Loncastuximab tesirine (DLBCL and HGBL)

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 *Loncastuximab tesirin (DLBCL und HGBL) – 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 his 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 Bernhard Jochheim.

IQWiG thanks the respondent for participating in the written exchange about how he experienced the disease and its treatment and about the treatment goals. The respondent was not involved in the actual preparation of the dossier assessment.

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Keywords

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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
AE	adverse event
BCL2	B-cell lymphoma 2
BCL6	B-cell lymphoma 6
BSG	Bundessozialgericht (Federal Social Court)
CAR-T	chimeric antigen receptor T-cell
DLBCL	diffuse large B-cell lymphoma
FDA	Food and Drug Administration
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HGBL	high-grade B-cell lymphoma
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MYC	myelocytomatosis oncogene
NOS	not otherwise specified
ORR	overall response rate
PMBCL	primary mediastinal large B-cell lymphoma
RCT	randomized controlled trial
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)
SPC	Summary of Product Characteristics
WHO	World Health Organization

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 loncastuximab tesirine. 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 15 May 2023.

Research question

The aim of the present report is to assess the added benefit of loncastuximab tesirine as monotherapy in comparison with the appropriate comparator therapy (ACT) for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) in adults after ≥ 2 lines of systemic therapy.

The research questions shown in Table 2 are derived from the ACT specified by the G-BA.

Table 2: Research questions of the benefit assessment of loncastuximab tesirine

Research question	Therapeutic indication	ACT[a]
1	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are eligible for high-dose therapy[b]	Treatment of physician's choice[c], taking into account ▪ tisagenlecleucel[d] ▪ axicabtagene ciloleucel[d] ▪ induction therapy with MINE followed by high-dose therapy with autologous stem cell transplantation if there is a response to induction therapy ▪ induction therapy with MINE followed by high-dose therapy with allogeneic stem cell transplantation if there is a response to induction therapy
2	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are not eligible for high-dose therapy	Treatment of physician's choice, taking into account ▪ CEOP ▪ dose-adjusted EPOCH ▪ polatuzumab vedotin + bendamustine + rituximab[d] ▪ tafasitamab + lenalidomide[d] ▪ pixantrone monotherapy ▪ radiation ▪ best supportive care

a. Presented is the respective ACT specified by the G-BA. Present guidelines and scientific-medical societies and/or the Drug Commission of the German Medical Association in accordance with §35a (para. 7, sentence 4) SGB V list both approved and unapproved drug therapies for the treatment of relapsed or refractory DLBCL and HGBL after at least 2 prior therapies. Drugs that are not approved for the present therapeutic indication and whose prescribability in off-label use has also not been recognized by the G-BA in the Pharmaceuticals Directive are generally not considered as ACT in the narrower sense of §2 (para. 1, sentence 3) §12 SGB V, according to the BSG comments on the judgment of 22 February 2023 (reference number: B 3 KR 14/21 R).

b. It is assumed that patients are eligible for high-dose therapy with curative intent.

c. When selecting the treatment options of the ACT, the patients' pretreatment with CAR T-cell therapy, autologous stem cell transplantation or allogeneic stem cell transplantation should be taken into account accordingly. In patients who have not yet been treated with autologous stem cell transplantation, allogeneic stem cell transplantation is an option in patients who have a very high risk of relapse or in whom sufficient stem cell collection for autologous stem cell transplantation was not possible.

d. The approvals of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel relate exclusively to DLBCL and PMBCL (approval between 2018 and 2021). With the updated WHO classification of 2022, HGBL was newly listed as a definite entity. Previously, aggressive lymphomas with MYC and BCL2/6 rearrangements were assigned to DLBCL, so that HGBL was not specified separately in the therapeutic indication at the time of approval of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel. Therefore, the G-BA considered designating these treatment options for both DLBCL and HGBL to be appropriate.

