Epcoritamab (follicular lymphoma)

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

EXTRACT

Project: A24-95 Version: 1.0 Status: 10 Dec 2024 DOI: 10.60584/A24-95_en

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Epcoritamab (follikuläres Lymphom) – 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.

Publishing details

Publisher

Institute for Quality and Efficiency in Health Care

Topic

Epcoritamab (follicular lymphoma) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

16 September 2024

Internal Project No.

A24-95

DOI-URL

https://doi.org/10.60584/A24-95_en

Address of publisher

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Siegburger Str. 237
50679 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Medical and scientific advice

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

Patient and family involvement

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

IQWiG employees involved in the dossier assessment

- Annette Christoph
- Tobias Effertz
- Charlotte Guddat
- Lisa Junge
- Claudia Kapp
- Philip Kranz
- Veronika Schneck
- Pamela Wronski

Keywords

Epcoritamab, Lymphoma – Follicular, Benefit Assessment

Part I: Benefit assessment

I Table of contents

I List of tables[2]

Page

[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)

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 epcoritamab. 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 16 September 2024.

Research question

The aim of the present report is to assess the added benefit of epcoritamab as monotherapy in comparison with the appropriate comparator therapy (ACT) in adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic therapy.

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 epcoritamab

Therapeutic indication	**ACT**[a]
Adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic therapy[b, c]	Individualized therapy taking into account prior therapy, course of disease, and general health, selecting from ▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per approval, ▪ lenalidomide + rituximab, ▪ rituximab monotherapy, ▪ mosunetuzumab, ▪ tisagenlecleucel
a. Presented is the ACT specified by the G-BA. b. According to the G-BA, it is assumed that epcoritamab is not an option for the treatment of diagnosed grade 3b follicular lymphomas in the present therapeutic indication. c. In the present therapeutic indication, it is assumed (according to the G-BA) that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to a correspondingly advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. Moreover, it is assumed that stem cell transplantation is not indicated at the time of treatment and that radiotherapy is not therapeutically indicated. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; GELF: Groupe d'Étude des Lymphomes Folliculaires	

Deviating from the ACT specified by the G-BA, the company named 2 further therapy options within the individualized treatment (axicabtagene-ciloleucel, zanubrutinib + obinutuzumab as combination therapy). The company's deviation from the ACT specified by the G-BA will not be further commented below, as the company did not present any suitable data for the benefit assessment – neither compared with a comparator therapy designated by the company nor compared with the ACT specified by the G-BA.

The assessment was conducted in comparison with the ACT specified by the G-BA and by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Results

Concurring with the company, the check of the completeness of the study pool produced no randomized controlled trials (RCTs) on the direct comparison of epcoritamab versus the ACT. However, the company identified the single-arm study GCT3013-01 with epcoritamab among further studies and stated that it would use results on the subpopulation with grade 1 to 3A follicular lymphoma after at least 2 lines of systemic therapy for the assessment of the added benefit of epcoritamab. However, the company did not claim an added benefit. It justified this by stating that, based on the formal requirements of the G-BA, no added benefit of epcoritamab could be demonstrated.

The analyses presented by the company are unsuitable for the benefit assessment of epcoritamab as they do not permit a comparison with the ACT.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of epcoritamab 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 shows a summary of probability and extent of the added benefit of epcoritamab.

[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].

Table 3: Epcoritamab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic therapy[b, c]	Individualized therapy taking into account prior therapy, course of disease, and general health, selecting from ▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per approval, ▪ lenalidomide + rituximab, ▪ rituximab monotherapy, ▪ mosunetuzumab, ▪ tisagenlecleucel	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, it is assumed that epcoritamab is not an option for the treatment of diagnosed grade 3b follicular lymphomas in the present therapeutic indication.
c. In the present therapeutic indication, it is assumed (according to the G-BA) that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to a correspondingly advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. Moreover, it is assumed that stem cell transplantation is not indicated at the time of treatment and that radiotherapy is not therapeutically indicated.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; GELF: Groupe d'Étude des Lymphomes Folliculaires

The G-BA decides on the added benefit.

I 2 Research question

The aim of the present report is to assess the added benefit of epcoritamab as monotherapy in comparison with the ACT in adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic therapy.

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 epcoritamab

Therapeutic indication	**ACT[a]**
Adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic therapy[b, c]	Individualized therapy taking into account prior therapy, course of disease, and general health, selecting from ▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per approval ▪ lenalidomide + rituximab, ▪ rituximab monotherapy, ▪ mosunetuzumab, ▪ tisagenlecleucel
a. Presented is the ACT specified by the G-BA. b. According to the G-BA, it is assumed that epcoritamab is not an option for the treatment of diagnosed grade 3b follicular lymphomas in the present therapeutic indication. c. In the present therapeutic indication, it is assumed (according to the G-BA) that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to a correspondingly advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. Moreover, it is assumed that stem cell transplantation is not indicated at the time of treatment and that radiotherapy is not therapeutically indicated. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; GELF: Groupe d'Étude des Lymphomes Folliculaires	

Deviating from the ACT specified by the G-BA, the company named 2 further therapy options within the individualized treatment (axicabtagene-ciloleucel, zanubrutinib + obinutuzumab as combination therapy). The company's deviation from the ACT specified by the G-BA will not be further commented below, as the company did not present any suitable data for the benefit assessment – neither compared with a comparator therapy designated by the company nor compared with the ACT specified by the G-BA.

