Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive: Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Epcoritamab (repeal of regulatory orphan status: diffuse large B-cell lymphoma (DLBCL), after ≥ 2 previous therapies)

of 17 April 2025

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1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of all reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The medicinal product Tepkinly with the active ingredient epcoritamab was first approved as a medicinal product for the treatment of rare diseases (orphan drug) under Regulation (EC) Number 141/2000 of the European Parliament and of the Council of 16 December 1999. This marketing authorisation as orphan drug was granted for the therapeutic indication "Tepkinly as monotherapy is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy."

On 4 April 2024, the G-BA decided on the benefit assessment of epcoritamab for this therapeutic indication on the basis of the statutory provisions on the benefit assessment of medicinal products for the treatment of a rare disease (Section 35a, paragraph 1, sentence 11 SGB V).

On 19 July 2024, the orphan designation for the medicinal product Tepkinly was withdrawn from the Community register of orphan drugs. This cancelled the orphan drug status. As a result, the pharmaceutical company was requested by the G-BA in a letter dated 13

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September 2024 to submit evidence in accordance with Chapter 5 Section 5, paragraphs 1 to 6 of the VerfO and to demonstrate the additional benefit compared with the appropriate comparator therapy.

On 31 October 2024, i.e. within three months of receiving the G-BA's request, the pharmaceutical company submitted a dossier for the active ingredient epcoritamab in accordance with Section 35a, paragraph 1, sentence 10 SGB V in conjunction with Chapter 5 Section 8, paragraph 1, number 6 and Section 12, number 2 of the Rules of Procedure of the G-BA (VerfO).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 3 February 2025 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of epcoritamab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of epcoritamab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of Epcoritamab (Tepkinly) in accordance with the product information

Tepkinly as monotherapy is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy.

Therapeutic indication of the resolution (resolution of 17 April 2025):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are eligible for CAR-T cell therapy or stem cell transplantation

Appropriate comparator therapy for epcoritamab as monotherapy:

Individualised therapy with selection of

- tisagenlecleucel,

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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- axicabtagene ciloleucel,
- lisocabtagene maraleucel,
- an induction therapy with
  - R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin and carboplatin) *or*
  - R-DHAP (rituximab, dexamethasone, cisplatin, cytarabine) *or*
  - R-ICE (rituximab, ifosfamide, carboplatin, etoposide)

  followed by high-dose therapy with autologous stem cell transplantation if there is a response to induction therapy and
- an induction therapy with
  - R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin and carboplatin) or
  - R-DHAP (rituximab, dexamethasone, cisplatin, cytarabine) or
  - R-ICE (rituximab, ifosfamide, carboplatin, etoposide)

  followed by high-dose therapy with allogeneic stem cell transplantation if there is a response to induction therapy

b) <u>Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation</u>

Appropriate comparator therapy for epcoritamab as monotherapy:

Individualised therapy with selection of

- polatuzumab vedotin + bendamustine + rituximab,
- tafasitamab + lenalidomide and
- radiotherapy

<u>Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):</u>

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application, unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

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According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

<u>Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:</u>

On 1. In addition to epcoritamab, the following active ingredients are approved for the present therapeutic indication:

Bleomycin, cyclophosphamide, cytarabine, dexamethasone, doxorubicin, etoposide, glofitamab, ifosfamide, melphalan, methotrexate, methylprednisolone, mitoxantrone, odronextamab, polatuzumab vedotin, prednisolone, prednisone, tafasitamab, trofosfamide, vinblastine, vincristine, vindesine, rituximab, loncastuximab tesirine, axicabtagene ciloleucel, lisocabtagene maraleucel and tisagenlecleucel.

Some of the medicinal products listed have a marketing authorisation for the superordinate therapeutic indication "non-Hodgkin lymphoma". The marketing authorisations are partly linked to (specified) concomitant active ingredients or do not fully cover the present therapeutic indication.

On 2. In principle, autologous or allogeneic stem cell transplantation can be considered as a non-medicinal treatment for relapsed or refractory DLBCL. In addition, radiotherapy can be administered, for example, to treat localised residual manifestations of the lymphoma after completion of chemotherapy.