BCL2: B-cell lymphoma 2; BCL6: B-cell lymphoma 6; BSG: Federal Social Court; CAR T-cells: chimeric antigen receptor T-cells; CEOP: cyclophosphamide, etoposide, vincristine, prednisone; DLBCL: diffuse large B-cell lymphoma; EPOCH: etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone; G-BA: Federal Joint Committee; HGBL: high-grade B-cell lymphoma; MINE: mesna, ifosfamide, mitoxantrone, etoposide; MYC: myelocytomatosis oncogene; PMBCL: primary mediastinal large B-cell lymphoma; SGB: Social Code Book V; WHO: World Health Organization

In connection with the determination of the ACT, the G-BA pointed out that present guidelines and scientific-medical societies and/or the Drug Commission of the German Medical Association in accordance with §35a (para. 7, sentence 4) SGB V list both approved and unapproved drug therapies for the treatment of relapsed or refractory DLBCL and HGBL after at least 2 prior therapies. Drugs that are not approved for the present therapeutic indication and whose prescribability in off-label use has also not been recognized by the G-BA in the Pharmaceuticals Directive are generally not considered as ACT in the narrower sense of §2 (para. 1, sentence 3) §12 SGB V, according to the Federal Social Court (BSG) comments on the judgment of 22 February 2023 (reference number: B 3 KR 14/21 R).

In deviation from the ACT according to Table 2, the company, in Module 3 A of the dossier, designated patient-specific therapy, taking into account the biology of the disease, the prior therapy, the course of disease and the general condition, with the comparators chimeric antigen receptor T-cell (CAR-T) therapy (tisagenlecleucel, axicabtagene ciloleucel and lisocabtagene maraleucel), allogeneic stem cell transplantation, autologous stem cell transplantation, polatuzumab vedotin + bendamustine + rituximab and tafasitamab + lenalidomide as ACT for the entire approval population, i.e. without differentiating between the 2 research questions. The company's deviation from the ACT specified by the G-BA will not be further commented on 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 is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier in comparison with the adapted ACT.

Since no suitable data are available for either of the 2 research questions designated by the G-BA, the assessment below is performed in a joint section of the report.

Results

The check of completeness of the study pool found no randomized controlled trial (RCT) of direct comparison of loncastuximab tesirine versus the ACT. The company also did not identify any RCTs versus its ACT. Among the further investigations, the company identified the single-arm study LOTIS-2 (ADCT-402-201) for loncastuximab tesirine and used this study to derive the added benefit. The LOTIS-2 study is unsuitable for the derivation of an added benefit because, as a single-arm study, it does not permit a comparison with the ACT. Beyond that, the company did not conduct any information retrieval for further investigations 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 loncastuximab tesirine in comparison with the ACT for both research questions of the present benefit assessment; 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 loncastuximab tesirine.

[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: Loncastuximab tesirine – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are eligible for high-dose therapy[b]	Treatment of physician's choice[c], taking into account ▪ tisagenlecleucel[d] ▪ axicabtagene ciloleucel[d] ▪ induction therapy with MINE followed by high-dose therapy with autologous stem cell transplantation if there is a response to induction therapy ▪ induction therapy with MINE followed by high-dose therapy with allogeneic stem cell transplantation if there is a response to induction therapy	Added benefit not proven
2	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are not eligible for high-dose therapy	Treatment of physician's choice, taking into account ▪ CEOP ▪ dose-adjusted EPOCH ▪ polatuzumab vedotin + bendamustine + rituximab[d] ▪ tafasitamab + lenalidomide[d] ▪ pixantrone monotherapy ▪ radiation ▪ best supportive care	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA. Present guidelines and scientific-medical societies and/or the Drug Commission of the German Medical Association in accordance with §35a (para. 7, sentence 4) SGB V list both approved and unapproved drug therapies for the treatment of relapsed or refractory DLBCL and HGBL after at least 2 prior therapies. Drugs that are not approved for the present therapeutic indication and whose prescribability in off-label use has also not been recognized by the G-BA in the Pharmaceuticals Directive are generally not considered as ACT in the narrower sense of §2 (para. 1, sentence 3) §12 SGB V, according to the BSG comments on the judgment of 22 February 2023 (reference number: B 3 KR 14/21 R).

b. It is assumed that patients are eligible for high-dose therapy with curative intent.

c. When selecting the treatment options of the ACT, the patients' pretreatment with CAR T-cell therapy, autologous stem cell transplantation or allogeneic stem cell transplantation should be taken into account accordingly. In patients who have not yet been treated with autologous stem cell transplantation, allogeneic stem cell transplantation is an option in patients who have a very high risk of relapse or in whom sufficient stem cell collection for autologous stem cell transplantation was not possible.

d. The approvals of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel relate exclusively to DLBCL and PMBCL (approval between 2018 and 2021). With the updated WHO classification of 2022, HGBL was newly listed as a definite entity. Previously, aggressive lymphomas with MYC and BCL2/6 rearrangements were assigned to DLBCL, so that HGBL was not specified separately in the therapeutic indication at the time of approval of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel. Therefore, the G-BA considered designating these treatment options for both DLBCL and HGBL to be appropriate.