The assessment was conducted in comparison with the ACT specified by the G-BA and by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

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 epcoritamab (status: 03 July 2024)
- bibliographical literature search on epcoritamab (last search on 03 July 2024)
- search in trial registries/trial results databases for studies on epcoritamab (last search on 03 July 2024)
- search on the G-BA website for epcoritamab (last search on 03 July 2024)

To check the completeness of the study pool:

- search in trial registries for studies on epcoritamab (last search on 24 September 2024); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check for the completeness of the study pool produced no RCT on the direct comparison of epcoritamab versus the ACT.

Since the company had not identified any RCT with epcoritamab, it conducted an information retrieval for other study types and identified the single-arm study GCT3013-01 [3,4], which was decisive for the approval of epcoritamab in the present therapeutic indication. The company conducted no information retrieval on further studies with the ACT.

The company stated that it used the results of the GCT3013-01 study to assess the added benefit of epcoritamab. However, the company does not claim an added benefit. It justified this by stating that no added benefit of epcoritamab could be demonstrated based on the formal requirements of the G-BA.

Concurring with the company, no added benefit of epcoritamab was derived. The reason for this is that the single-arm GCT3013-01 study does not enable a comparison versus the ACT.

Evidence provided by the company

Study GCT3013-01

The GC3013-01 study is an ongoing, single-arm, open-label, multicentre phase 1 and 2 study on epcoritamab in adult patients with relapsed, progressive or refractory B-cell lymphoma. The study is divided into a dose escalation phase (to determine the dosage of epcoritamab for the subsequent phases), a dose expansion phase and a dose optimization phase. Included were patients with different histological subtypes of B-cell neoplasia according to the 2016 classification of the World Health Organization [5] or 2008 [6] (e.g. grade 1 to 3a follicular

lymphoma). To be included in the dose expansion phase or the dose optimization phase of the study, patients had to have relapsed or refractory, measurable disease after 2 or more prior systemic antineoplastic therapies, including at least 1 monoclonal antibody therapy directed against the epitope cluster of differentiation (CD) 20.

The primary outcome of the dose expansion phase of the GCT3013-01 study is the overall response rate. Primary outcome of the dose optimization phase is the proportion of patients with grade 2 or higher cytokine release syndrome as well as cytokine release syndrome of any grade from the 1st administration of epcoritamab until 7 days after administration of the 2nd full dose of epcoritamab.

In Module 4 A of the dossier, the company presented results on epcoritamab for the subpopulation with grade 1 to 3A follicular lymphoma in the dose optimization phase (N = 86). In addition, it presents results on patient-reported outcomes for patients with grade 1 to 3A follicular lymphoma (N = 128) from the dose expansion phase.

Assessment of the evidence presented by the company

The analyses presented by the company are unsuitable for the benefit assessment of epcoritamab in comparison with the ACT. The consideration of single-arm data on the treatment with epcoritamab from the GCT3013-01 study does not allow a comparison with the ACT. Therefore, the GCT3013-01 study is not suitable for the benefit assessment.

I 4 Results on added benefit

No suitable data are available to assess the added benefit of epcoritamab compared with the ACT in adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic treatment. There is no hint of an added benefit of epcoritamab in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of epcoritamab in comparison with the ACT is summarized in Table 5.

Table 5: Epcoritamab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adult patients with relapsed or refractory follicular lymphoma after 2 or more lines of systemic therapy[b, c]	Individualized therapy taking into account prior therapy, course of disease, and general health, selecting from ▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per approval, ▪ lenalidomide + rituximab, ▪ rituximab monotherapy, ▪ mosunetuzumab, ▪ tisagenlecleucel	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, it is assumed that epcoritamab is not an option for the treatment of diagnosed grade 3b follicular lymphomas in the present therapeutic indication.
c. In the present therapeutic indication, it is assumed (according to the G-BA) that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to a correspondingly advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. Moreover, it is assumed that stem cell transplantation is not indicated at the time of treatment and that radiotherapy is not therapeutically indicated.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; GELF: Groupe d'Étude des Lymphomes Folliculaires

The assessment described above concurs with that by 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: 02.09.2024]. 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.

3. Linton KM, Vitolo U, Jurczak W et al. Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma (EPCORE NHL-1); a phase 2 cohort of a single-arm, multicentre study. Lancet Haematol 2024. https://doi.org/10.1016/s2352-3026(24)00166-2.

4. Hutchings M, Mous R, Clausen MR et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study. Lancet 2021; 398(10306): 1157-1169. https://doi.org/10.1016/s0140-6736(21)00889-8.

5. Swerdlow SH, Campo E, Pileri SA et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016; 127(20): 2375-2390. https://doi.org/10.1182/blood-2016-01-643569.

6. WHO. Tumours of Haematopoietic and Lymphoid Tissues. 2008.

The full report (German version) is published under https://www.iqwig.de/en/projects/a24-95.html.