On 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- epcoritamab (resolution of 4 April 2024)
- tisagenlecleucel (resolution of 15 February 2024)
- glofitamab (resolution of 1 February 2024)
- axicabtagene ciloleucel (resolution of 21 December 2023)
- loncastuximab tesirine (resolution of 2 November 2023)

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- lisocabtagene maraleucel (resolution of 6 April 2023)
- tafasitamab (resolution of 3 March 2022)
- polatuzumab vedotin (resolution of 20 June 2024)
- pixantrone (resolution of 16 May 2013)

Directive on Inpatient Treatment Methods (last revised 7 December 2022: allogeneic stem cell transplantation for aggressive B-non-Hodgkin lymphomas):

- Section 4 Excluded methods: Allogeneic stem cell transplantation in adult patients with aggressive B-non-Hodgkin lymphoma who have not yet been treated with autologous stem cell transplantation (exceptions: a) patients who have a very high risk of recurrence and who achieve a response at least in the sense of stable disease after salvage therapy; b) patients in whom sufficient stem cell harvesting for autologous stem cell transplantation was not possible and who achieve a response at least in the sense of stable disease after salvage therapy).
- Annex I - Methods required for hospital care: Allogeneic stem cell transplantation in adult patients with aggressive B-cell non-Hodgkin lymphomas who relapse after autologous stem cell transplantation and achieve a response at least in the sense of stable disease after salvage therapy.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V.

Among the approved active ingredients listed under 1., only certain active ingredients named below will be included in the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of care.

Overall, the evidence on treatment options for the present advanced treatment setting of relapsed or refractory DLBCL after at least two lines of therapy is limited.

The approved therapeutic indication generally refers to patients with relapsed or refractory (r/r) DLBCL, after two or more lines of systemic therapy, and is not limited in terms of patient eligibility or ineligibility for an intensive therapeutic approach. According to the S3 guideline, there are distinct treatment recommendations for therapy with a primarily curative intention, such as CAR-T cell therapy and stem cell transplantation on the one hand, and therapy with a primarily palliative intention on the other. The joint statement of the German Society for Haematology and Medical Oncology (DGHO) and the German Lymphoma Alliance (GLA) also indicates that suitability for CAR-T cell therapy is a relevant parameter with regard to the treatment decision in the event of relapse or refractoriness. The G-BA therefore considers it appropriate to differentiate between two patient groups depending on their suitability for CAR-T cell therapy or stem cell transplantation when determining the appropriate comparator therapy.

<u>Patient group a)</u>

For patient group a), it is assumed that the patients are eligible for a therapy with curative intent.

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According to the S3 guideline, CAR-T cell therapy should be carried out from the second relapse onwards if it has not already been carried out in second-line therapy. The CAR-T cell therapies axicabtagene ciloleucel, tisagenlecleucel and lisocabtagene maraleucel are available in this therapeutic indication. For axicabtagene ciloleucel, it was determined by the G-BA's resolution of 21 December 2023 that an additional benefit is not proven, as no suitable data were available to enable an assessment of the additional benefit. A hint for a non-quantifiable additional benefit was identified for tisagenlecleucel by resolution of 15 February 2024 within the scope of an orphan drug assessment since the scientific data did not allow quantification. For lisocabtagene maraleucel, it was determined by resolution of 6 April 2023 that an additional benefit is not proven, as no data were available to enable an assessment of the additional benefit.

According to the available guidelines, salvage chemoimmunotherapy including stem cell transplantation (autologous or allogeneic) is a treatment option, especially after CAR-T cell therapy or for patients who are ineligible for such therapy. This is particularly the case for patients who have not undergone stem cell transplantation in the second line of therapy. A salvage chemoimmunotherapy followed by an autologous or allogeneic stem cell transplantation is therefore considered by the G-BA to be a further suitable comparator in the context of individualised therapy.

According to the guidelines[2,3], platinum-based chemoimmunotherapy is used as standard for induction therapy, with the platinum-containing combinations GDP (gemcitabine, dexamethasone, cisplatin or carboplatin) and ICE (ifosfamide, carboplatin, etoposide), each in combination with rituximab, being recommended as specific therapy regimens. In accordance with the S3 guidelines, these treatment regimens were compared with each other in prospective randomised studies, whereby differences in toxicity were found with the same efficacy.[4,5]

The protocols R-GDP, R-DHAP and R-ICE have already been used as standard protocols for induction therapy in this therapeutic indication as part of the G-BA's assessment of the "allogeneic stem cell transplantation for B-cell non-Hodgkin lymphomas" method.[6] Rituximab is only approved in the present indication in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone), and individual components of the combination therapies mentioned (cisplatin, carboplatin, gemcitabine) are also not approved in the present indication.

