Glofitamab
(DLBCL, combination with gemcitabine and oxaliplatin)

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

EXTRACT

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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 families were involved in 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
CAR	chimeric antigen receptor
DLBCL	diffuse large B-cell lymphoma
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MYC	myelocytomatosis oncogene
NOS	not otherwise specified
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
WHO	World Health Organization

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 glofitamab (in combination with gemcitabine and oxaliplatin). 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 May 2025.

Research question

The aim of this report is to assess the added benefit of glofitamab in combination with gemcitabine and oxaliplatin (hereinafter referred to as glofitamab + gemcitabine + oxaliplatin) compared with the appropriate comparator therapy (ACT) in adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS) and who are ineligible for autologous stem cell transplant.

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 glofitamab + gemcitabine + oxaliplatin

Therapeutic indication	**ACT**[a, b, c]
Adults with relapsed or refractory DLBCL NOS who are ineligible for autologous stem cell transplant	▪ tafasitamab in combination with lenalidomide or ▪ polatuzumab vedotin in combination with bendamustine and rituximab
a. Presented is the ACT specified by the G-BA. b. According to the G-BA, due to the study population of the STARGLO study (GO41944) and the combination therapy with gemcitabine and oxaliplatin used, it is assumed that high-dose therapy with subsequent autologous or allogeneic stem cell transplant or CAR T-cell therapy is not an option for patients in the therapeutic indication of glofitamab. c. According to the S3 guideline, radiotherapy can be a suitable method for local disease control in palliative situations and should be offered to patients with 2 or more prior systemic therapies, if indicated, in both study arms. ACT: appropriate comparator therapy; CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Federal Joint Committee; NOS: not otherwise specified	

On 6 May 2025, shortly before the dossier was submitted by the company, the G-BA modified the ACT to that shown in Table 2. In its dossier, the company referred to the ACT from its consultation with the G-BA in 2021.

The company modified the specified ACT and justified this with numerous new treatment options that it said have significantly changed the treatment landscape in recent years. It

therefore distinguished between 4 research questions depending on the number of previous lines of treatment (1 / ≥ 2) and suitability for chimeric antigen receptor (CAR) T-cell therapy (yes/no). Consistent with the information in Module 3 A, the company defined the ACT as follows:

- Subpopulation 1: Patients who have failed first-line treatment and are eligible for CAR T-cell therapy
  - axicabtagene ciloleucel or lisocabtagene maraleucel
- Subpopulation 2: Patients who have failed first-line treatment and are ineligible for CAR T-cell therapy
  - tafasitamab in combination with lenalidomide (tafasitamab + lenalidomide) or polatuzumab vedotin in combination with bendamustine and rituximab (polatuzumab vedotin + bendamustine + rituximab)
- Subpopulation 3: Patients after at least 2 lines of treatment who are eligible for CAR T-cell therapy
  - axicabtagene ciloleucel or lisocabtagene maraleucel or tisagenlecleucel
- Subpopulation 4: Patients after at least 2 lines of treatment who are ineligible for CAR T-cell therapy
  - Treatment of physician's choice, selecting from epcoritamab or glofitamab or loncastuximab tesirine or polatuzumab vedotin + bendamustine + rituximab or tafasitamab + lenalidomide

This benefit assessment was conducted in comparison with the ACT specified by the G-BA on 6 May 2025. The company's deviation from the G-BA's ACT remained without consequence, as the company did not present any suitable data for the benefit assessment – neither versus the comparator therapy it had specified nor versus 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) were used to derive the added benefit. This concurred with the company's inclusion criteria.

Results

Consistent with the findings of the company, a review of the completeness of the study pool did not identify any relevant RCTs for the direct comparison of glofitamab + gemcitabine + oxaliplatin with the ACT specified by the G-BA in the given therapeutic indication. Nevertheless, the company presented data on its RCT GO41944 (hereinafter referred to as the STARGLO study), in which glofitamab + gemcitabine + oxaliplatin was compared with rituximab in combination with gemcitabine and oxaliplatin (hereinafter referred to as

rituximab + gemcitabine + oxaliplatin). The treatment in the comparator arm did not concur with the ACT, so no data were available on the comparison of glofitamab + gemcitabine + oxaliplatin with the comparator therapy specified by the G-BA.

