Polatuzumab Vedotin (combination with bendamustine and rituximab, relapsed or refractory DLBCL)

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

EXTRACT

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[1] Translation of Sections I 1 to I 5 of the dossier assessment *Polatuzumab Vedotin (Kombination mit Bendamustin und Rituximab, rezidivierendes oder refraktäres DLBCL) – 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

No feedback of persons concerned was received within the framework of 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
DLBCL	relapsed or refractory diffuse large B-cell lymphoma
FL	follicular lymphoma
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IPD	individual patient data
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 polatuzumab vedotin (in combination with bendamustine and rituximab). 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 21 December 2023.

Research question

The aim of this report is to assess the added benefit of polatuzumab vedotin in combination with bendamustine and rituximab (hereinafter referred to as "polatuzumab vedotin + bendamustine + rituximab") compared with the appropriate comparator therapy (ACT) in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), for whom haematopoietic stem cell transplantation is not an option.

The research questions presented in Table 2 result from the ACT specified by the G-BA.

Table 2: Research questions of the benefit assessment of polatuzumab vedotin + bendamustine + rituximab

Research question	Therapeutic indication	ACT[a, b]
1	Adults with relapsed or refractory DLBCL after failure of 1 line of systemic therapy for whom haematopoietic stem cell transplantation is not an option	Tafasitamab in combination with lenalidomide[c]
2	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy is an option and haematopoietic stem cell transplantation is not an option	▪ Tisagenlecleucel or ▪ axicabtagene ciloleucel or ▪ lisocabtagene maraleucel
3	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy and haematopoietic stem cell transplantation are not an option	Treatment of physician's choice, taking into account[d]: ▪ tafasitamab in combination with lenalidomide, ▪ pixantrone monotherapy and ▪ radiation

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, the available evidence does not imply that the off-label use of rituximab in combination with gemcitabine and oxaliplatin and of rituximab in combination with bendamustine is generally preferable over the drugs approved in the therapeutic indication so far, or over the drugs approved for relevant patient groups or therapeutic indications so far based on the generally recognized state of medical knowledge. Rituximab in combination with gemcitabine and oxaliplatin and rituximab in combination with bendamustine are therefore not specified as an ACT.
c. Patients with a PET-positive residual tumour after systemic second-line therapy should receive consolidation radiotherapy.
d. A single-comparator study is generally insufficient for implementing treatment of physician's choice in a study of direct comparison. The investigators are expected to have a choice between several treatment options (multi-comparator study). The choice and, if necessary, limitation of treatment options must be justified.

CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Joint Federal Committee; PET: positron emission tomography

The company deviated from the G-BA's specification for differentiating between the different research questions and the respective ACTs. In its dossier, it addresses only 2 research questions by differentiating the therapeutic indication solely by the number of treatment lines: after failure of 1 and after failure of ≥ 2 lines of systemic therapy. However, after failure of ≥ 2 lines of systemic therapy, it does not differentiate further within the population depending on the eligibility for CAR T-cell therapy.

In addition, the company is inconsistent in naming the ACT within the dossier. However, none of the comparator therapies listed by the company corresponded to the G-BA's ACT.

The present assessment was conducted on the basis of the research questions specified by the G-BA (populations and corresponding ACTs).

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) are used to derive the added benefit.

Since no suitable data are available for either of the 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 did not reveal any relevant study for assessing the added benefit of polatuzumab vedotin + bendamustine + rituximab in comparison with the ACT for the present research questions.

The studies GO29365 and YO41543 included by the company are not suitable for the assessment of the added benefit of polatuzumab vedotin + bendamustine + rituximab versus the ACT because the ACT was not implemented in both studies. This is justified below.

Evidence provided by the company

GO29365

GO29365 is a completed, multicentre, open-label phase IB/II study comparing polatuzumab vedotin in combination with bendamustine and rituximab or bendamustine and obinutuzumab. It included adult patients with relapsed or refractory DLBCL or follicular lymphoma (FL) after at least 1 systemic therapy for whom autologous haematopoietic stem cell transplantation was not an option. The disease was considered refractory if patients showed progression or no response (stable disease) within < 6 months after start of the previous therapy, and relapsing if patients showed a relapse after an initial response ≥ 6 months of initiating the previous therapy.