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[2] Guideline program in oncology (German Cancer Society, German Cancer Aid, Association of the Scientific Medical Societies): Diagnostics, therapy and after-care for adult patients with diffuse large B-cell lymphoma and related entities, long version 1.0, 2022, AWMF registry number: 018/038OL https://www.leitlinienprogramm-onkologie.de/leitlinien/dlbcl/; accessed [04.03.2025]

[3] National Institute for Health and Care Excellence (NICE). Non-Hodgkin's lymphoma: diagnosis and management [online]. 10.2021. London (GBR): NICE; 2016. [Accessed: 11.07.2024]. (NICE Guideline; Band NG52). URL: https://www.nice.org.uk/guidance/ng52/resources/nonhodgkins-lymphoma-diagnosis-and-management-pdf-1837509936325.

[4] Gisselbrecht C, Glass B, Mounier N, Linch D, Gill D, Trneny M. R-ICE versus R-DHAP in relapsed patients with CD20 diffuse large B-cell lymphoma (DLBCL) followed by autologous stem cell transplantation: CORAL study. 2009;27:15s

[5] Crump M, Kuruvilla J, Couban S, MacDonald D, Kukreti V, Kouroukis C, et al. Randomized comparison of gemcitabine, dexamethasone, and cisplatin versus dexamethasone, cytarabine, and cisplatin chemotherapy before autologous stem-cell transplantation for relapsed and refractory aggressive lymphomas: NCIC-CTG LY12. J Clin Oncol. 2014;32:3490-6. URL: https://pubmed.ncbi.nlm.nih.gov/25267740/

[6] Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Directive on Inpatient Treatment Methods: Allogeneic stem cell transplantation for aggressive B-cell non-Hodgkin lymphomas; 9 April 2020

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Of the active ingredients approved for the treatment of non-Hodgkin lymphoma, only the platinum-free induction therapy MINE (mesna, ifosfamide, mitoxantrone, etoposide), which is mentioned in the American guideline of the National Comprehensive Cancer Network (NCCN) as another possible treatment regimen of lower priority, is available.[7] From the statements of the clinical experts in the benefit assessment procedures for axicabtagene ciloleucel for the treatment of relapsed/ refractory DLBCL in the second line of therapy or relapsed/ refractory DLBCL and relapsed/ refractory primary mediastinal large B-cell lymphoma (PMBCL) in the third line of therapy indicate that MINE has no relevant value in this therapeutic indication and, if used separately in the past, was consolidated with a platinum-containing therapy. In agreement with the estimate of the clinical experts, all the available guidelines unanimously recommend platinum-containing induction therapy with R-GDP, R-ICE or R-DHAP, although it should be noted that the platinum-free induction therapy MINE is not mentioned at all in the S3 guideline relevant to the German healthcare context.

In summary, if CAR-T cell therapy has already been carried out or is not an option for medical reasons, salvage chemoimmunotherapy consisting of R-GDP, R-ICE or R-DHAP should be accordingly carried out with the inclusion of stem cell transplantation. In these cases, the use of induction therapy with R-GDP, R-ICE or R-DHAP is generally preferable to induction therapy with MINE for this relevant patient group in accordance with Section 6, paragraph 2, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV). Therefore, it is appropriate to determine the off-label use of these combinations of medicinal products as the appropriate comparator therapy for this patient population. The other approved active ingredients listed under 1 do not correspond to the therapy recommendations for the present indication and to the therapy standard in the reality of care as set out in the guidelines and in the written statement of the scientific-medical societies.

Overall, an individualised therapy is therefore determined as an appropriate comparator therapy, with selection of tisagenlecleucel, axicabtagene ciloleucel and lisocabtagene maraleucel, an induction therapy with R-GDP, R-ICE or R-DHAP followed by a high-dose therapy with autologous or allogeneic stem cell transplantation in response to the induction therapy.

When selecting therapy options as part of an individualised therapy, the patients' previous therapy with CAR-T cell therapy, autologous stem cell transplantation or allogeneic stem cell transplantation must accordingly be taken into account.