BCL2: B-cell lymphoma 2; BCL6: B-cell lymphoma 6; BSG: Federal Social Court; CAR T-cells: chimeric antigen receptor T-cells; CEOP: cyclophosphamide, etoposide, vincristine, prednisone; DLBCL: diffuse large B-cell lymphoma; EPOCH: etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone; G-BA: Federal Joint Committee; HGBL: high-grade B-cell lymphoma; MINE: mesna, ifosfamide, mitoxantrone, etoposide; MYC: myelocytomatosis oncogene; PMBCL: primary mediastinal large B-cell lymphoma; SGB: Social Code Book V; WHO: World Health Organization

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 loncastuximab tesirine as monotherapy in comparison with the ACT for the treatment of relapsed or refractory DLBCL and HGBL in adults after ≥ 2 lines of systemic therapy.

The research questions shown in Table 4 are derived from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of loncastuximab tesirine

Research question	Therapeutic indication	ACT[a]
1	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are eligible for high-dose therapy[b]	Treatment of physician's choice[c], taking into account ▪ tisagenlecleucel[d] ▪ axicabtagene ciloleucel[d] ▪ induction therapy with MINE followed by high-dose therapy with autologous stem cell transplantation if there is a response to induction therapy ▪ induction therapy with MINE followed by high-dose therapy with allogeneic stem cell transplantation if there is a response to induction therapy
2	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are not eligible for high-dose therapy	Treatment of physician's choice, taking into account ▪ CEOP ▪ dose-adjusted EPOCH ▪ polatuzumab vedotin + bendamustine + rituximab[d] ▪ tafasitamab + lenalidomide[d] ▪ pixantrone monotherapy ▪ radiation ▪ best supportive care

a. Presented is the respective ACT specified by the G-BA. Present guidelines and scientific-medical societies and/or the Drug Commission of the German Medical Association in accordance with §35a (para. 7, sentence 4) SGB V list both approved and unapproved drug therapies for the treatment of relapsed or refractory DLBCL and HGBL after at least 2 prior therapies. Drugs that are not approved for the present therapeutic indication and whose prescribability in off-label use has also not been recognized by the G-BA in the Pharmaceuticals Directive are generally not considered as ACT in the narrower sense of §2 (para. 1, sentence 3) §12 SGB V, according to the BSG comments on the judgment of 22 February 2023 (reference number: B 3 KR 14/21 R).

b. It is assumed that patients are eligible for high-dose therapy with curative intent.

c. When selecting the treatment options of the ACT, the patients' pretreatment with CAR T-cell therapy, autologous stem cell transplantation or allogeneic stem cell transplantation should be taken into account accordingly. In patients who have not yet been treated with autologous stem cell transplantation, allogeneic stem cell transplantation is an option in patients who have a very high risk of relapse or in whom sufficient stem cell collection for autologous stem cell transplantation was not possible.

d. The approvals of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel relate exclusively to DLBCL and PMBCL (approval between 2018 and 2021). With the updated WHO classification of 2022 [3], HGBL was newly listed as a definite entity. Previously, aggressive lymphomas with MYC and BCL2/6 rearrangements were assigned to DLBCL, so that HGBL was not specified separately in the therapeutic indication at the time of approval of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel. Therefore, the G-BA considered designating these treatment options for both DLBCL and HGBL to be appropriate.

BCL2: B-cell lymphoma 2; BCL6: B-cell lymphoma 6; BSG: Federal Social Court; CAR T-cells: chimeric antigen receptor T-cells; CEOP: cyclophosphamide, etoposide, vincristine, prednisone; DLBCL: diffuse large B-cell lymphoma; EPOCH: etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone; G-BA: Federal Joint Committee; HGBL: high-grade B-cell lymphoma; MINE: mesna, ifosfamide, mitoxantrone, etoposide; MYC: myelocytomatosis oncogene; PMBCL: primary mediastinal large B-cell lymphoma; SGB: Social Code Book V; WHO: World Health Organization

In connection with the determination of the ACT, the G-BA pointed out that present guidelines and scientific-medical societies and/or the Drug Commission of the German Medical Association in accordance with §35a (para. 7, sentence 4) SGB V list both approved and unapproved drug therapies for the treatment of relapsed or refractory DLBCL and HGBL after at least 2 prior therapies. Drugs that are not approved for the present therapeutic indication and whose prescribability in off-label use has also not been recognized by the G-BA in the Pharmaceuticals Directive are generally not considered as ACT in the narrower sense of §2 (para. 1, sentence 3) §12 SGB V, according to the BSG comments on the judgment of 22 February 2023 (reference number: B 3 KR 14/21 R).