The study comprised a phase Ib safety run-in phase to determine the dose for phase II and a phase II, which were conducted consecutively and separately according to histology (DLBCL and FL). Study arms C and D comprised the randomized, controlled comparison of polatuzumab vedotin + bendamustine + rituximab with bendamustine + rituximab in adults with relapsed or refractory DLBCL.

A total of 80 patients with relapsed or refractory DLBCL were included and randomized in a 1:1 ratio to treatment with polatuzumab vedotin + bendamustine + rituximab (N = 40) or to the comparator therapy consisting of bendamustine + rituximab (N = 40).

Treatment with polatuzumab vedotin + bendamustine + rituximab was generally in accordance with the information provided in the Summary of Product Characteristics (SPC). However, patients in study arms C and D were treated with the liquid formulation of polatuzumab vedotin and not with the approved lyophilised formulation.

Primary outcome of the study was complete remission as assessed by an independent review committee, recorded 6 to 8 weeks after Day 1 of Cycle 6 or the last dose of study medication.

YO41543

YO41543 is a completed, double-blind RCT comparing polatuzumab vedotin + bendamustine + rituximab with placebo + bendamustine + rituximab. It included adult Chinese patients with relapsed or refractory DLBCL after at least 1 systemic therapy for whom autologous haematopoietic stem cell transplantation was not an option. The disease was considered refractory if patients showed progression or no response (stable disease) within < 6 months after start of the previous therapy, and relapsing if patients showed a relapse after an initial response ≥ 6 months of initiating the previous therapy.

A total of 42 patients with relapsed or refractory DLBCL were included and randomized in a 2:1 ratio to treatment with polatuzumab vedotin + bendamustine + rituximab (N = 28) or to the comparator therapy consisting of placebo + bendamustine + rituximab (N = 14).

Treatment with polatuzumab vedotin + bendamustine + rituximab was in accordance with the information provided in the SPC.

Primary outcome of the study was complete remission as assessed by an IRC, recorded 6 to 8 weeks after Day 1 of Cycle 6 or the last dose of study medication.

ACT specified by the G-BA not implemented

The meta-analysis based on individual patient data (IPD) of the studies GO29365 and YO41543 presented by the company is not suitable for any of the 3 research questions of the benefit assessment. This is due to the fact that the ACT had not been implemented in either of the two studies presented by the company. Bendamustine + rituximab was used in the comparator arm of each study. The combination of bendamustine + rituximab is not approved in the present therapeutic indication and is not recommended by the guidelines as a second or third-line therapy. Accordingly, the G-BA did not specify bendamustine + rituximab as an ACT. Consequently, the studies presented by the company do not allow a comparison with the ACT. Thus, there is no relevant study to derive an added benefit in comparison with the ACT for any of the research questions.

Results on added benefit

Since no suitable data are available for the present research questions, there is no hint of added benefit of polatuzumab vedotin + bendamustine + rituximab 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 polatuzumab vedotin + bendamustine + rituximab .

[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: Polatuzumab vedotin + bendamustine + rituximab – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
1	Adults with relapsed or refractory DLBCL after failure of 1 line of systemic therapy for whom haematopoietic stem cell transplantation is not an option	Tafasitamab in combination with lenalidomide[c]	Added benefit not proven
2	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy is an option and haematopoietic stem cell transplantation is not an option	▪ Tisagenlecleucel or ▪ axicabtagene ciloleucel or ▪ lisocabtagene maraleucel	Added benefit not proven
3	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy and haematopoietic stem cell transplantation are not an option	Treatment of physician's choice, taking into account[d]: ▪ tafasitamab in combination with lenalidomide, ▪ pixantrone monotherapy and ▪ radiation	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, the available evidence does not imply that the off-label use of rituximab in combination with gemcitabine and oxaliplatin and of rituximab in combination with bendamustine is generally preferable over the drugs approved in the therapeutic indication so far, or over the drugs approved for relevant patient groups or therapeutic indications so far based on the generally recognized state of medical knowledge. Rituximab in combination with gemcitabine and oxaliplatin and rituximab in combination with bendamustine are therefore not specified as an ACT.
c. Patients with a PET-positive residual tumour after systemic second-line therapy should receive consolidation radiotherapy.
d. A single-comparator study is generally insufficient for implementing treatment of physician's choice in a study of direct comparison. The investigators are expected to have a choice between several treatment options (multi-comparator study). The choice and, if necessary, limitation of treatment options must be justified.

CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Joint Federal Committee; PET: positron emission tomography

The G-BA decides on the added benefit.