Results on added benefit

Since no suitable data were available for the benefit assessment, there is no hint of an added benefit of glofitamab + gemcitabine + oxaliplatin 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 the probability and extent of the added benefit of glofitamab + gemcitabine + oxaliplatin.

Table 3: Glofitamab + gemcitabine + oxaliplatin – probability and extent of added benefit

Therapeutic indication	ACT[a, b, c]	Probability and extent of added benefit
Adults with relapsed or refractory DLBCL NOS who are ineligible for autologous stem cell transplant	▪ tafasitamab in combination with lenalidomide or ▪ polatuzumab vedotin in combination with bendamustine and rituximab	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, due to the study population of the STARGLO study (GO41944) and the combination therapy with gemcitabine and oxaliplatin used, it is assumed that high-dose therapy with subsequent autologous or allogeneic stem cell transplant or CAR T-cell therapy is not an option for patients in the therapeutic indication of glofitamab.
c. According to the S3 guideline, radiotherapy can be a suitable method for local disease control in palliative situations and should be offered to patients with 2 or more prior systemic therapies, if indicated, in both study arms.

ACT: appropriate comparator therapy; CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Federal Joint Committee; NOS: not otherwise specified

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 glofitamab in combination with gemcitabine and oxaliplatin (hereinafter referred to as glofitamab + gemcitabine+ oxaliplatin) compared with the ACT in adult patients with relapsed or refractory DLBCL NOS and who are ineligible for autologous stem cell transplant.

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 glofitamab + gemcitabine + oxaliplatin

Therapeutic indication	**ACT**[a, b, c]
Adults with relapsed or refractory DLBCL NOS who are ineligible for autologous stem cell transplant	▪ tafasitamab in combination with lenalidomide or ▪ polatuzumab vedotin in combination with bendamustine and rituximab
a. Presented is the ACT specified by the G-BA. b. According to the G-BA, due to the study population of the STARGLO study (GO41944) and the combination therapy with gemcitabine and oxaliplatin used, it is assumed that high-dose therapy with subsequent autologous or allogeneic stem cell transplant or CAR T-cell therapy is not an option for patients in the therapeutic indication of glofitamab. c. According to the S3 guideline, radiotherapy can be a suitable method for local disease control in palliative situations and should be offered to patients with 2 or more prior systemic therapies, if indicated, in both study arms. ACT: appropriate comparator therapy; CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Federal Joint Committee; NOS: not otherwise specified	

On 6 May 2025, shortly before the dossier was submitted by the company, the G-BA modified the ACT to that shown in Table 4. In its dossier, the company referred to the ACT from its consultation with the G-BA in 2021.

The company modified the specified ACT and justified this with numerous new treatment options that it said have significantly changed the treatment landscape in recent years. It therefore distinguished between 4 research questions depending on the number of previous lines of treatment (1 / ≥ 2) and suitability for CAR T-cell therapy (yes/no). Consistent with the information in Module 3 A, the company defined the ACT as follows:

- Subpopulation 1: Patients who have failed first-line treatment and are eligible for CAR T-cell therapy
  - axicabtagene ciloleucel or lisocabtagene maraleucel
- Subpopulation 2: Patients who have failed first-line treatment and are ineligible for CAR T-cell therapy

- tafasitamab in combination with lenalidomide (tafasitamab + lenalidomide) or polatuzumab vedotin in combination with bendamustine and rituximab (polatuzumab vedotin + bendamustine + rituximab)

- Subpopulation 3: Patients after at least 2 lines of treatment who are eligible for CAR T-cell therapy
  - axicabtagene ciloleucel or lisocabtagene maraleucel or tisagenlecleucel
- Subpopulation 4: Patients after at least 2 lines of treatment who are ineligible for CAR T-cell therapy
  - Treatment of physician's choice, selecting from epcoritamab or glofitamab or loncastuximab tesirine or polatuzumab vedotin + bendamustine + rituximab or tafasitamab + lenalidomide

This benefit assessment was conducted in comparison with the ACT specified by the G-BA on 6 May 2025. The company's deviation from the G-BA's ACT remained without consequence, as the company did not present any suitable data for the benefit assessment – neither versus the comparator therapy it had specified nor versus the ACT specified by the G-BA (see Chapter I 3).