In deviation from the ACT according to Table 4, the company, in Module 3 A of the dossier, designated patient-specific therapy, taking into account the biology of the disease, the prior therapy, the course of disease and the general condition, with the comparators CAR-T therapy (tisagenlecleucel, axicabtagene ciloleucel and lisocabtagene maraleucel), allogeneic stem cell transplantation, autologous stem cell transplantation, polatuzumab vedotin + bendamustine + rituximab and tafasitamab + lenalidomide as ACT for the entire approval population, i.e. without differentiating between the 2 research questions. The company's deviation from the ACT specified by the G-BA will not be further commented on 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 is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier in comparison with the adapted ACT.

Since no suitable data are available for either of the 2 research questions designated by the G-BA, the assessment below is performed in a joint section of the report.

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 loncastuximab tesirine (status: 6 March 2023)
- bibliographical literature search on loncastuximab tesirine alfa (last search on 6 March 2023)
- search in trial registries/trial results databases for studies on loncastuximab tesirine (last search on 6 March 2023)
- search on the G-BA website for loncastuximab tesirine (last search on 6 March 2023)

To check the completeness of the study pool:

- search in trial registries for studies on loncastuximab tesirine (last search on 23 May 2023); for search strategies, see I Appendix A of the full dossier assessment

Direct comparison

The check of completeness of the study pool found no RCT of direct comparison of loncastuximab tesirine versus the ACT in the present therapeutic indication.

Further investigations

As the company also did not identify any studies for a direct comparison, it carried out an information retrieval for further investigations with loncastuximab tesirine and presented data on the single-arm study LOTIS-2 (ADCT-402-201) [4] in the dossier. The company conducted no information retrieval on other investigations with the ACT.

A check for completeness of the study pool presented by the company for other investigations was foregone because the data submitted by the company under “Other investigations” are unsuitable for the benefit assessment due to the lack of comparison with the ACT. This is explained below.

LOTIS-2 study

The LOTIS-2 study is a single-arm study on treatment with loncastuximab tesirine, which included adults with relapsed or refractory DLBCL not otherwise specified (NOS), HGBL with myelocytomatosis oncogene (MYC) and B-cell lymphoma (BCL)2 and/or BCL6 rearrangements and primary mediastinal large B-cell lymphoma (PMBCL) as defined by the 2016 World Health Organization (WHO) classification of lymphoid neoplasms [5]. A total of 145 patients were enrolled, including 127 (87.6%) with DLBCL, 11 (7.6%) with HGBL, and 7 (4.8%) with PMBCL, with the latter not comprised by the approved therapeutic indication of loncastuximab

tesirine. All patients had to have already received ≥ 2 lines of systemic therapy and have measurable disease as defined by the 2014 Lugano Classification [6].

Loncastuximab tesirine treatment was generally administered in accordance with the specifications provided in the Summary of Product Characteristics (SPC) [7]. In addition to the approved formulation (powder for concentrate for solution for infusion), some of the patients were treated with a liquid formulation. In total, 35 of the 145 patients (24.1%) received the latter formulation.

The primary outcome was the overall response rate (ORR) according to the 2014 Lugano classification [6]. Secondary outcomes include outcomes from the categories of mortality, morbidity, health-related quality of life and side effects.

According to the information provided by the company in Module 4 A of the dossier, 5 data cut-offs were performed for the LOTIS-2 study: the first data cut-off on 6 April 2020 (submission for approval to the Food and Drug Administration [FDA]); the second data cut-off on 6 August 2020 (120-day safety follow-up for approval to the FDA); the third data cut-off on 1 March 2021 (submission for approval to the European Medicines Agency); the fourth data cut-off on 1 March 2022 (internal data cut-off), and the fifth data cut-off on 15 September 2022 (final overall survival analysis). In Module 4 A, the company presented the results of the individual outcomes for both the first and the third data cut-off, as well as for the outcome of overall survival for the fifth data cut-off.