Supplementary note

The result of the assessment deviates from the result of the G-BA's assessment in the context of the market launch in 2020. There, the G-BA had determined a non-quantifiable added benefit of polatuzumab vedotin + bendamustine + rituximab. However, in this assessment, the added benefit had been regarded as proven by the approval irrespective of the underlying data because of the special situation for orphan drugs.

I 2 Research question

The aim of this report is to assess the added benefit of polatuzumab vedotin in combination with bendamustine and rituximab (hereinafter referred to as "polatuzumab vedotin + bendamustine + rituximab") compared with the ACT in adult patients with relapsed or refractory DLBCL, for whom haematopoietic stem cell transplantation is not an option.

The research questions presented in Table 4 result from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of polatuzumab vedotin + bendamustine + rituximab

Research question	Therapeutic indication	ACT[a, b]
1	Adults with relapsed or refractory DLBCL after failure of 1 line of systemic therapy for whom haematopoietic stem cell transplantation is not an option	Tafasitamab in combination with lenalidomide[c]
2	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy is an option and haematopoietic stem cell transplantation is not an option	▪ Tisagenlecleucel or ▪ axicabtagene ciloleucel or ▪ lisocabtagene maraleucel
3	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy and haematopoietic stem cell transplantation are not an option	Treatment of physician's choice, taking into account[d]: ▪ tafasitamab in combination with lenalidomide, ▪ pixantrone monotherapy and ▪ radiation

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, the available evidence does not imply that the off-label use of rituximab in combination with gemcitabine and oxaliplatin and of rituximab in combination with bendamustine is generally preferable over the drugs approved in the therapeutic indication so far, or over the drugs approved for relevant patient groups or therapeutic indications so far based on the generally recognized state of medical knowledge. Rituximab in combination with gemcitabine and oxaliplatin and rituximab in combination with bendamustine are therefore not specified as an ACT.
c. Patients with a PET-positive residual tumour after systemic second-line therapy should receive consolidation radiotherapy.
d. A single-comparator study is generally insufficient for implementing treatment of physician's choice in a study of direct comparison. The investigators are expected to have a choice between several treatment options (multi-comparator study). The choice and, if necessary, limitation of treatment options must be justified.

CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Joint Federal Committee; PET: positron emission tomography

The company deviated from the G-BA's specification for differentiating between the different research questions and the respective ACTs. In its dossier, it addresses only 2 research

questions by differentiating the therapeutic indication solely by the number of treatment lines: after failure of 1 and after failure of ≥ 2 lines of systemic therapy. However, after failure of ≥ 2 lines of systemic therapy, it does not differentiate further within the population depending on the eligibility for CAR T-cell therapy.

In addition, the company is inconsistent in naming the ACT within the dossier. In Module 3 A, the company names one therapy of physician choice each as an ACT, taking into account various drugs and drug combinations (a complete list can be found in Module 3 A of the dossier). The drugs and drug combinations listed by the company in the context of a treatment of physician's choice differ from those considered suitable by the G-BA within the framework of the various ACT determinations. In Module 4 A, however, it describes a patient-specific therapy under the research question of bendamustine + rituximab and under the inclusion criteria, taking into account the biology of the disease, the previous therapy, the course of the disease and the general condition as a comparator therapy, without differentiating between the questions specified by it.

The approach of the company is not appropriate. Firstly, the company itself describes that the unsuitability of high-dose therapy for patients followed by stem cell transplantation is not to be equated with the unsuitability of CAR-T cell therapy. Secondly, the company justified the choice of bendamustine + rituximab as comparator therapy by stating that the combination was a clinically established chemoimmunotherapy specified as a comparator by the G-BA and was relevant at the time of the study, and that its off-label use was still recommended in the current guidelines. The company’s reasoning is not sound. The G-BA does not specify the combination of bendamustine + rituximab as an ACT, nor do the guidelines [3,4] recommend the off-label use of this combination as a second or third-line therapy.

The present assessment was conducted on the basis of the research questions specified by the G-BA (populations and corresponding ACTs).

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs are used to derive the added benefit. This concurs with the company’s inclusion criteria.

Since no suitable data are available for any of the research questions named by the G-BA, the assessment below is performed in a joint section of the report (see Chapters I 3 to I 5).

