research question for the benefit assessment of faricimab

Therapeutic indication	**ACT**[a]
Adult patients with neovascular (wet) age-related macular degeneration	Ranibizumab or **aflibercept**
a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in **bold**. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification by choosing aflibercept as the ACT.

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 are used for the derivation of added benefit. This does not correspond to the company's inclusion criteria, which did not specify a minimum duration. This deviation has no consequence for the present benefit assessment, as no suitable data are available to compare faricimab and aflibercept, regardless of the study duration (see Chapter I 3).

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 list on faricimab (status: 8 August 2022)
- bibliographical literature search on faricimab (last search on 8 August 2022)
- search in trial registries/trial results databases for studies on faricimab (last search on 8 August 2022)
- search on the G-BA website for faricimab (last search on 8 August 2022)

To check the completeness of the study pool:

- search in trial registries for studies on faricimab (last search on 25 October 2022); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check of the study pool did not identify any relevant study which would allow a comparison of faricimab with aflibercept.

Approach of the company

In its information retrieval, the company did not identify any relevant data for the present research question, but presented the results of the studies TENAYA [3] and LUCERNE [3] as supplementary information in its dossier. Both studies compared the drugs faricimab and aflibercept for the treatment of neovascular age-related macular degeneration.

In this context, the company referred to the resolution of the G-BA [4] on the benefit assessment of brolucizumab in the therapeutic indication of neovascular age-related macular degeneration [5]. As in the studies TENAYA and LUCERNE submitted by the company as supplementary information, the brolucizumab studies did not allow the individual adjustment of the dosing regimen for aflibercept recommended in the SPC, so that the studies were not used for the benefit assessment of brolucizumab. According to the company, it had followed the G-BA's resolution on the benefit assessment of brolucizumab in the therapeutic indication of neovascular age-related macular degeneration [4] and therefore did not use the studies TENAYA and LUCERNE to derive the added benefit.

The company's approach is appropriate. This is explained below.

Lack of consideration of individual treatment adjustment of aflibercept in the studies TENAYA and LUCERNE

The studies TENAYA and LUCERNE are double-blind, multicentre RCTs comparing faricimab and aflibercept in patients aged 50 years and older with neovascular age-related macular degeneration.

According to the SPC, treatment with aflibercept should be initiated with one injection per month for 3 consecutive doses [6,7]. The treatment interval should then be extended to 2 months. Based on the physician's judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at 2 months or further extended using a treat-and-extend dosing regimen, where injection intervals are increased in 2- or 4-weekly increments on a patient-specific basis. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly.

In the studies TENAYA and LUCERNE, after initiation with 3 monthly injections, aflibercept was administered on a fixed regimen every 8 weeks for a total study period of 2 years. The individual adjustment of the treatment interval recommended by the SPC was thus not possible in the comparator arms of the studies. In the intervention arms of both studies, however, in compliance with the SPC of faricimab [8], a flexible dosing regimen with personalized treatment intervals of up to 16 weeks depending on disease activity was used starting at 20 or 24 weeks after treatment initiation.

The lack of consideration of an individual treatment adjustment in the comparator arm as recommended in the SPC may have a relevant influence on the treatment result. According to the German Ophthalmological Society, the Retinological Society, and the Professional Association of German Ophthalmologists, consistent control examinations and optimization of individualized therapy according to the principle "as much as necessary, as little as possible" are crucial, with patient adherence being of key importance [9]. According to the information provided by the company in Module 4 B, fewer injections mean a lower treatment burden and treatment barrier. This facilitates therapy adherence and enables long-term preservation of vision. The differences between the dosing regimens in the different study arms resulted in a disparity between the faricimab and aflibercept treatment arms.

The studies TENAYA and LUCERNE are therefore not suitable for the benefit assessment.

I 4 Results on added benefit

No suitable data are available for the assessment of added benefit of faricimab in adult patients with neovascular (wet) age-related macular degeneration. There is no hint of an added benefit of faricimab in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

Table 5 summarizes the results of the assessment of added benefit of faricimab in comparison with the ACT.

Table 5: Faricimab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Adult patients with neovascular (wet) age-related macular degeneration	Ranibizumab or **aflibercept**	Added benefit not proven

a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.

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

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.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a22-110.html.