For patients who have not yet been treated with autologous stem cell transplantation, allogeneic stem cell transplantation is an option for patients who have a very high risk of recurrence or for whom stem cell harvesting was not possible for autologous stem cell transplantation.

Patient group b)

For patient group b), it is assumed that the patients are not eligible for a therapy with curative intent. For these patients who are ineligible for CAR-T cell therapy and stem cell transplantation due to the course of their disease or their general condition, various chemo or chemo-immunotherapies as well as newer substances represent treatment options according to guidelines and statement of the German Society for Haematology and Medical Oncology and GLA.

[7] National Comprehensive Cancer Network (NCCN). B-Cell lymphomas; Vers. 05.2022 [online]. Fort Washington (USA): NCCN; 2022. (NCCN Clinical Practice Guidelines in Oncology)

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The antibody-drug conjugate polatuzumab vedotin is approved in combination with bendamustine and rituximab (Pola-BR) for the treatment of adults with relapsed or refractory DLBCL if they are ineligible for haematopoietic stem cell transplantation. By resolution of 20 August 2020, a hint for a non-quantifiable additional benefit over bendamustine in combination with rituximab was identified for polatuzumab vedotin within the scope of a first orphan drug assessment since the scientific data did not allow quantification. As part of a new benefit assessment because of exceeding the EUR 30 million turnover limit, the additional benefit of polatuzumab vedotin was determined as not proven by resolution of 20 June 2024.

The CD19-specific antibody tafasitamab is approved in combination with lenalidomide for the treatment of patients with relapsed or refractory DLBCL for who are ineligible for autologous stem cell transplantation. By resolution of 3 March 2022, a hint for a non-quantifiable additional benefit was identified for tafasitamab within the scope of an orphan drug assessment since the scientific data did not allow quantification.

According to the S3 guideline, radiotherapy can be a suitable method for local disease control in palliative situations.

The combination chemotherapies CEOP (cyclophosphamide, etoposide, vincristine, prednisone) and EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone) are also approved for this indication. From the statements of the clinical experts in the benefit assessment procedure for loncastuximab tesirine, it emerged that the combination chemotherapies mentioned have no relevant significance in the present treatment setting - especially as the combination therapies mentioned or the active ingredients contained in these combination therapies have already been used previously within the therapeutic sequence. The combination therapies mentioned are not designated as an appropriate comparator therapy.

The active ingredients loncastuximab tesirine and glofitamab are treatment options in the present therapeutic indication. For loncastuximab tesirine, it was determined by the G-BA's resolution of 2 November 2023 that an additional benefit is not proven, as no suitable data were available to enable an assessment of the additional benefit. A hint for a non-quantifiable additional benefit was identified for glofitamab by resolution of 1 February 2024 within the scope of an orphan drug benefit assessment since the scientific data did not allow quantification.

Based on the generally recognised state of medical knowledge, loncastuximab tesirine and glofitamab are therefore not determined to be an appropriate comparator therapy.

The active ingredient odronextamab is a new treatment option in the present therapeutic indication. The active ingredient was only recently approved (marketing authorisation on 22 August 2024). The medicinal product with the active ingredient odronextamab has not yet been placed on the market in Germany. Based on the generally accepted state of medical knowledge, odronextamab is not determined to be an appropriate comparator therapy.

Against this background, an individualised therapy with selection of pola-BR, tafasitamab + lenalidomide and radiotherapy is determined as the appropriate comparator therapy for patient group b).

Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

Editorial note: The term "individualised therapy" is used instead of previously used terms such as "patient-individual therapy" or "therapy according to doctor's

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instructions". This harmonises the terms used in the European assessment procedures (EU-HTA).

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of epcoritamab is assessed as follows:

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are eligible for CAR-T cell therapy or stem cell transplantation

The additional benefit is not proven for patient group a).

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation

The additional benefit is not proven for patient group b).

Justification:

For the demonstration of an additional benefit of epcoritamab in patients with relapsed or refractory DLBCL, the pharmaceutical company did not identify any relevant studies compared to the appropriate comparator therapy. In the dossier, the pharmaceutical company presented the results of the uncontrolled approval study GCT3013-01 as the best available evidence.