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 polatuzumab vedotin (status: 4 October 2023)
- bibliographical literature search on polatuzumab vedotin (last search on 4 October 2023)
- search in trial registries/trial results databases for studies on polatuzumab vedotin (last search on 4 October 2023)
- search on the G-BA website for polatuzumab vedotin (last search on 4 October 2023)

To check the completeness of the study pool:

- search in trial registries for studies on polatuzumab vedotin (last search on 10 January 2024); for search strategies, see Appendix A of the full dossier assessment

The check of completeness of the study pool did not reveal any relevant study for assessing the added benefit of polatuzumab vedotin + bendamustine + rituximab in comparison with the ACT for the present research questions.

This deviates from the assessment of the company, whose information retrieval identified the RCTs GO29365 [5] und YO41543 [6]. For these studies, it presented data on 2 subpopulations as a meta-analysis based on IPD, subdivided according to the respective treatment lines, which it uses for the assessment of added benefit.

The studies GO29365 and YO41543 included by the company are not suitable for the assessment of the added benefit of polatuzumab vedotin + bendamustine + rituximab versus the ACT because the ACT was not implemented in both studies. This is justified below. For this purpose, the studies used by the company are first described. It is then explained why the studies for the assessment of the added benefit of polatuzumab vedotin + bendamustine + rituximab compared with the ACT are not suitable for any of the 3 research questions.

Evidence provided by the company

GO29365

GO29365 is a completed, multicentre, open-label phase IB/II study comparing polatuzumab vedotin in combination with bendamustine and rituximab or bendamustine and obinutuzumab. It included adult patients with relapsed or refractory DLBCL or FL after at least 1 systemic therapy for whom autologous haematopoietic stem cell transplantation was not an option. The disease was considered refractory if patients showed progression or no response (stable disease) within < 6 months after start of the previous therapy, and relapsing

if patients showed a relapse after an initial response ≥ 6 months of initiating the previous therapy. Patients who had a primary or secondary lymphoma of the central nervous system or who had received CAR-T cell therapy within 100 days prior to the first treatment were excluded from the study.

The study comprised a phase Ib safety run-in phase to determine the dose for phase II and a phase II, which were conducted consecutively and separately according to histology (DLBCL and FL). Phase II consists of a randomization phase (study arms A to D) and a non-randomized expansion phase (study arms E and F). 2 further study arms (G and H) were only added with protocol version 5.0 (16 November 2017) and 7.0 (2 October 2018) to investigate the pharmacokinetics, safety and efficacy of the lyophilised formulation of polatuzumab vedotin in combination with bendamustine + rituximab in patients with relapsed or refractory DLBCL. The further study description refers to the randomized, controlled comparison of polatuzumab vedotin + bendamustine + rituximab with bendamustine + rituximab in adults with relapsed or refractory DLBCL (study arms C and D).

A total of 80 patients with relapsed or refractory DLBCL were included and randomized in a 1:1 ratio to treatment with polatuzumab vedotin + bendamustine + rituximab (N = 40) or to the comparator therapy consisting of bendamustine + rituximab (N = 40). Stratification was based on the duration of response to the last therapy (≤ 12 months vs. > 12 months).

Treatment with polatuzumab vedotin + bendamustine + rituximab was generally in compliance with the information provided in the SPC [7]. However, patients in study arms C and D were treated with the liquid formulation of polatuzumab vedotin and not with the approved lyophilised formulation.

The end of the study was defined as the time at which all patients included in the study had been followed up for at least 2 years or withdrawn from the study. The analyses presented by the company are based on the data cut-off of 21 October 2021, on which the final visit of the last patient took place.

Primary outcome of the study was complete remission as assessed by an IRC, recorded 6 to 8 weeks after Day 1 of Cycle 6 or the last dose of study medication.

YO41543

YO41543 is a completed, double-blind RCT comparing polatuzumab vedotin + bendamustine + rituximab with placebo + bendamustine + rituximab. It included adult Chinese patients with relapsed or refractory DLBCL after at least 1 systemic therapy for whom autologous haematopoietic stem cell transplantation was not an option. The disease was considered refractory if patients showed progression or no response (stable disease) within < 6 months after start of the previous therapy, and relapsing if patients showed a relapse after an initial

response ≥ 6 months of initiating the previous therapy. Patients who had a primary or secondary lymphoma of the central nervous system or who had received prior CAR-T cell therapy were excluded from the study.