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs were used to derive the added benefit. This concurred 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 glofitamab + gemcitabine + oxaliplatin (status 11 March 2025)
- Bibliographical literature search on glofitamab + gemcitabine + oxaliplatin (last search on 11 March 2025)
- Search of trial registries/trial results databases for studies on glofitamab + gemcitabine + oxaliplatin (last search on 11 March 2025)
- Search on the G-BA website for glofitamab + gemcitabine + oxaliplatin (last search on 11 March 2025)

To check the completeness of the study pool:

- Search of trial registries for studies on glofitamab (last search on 27 May 2025); for search strategies, see I Appendix A of the full dossier assessment

Consistent with the findings of the company, a review of the completeness of the study pool did not identify any relevant RCTs for the direct comparison of glofitamab + gemcitabine + oxaliplatin with the ACT specified by the G-BA in the given therapeutic indication.

Nevertheless, the company presented data on its RCT GO41944 (hereinafter referred to as the STARGLO study) [3], on the basis of which the marketing authorization of glofitamab + gemcitabine + oxaliplatin was granted. The study investigated glofitamab + gemcitabine + oxaliplatin in comparison with rituximab in combination with gemcitabine and oxaliplatin (hereinafter referred to as rituximab + gemcitabine + oxaliplatin). STARGLO is briefly described below.

The STARGLO study

STARGLO is an ongoing, open-label RCT comparing glofitamab + gemcitabine + oxaliplatin with rituximab + gemcitabine + oxaliplatin for the treatment of adult patients with relapsed/refractory DLBCL NOS. Patients who were refractory or relapsed after at least one line of prior systemic therapy were included. Patients for whom only one prior line of therapy had failed were not allowed to be eligible for a stem cell transplant. The following patients, among others, were excluded from study participation: patients eligible for CAR T-cell therapy (this only applied to Germany and France), patients with high-grade B-cell lymphoma with myelocytomatosis oncogene (MYC) and B-cell lymphoma 2 (BCL2) and/or BCL6 translocations, with high-grade B-cell lymphoma NOS (according to the World Health Organization [WHO]

classification 2016) and with primary mediastinal B-cell lymphoma. Overall survival was the primary outcome of STARGLO.

In Module 4 A of the dossier, the company presented data on the STARGLO patients (N = 274) for the data cut-off of 16 February 2024, divided into 2 subpopulations: patients after failure of first-line treatment and patients after failure of at least 2 previous lines of treatment.

The treatment in the comparator arm of STARGLO did not concur with the ACT, so no data were available on the comparison of glofitamab + gemcitabine + oxaliplatin with the comparator therapy specified by the G-BA.

I 4 Results on added benefit

For the assessment of glofitamab + gemcitabine + oxaliplatin for the treatment of adult patients with relapsed or refractory DLBCL NOS who are ineligible for autologous stem cell transplant, no suitable data were available for comparison with the ACT specified by the G-BA. There is no hint of an added benefit of glofitamab + gemcitabine + oxaliplatin 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 glofitamab + gemcitabine + oxaliplatin in comparison with the ACT is summarized in Table 5.

Table 5: Glofitamab + gemcitabine + oxaliplatin – probability and extent of added benefit

Therapeutic indication	**ACT**[a, b, c]	**Probability and extent of added benefit**
Adults with relapsed or refractory DLBCL NOS who are ineligible for autologous stem cell transplant	▪ tafasitamab in combination with lenalidomide or ▪ polatuzumab vedotin in combination with bendamustine and rituximab	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, due to the study population of the STARGLO study (GO41944) and the combination therapy with gemcitabine and oxaliplatin used, it is assumed that high-dose therapy with subsequent autologous or allogeneic stem cell transplant or CAR T-cell therapy is not an option for patients in the therapeutic indication of glofitamab.
c. According to the S3 guideline, radiotherapy can be a suitable method for local disease control in palliative situations and should be offered to patients with 2 or more prior systemic therapies, if indicated, in both study arms.

ACT: appropriate comparator therapy; CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Federal Joint Committee; NOS: not otherwise specified

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.

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