GCT3013-01 study

The GCT3013-01 study is a single-arm, ongoing phase I/II study in adults with various disease entities of relapsed/ refractory (r/r) B-cell lymphoma. The study comprises three separate phases: a dose-finding phase, an expansion phase and a dose-optimisation phase. Enrolled patients could only participate in one of the three study phases. Relevant for the present benefit assessment is the cohort of patients with r/r DLBCL in the expansion phase of the study. In addition to patients with r/r DLBCL, patients with other diseases such as PMBCL, follicular lymphoma or mantle cell lymphoma are also being investigated in this study phase.

Patients with r/r DLBCL in the expansion phase of the study had to have CD20-positive disease and prior therapy with at least two lines of systemic antineoplastic therapy, including at least one anti-CD20 antibody-containing therapy. Patients who were eligible for curative intensive salvage therapy followed by high-dose chemotherapy with haematological stem cell transplantation (HSCT) were not enrolled in the study. Patients were treated with epcoritamab according to the product information.

Due to its single-arm study design, the study presented by the pharmaceutical company does not allow a comparison with the appropriate comparator therapy.

Conclusion:

Overall, the data presented are not suitable to demonstrate an additional benefit compared to the appropriate comparator therapy, which is why an additional benefit of epcoritamab as

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monotherapy for the treatment of adults with an r/r DLBCL after two or more lines of systemic therapy is not proven.

2.1.4 Summary of the assessment

The present assessment is a new benefit assessment of the active ingredient epcoritamab due to the repeal of the orphan drug status.

As an orphan drug, Tepkinly received a conditional marketing authorisation as monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B- lymphoma (DLBCL), after two or more lines of systemic therapy.

In the therapeutic indication to be considered, 2 patient groups were distinguished:

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are eligible for CAR-T cell therapy or stem cell transplantation

   and

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation

Patient group a)

An individualised therapy was determined as an appropriate comparator therapy, with selection of tisagenlecleucel, axicabtagene ciloleucel and lisocabtagene maraleucel, an induction therapy with R-GDP, R-ICE or R-DHAP followed by a high-dose therapy with autologous or allogeneic stem cell transplantation in response to the induction therapy.

Patient group b)

An individualised therapy with selection of pola-BR, tafasitamab + lenalidomide and radiotherapy was determined as the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company submitted the results of the GCT3013-01 study. Due to its single-arm study design, the GCT3013-01 study does not allow a comparison with the appropriate comparator therapy and is therefore unsuitable for the assessment of an additional benefit of epcoritamab. An additional benefit is therefore not proven.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The patient number determined by the pharmaceutical company is subject to uncertainties, but is comparable to the patient numbers treated with previous procedures in the therapeutic indication. Furthermore, the use of CAR-T cell therapy in the second line of therapy as a result of early relapse was taken into account for the first time in the calculation.

In addition, IQWiG calculated the patient numbers separately for patient groups a) and b), based on the information provided by the pharmaceutical company in the dossier (addendum to the benefit assessment of 4 April 2025). According to this calculation, the percentage of the two patient groups in the total target population is approximately 50% in each case. Uncertainties arise in particular due to the lack of standardised criteria for suitability for high-dose therapy and stem cell transplantation or for CAR-T cell therapy.

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2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Tepkinly (active ingredient: epcoritamab) at the following publicly accessible link (last access: 10 March 2025):

https://www.ema.europa.eu/en/documents/product-information/tepkinly-epar-product-information_en.pdf

Treatment with epcoritamab should only be initiated and monitored by specialists in internal medicine, haematology and oncology, experienced in the treatment of patients with diffuse large B-cell lymphoma (DLBCL).

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency EMA will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

In accordance with the EMA's requirements for additional risk minimisation measures, the pharmaceutical company must ensure that all healthcare professionals who may prescribe epcoritamab and each subject treated with epcoritamab receive a patient pass containing information on risks associated with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) as well as a warning for healthcare professionals treating the subjects and the contact details of the healthcare professional prescribing epcoritamab.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 1 April 2025).

For the cost representation, one year is assumed for all medicinal products.

The (daily) doses recommended in the product information or in the labelled publications were used as the basis for calculation.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or co-morbidities) are not taken into account when calculating the annual treatment costs.

CAR-T cell therapies

Axicabtagene ciloleucel, lisocabtagene maraleucel and tisagenlecleucel are genetically modified, patient's own (autologous) T cells, which are usually obtained by leukapheresis. Since leukapheresis is part of the manufacture of the medicinal product according to Section 4 paragraph 14 Medicinal Products Act, no further costs are incurred in this respect for these active ingredients as treatment options of the medicinal product to be assessed.