A total of 42 patients with relapsed or refractory DLBCL were included and randomized in a 2:1 ratio to treatment with polatuzumab vedotin + bendamustine + rituximab (N = 28) or to the comparator therapy consisting of placebo + bendamustine + rituximab (N = 14). Stratification was based on the duration of response to the last therapy (≤ 12 months vs. > 12 months) and the number of prior therapies (1 vs. ≥ 2).

Treatment with polatuzumab vedotin + bendamustine + rituximab was generally in compliance with the information provided in the SPC [7].

The end of the study was defined as the time at which two thirds of the patients included in the study had died or all patients had withdrawn from the study, whichever came first. The analyses presented by the company are based on the data cut-off of 07 February 2022, on which the final visit of the last patient took place.

Primary outcome of the study was complete remission as assessed by an IRC, recorded 6 to 8 weeks after Day 1 of Cycle 6 or the last dose of study medication.

ACT specified by the G-BA not implemented

The IPD meta-analysis of the studies GO29365 and YO41543 presented by the company is not suitable for any of the 3 research questions of the benefit assessment. This is due to the fact that the ACT had not been implemented in either of the two studies presented by the company. Bendamustine + rituximab was used in the comparator arm of each study. The combination of bendamustine + rituximab is not approved in the present therapeutic indication and is not recommended by the guidelines [3,4] as a second or third-line therapy. Accordingly, the G-BA did not specify bendamustine + rituximab as an ACT (see I 2). Consequently, the studies presented by the company do not allow a comparison with the ACT. Thus, there is no relevant study to derive an added benefit in comparison with the ACT for any of the research questions.

I 4 Results on added benefit

No suitable data are available for assessing the added benefit of polatuzumab vedotin + bendamustine + rituximab in comparison with the ACT for adult patients with relapsed or refractory DLBCL for whom haematopoietic stem cell transplantation is not an option. There is no hint of added benefit of polatuzumab vedotin + bendamustine + rituximab in comparison with the ACT for any of the 3 research questions; 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 polatuzumab vedotin + bendamustine + rituximab in comparison with the ACT is summarized in Table 5.

Table 5: Polatuzumab vedotin + bendamustine + rituximab – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
1	Adults with relapsed or refractory DLBCL after failure of 1 line of systemic therapy for whom haematopoietic stem cell transplantation is not an option	Tafasitamab in combination with lenalidomide[c]	Added benefit not proven
2	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy is an option and haematopoietic stem cell transplantation is not an option	▪ Tisagenlecleucel or ▪ axicabtagene ciloleucel or ▪ lisocabtagene maraleucel	Added benefit not proven
3	Adults with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy, for whom CAR-T cell therapy and haematopoietic stem cell transplantation are not an option	Treatment of physician's choice, taking into account[d]: ▪ tafasitamab in combination with lenalidomide, ▪ pixantrone monotherapy and ▪ radiation	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, the available evidence does not imply that the off-label use of rituximab in combination with gemcitabine and oxaliplatin and of rituximab in combination with bendamustine is generally preferable over the drugs approved in the therapeutic indication so far, or over the drugs approved for relevant patient groups or therapeutic indications so far based on the generally recognized state of medical knowledge. Rituximab in combination with gemcitabine and oxaliplatin and rituximab in combination with bendamustine are therefore not specified as an ACT.
c. Patients with a PET-positive residual tumour after systemic second-line therapy should receive consolidation radiotherapy.
d. A single-comparator study is generally insufficient for implementing treatment of physician's choice in a study of direct comparison. The investigators are expected to have a choice between several treatment options (multi-comparator study). The choice and, if necessary, limitation of treatment options must be justified.

CAR: chimeric antigen receptor; DLBCL: diffuse large B-cell lymphoma; G-BA: Joint Federal Committee; PET: positron emission tomography

For patients with relapsed or refractory DLBCL after failure of 1 line of systemic therapy, the assessment described above corresponds to that of the company. For patients with relapsed or refractory DLBCL after failure of ≥ 2 lines of systemic therapy , the assessment described above differs from that of the company, which derives proof of a considerable added benefit

without further differentiating the population depending on the eligibility for CAR-T cell therapy.

The G-BA decides on the added benefit.

Supplementary note

The result of the assessment deviates from the result of the G-BA's assessment in the context of the market launch in 2020. There, the G-BA had determined a non-quantifiable added benefit of polatuzumab vedotin + bendamustine + rituximab. However, in this assessment, the added benefit had been regarded as proven by the approval irrespective of the underlying data because of the special situation for orphan drugs.

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/a23-140.html.