Approach of the company

Based on its information retrieval, the company classified the single-arm study LOTIS-2 as the best available evidence. Although the company described that no added benefit can usually be derived for single-arm studies due to the lack of evidence in comparison with an ACT, it derived a hint of a non-quantifiable added benefit for loncastuximab tesirine in the overall assessment based on the third data cut-off (and for the outcome of overall survival additionally based on the fifth data cut-off) of the LOTIS-2 study because a high therapeutic need was addressed and there were clinical and therapeutic advantages.

Submitted data unsuitable for drawing conclusions on added benefit

The LOTIS-2 study is unsuitable for the derivation of an added benefit because, as a single-arm study, it does not permit a comparison with the ACT. Hence, there are no suitable data for deriving an added benefit in comparison with the ACT.

I 4 Results on added benefit

No suitable data are available to assess the added benefit of loncastuximab tesirine as monotherapy in comparison with the ACT for the treatment of relapsed or refractory DLBCL and HGBL in adults after ≥ 2 lines of systemic therapy. There is no hint of added benefit of loncastuximab tesirine in comparison with the ACT for either research question of the present benefit assessment; 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 loncastuximab tesirine in comparison with the ACT.

Table 5: Loncastuximab tesirine – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are eligible for high-dose therapy[b]	Treatment of physician's choice[c], taking into account ▪ tisagenlecleucel[d] ▪ axicabtagene ciloleucel[d] ▪ induction therapy with MINE followed by high-dose therapy with autologous stem cell transplantation if there is a response to induction therapy ▪ induction therapy with MINE followed by high-dose therapy with allogeneic stem cell transplantation if there is a response to induction therapy	Added benefit not proven
2	Adults with relapsed or refractory DLBCL and HGBL after ≥ 2 lines of systemic therapy who are not eligible for high-dose therapy	Treatment of physician's choice, taking into account ▪ CEOP ▪ dose-adjusted EPOCH ▪ polatuzumab vedotin + bendamustine + rituximab[d] ▪ tafasitamab + lenalidomide[d] ▪ pixantrone monotherapy ▪ radiation ▪ best supportive care	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA. Present guidelines and scientific-medical societies and/or the Drug Commission of the German Medical Association in accordance with §35a (para. 7, sentence 4) SGB V list both approved and unapproved drug therapies for the treatment of relapsed or refractory DLBCL and HGBL after at least 2 prior therapies. Drugs that are not approved for the present therapeutic indication and whose prescribability in off-label use has also not been recognized by the G-BA in the Pharmaceuticals Directive are generally not considered as ACT in the narrower sense of §2 (para. 1, sentence 3) §12 SGB V, according to the BSG comments on the judgment of 22 February 2023 (reference number: B 3 KR 14/21 R).

b. It is assumed that patients are eligible for high-dose therapy with curative intent.

c. When selecting the treatment options of the ACT, the patients' pretreatment with CAR T-cell therapy, autologous stem cell transplantation or allogeneic stem cell transplantation should be taken into account accordingly. In patients who have not yet been treated with autologous stem cell transplantation, allogeneic stem cell transplantation is an option in patients who have a very high risk of relapse or in whom sufficient stem cell collection for autologous stem cell transplantation was not possible.

d. The approvals of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel relate exclusively to DLBCL and PMBCL (approval between 2018 and 2021). With the updated WHO classification of 2022 [3], HGBL was newly listed as a definite entity. Previously, aggressive lymphomas with MYC and BCL2/6 rearrangements were assigned to DLBCL, so that HGBL was not specified separately in the therapeutic indication at the time of approval of polatuzumab vedotin + bendamustine + rituximab, tafasitamab + lenalidomide, tisagenlecleucel and axicabtagene ciloleucel. Therefore, the G-BA considered designating these treatment options for both DLBCL and HGBL to be appropriate.

BCL2: B-cell lymphoma 2; BCL6: B-cell lymphoma 6; BSG: Federal Social Court; CAR T-cells: chimeric antigen receptor T-cells; CEOP: cyclophosphamide, etoposide, vincristine, prednisone; DLBCL: diffuse large B-cell lymphoma; EPOCH: etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone; G-BA: Federal Joint Committee; HGBL: high-grade B-cell lymphoma; MINE: mesna, ifosfamide, mitoxantrone, etoposide; MYC: myelocytomatosis oncogene; PMBCL: primary mediastinal large B-cell lymphoma; SGB: Social Code Book V; WHO: World Health Organization

The assessment described above departs from that by the company, which derived a hint of non-quantifiable added benefit for the entire approval population of loncastuximab tesirine.

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/a23-45.html.