Axicabtagene ciloleucel, lisocabtagene maraleucel and tisagenlecleucel are listed on LAUER-TAXE®, but are only dispensed to appropriately qualified inpatient treatment facilities. Accordingly, the active ingredients are not subject to the Pharmaceutical Price Ordinance (Arzneimittelpreisverordnung) and no rebates according to Section 130 or Section 130a SGB V apply. The calculation is based on the purchase price of the respective clinic pack, in deviation from the LAUER-TAXE® data usually taken into account.

Courtesy translation – only the German version is legally binding.

Axicabtagene ciloleucel, lisocabtagene maraleucel and tisagenlecleucel are administered as a single intravenous infusion according to the requirements in the underlying product information.

Induction chemotherapy before stem cell transplantation

The induction chemotherapies R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin), R-ICE (rituximab + ifosfamide + carboplatin + etoposide) and R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin) do not have a marketing authorisation in the present therapeutic indication. In accordance with the recommendation of the S3 guideline, the G-BA uses 2 - 3 cycles as the basis for calculating costs in the context of off-label use of these combination therapies[8]. Furthermore, for the treatment regimens and dosages in relation to the combination therapy R-GDP, the study by Crump et al. (2014) [9] referenced in the S3 guideline and, in relation to the combination therapies R-ICE and R-DHAP, the study by Gisselbrecht et al. referenced in the S3 guideline (2010)[10] are taken into account.

Epcoritamab is administered with a dose escalation regimen: In cycle 1, 0.16 mg epcoritamab (step-up dose 1) is given on day 1, 0.8 mg (step-up dose 2) on day 8 and 48 mg (full dose in each case) on day 15 and day 22. Subsequently, 48 mg epcoritamab is administered weekly in cycles 2 - 3, every 2 weeks in cycles 4 - 9 and every 4 weeks from cycle 10 onwards. The product information describes that in cycle 1 all patients should receive premedication with diphenhydramine (or equivalent) and paracetamol. In addition, all patients in cycle 1 should receive premedication and post-medication with prednisolone or dexamethasone.

Inpatient treatments

Some treatment options of the appropriate comparator therapy are carried out on an inpatient basis. The inpatient costs are calculated on the basis of the case flat fee revenues, which result from the valuation ratios of the respective DRG (Diagnosis Related Group) multiplied by the federal base rate value of 2024 (€ 4,210.59). Furthermore, the nursing revenue, which is calculated from the average length of stay of the concerned Diagnosis Related Group (DRG) multiplied by the nursing fee according to Section 15 paragraph 2a German Hospital Fee Act (KHEntgG) and the treatment-specific nursing revenue valuation ratio, is taken into account in the inpatient costs. The calculation of the costs of the inpatient treatments is standardised in the following on the basis of the DRG case flat fee catalogue 2024 and the nursing revenue catalogue 2024, the Federal base rate value of 2024 as well as the nursing fee pursuant to Section 15, paragraph 2a German Hospital Fee Act (KHEntgG), since the federal base rate value for 2025 was not yet available at the time of the cost calculation (1 April 2025).

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[8] Association of the Scientific-Medical Societies (AWMF). Diagnostics, therapy and after-care for adult patients with diffuse large B-cell lymphoma and related entities; S3-guideline [online]. AWMF register number 018-038OL. Berlin (GER): Oncology guideline programme; 2022.

[9] Crump M, Kuruvilla J, Couban S, MacDonald D, Kukreti V, Kouroukis C, et al. Randomized comparison of gemcitabine, dexamethasone, and cisplatin versus dexamethasone, cytarabine, and cisplatin chemotherapy before autologous stem-cell transplantation for relapsed and refractory aggressive lymphomas: NCIC-CTG LY12. J Clin Oncol. 2014;32:3490-6.

[10] Gisselbrecht C, Glass B, Mounier N, Singh Gill D, Linch DC, Trneny M, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol 2010;28 (27):4184-90

Courtesy translation – only the German version is legally binding.

Treatment period:

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are eligible for CAR-T cell therapy or stem cell transplantation

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Epcoritamab	Cycle 1 – 3: 4 x per 28-day cycle Cycle 4 – 9: 2 x per 28-day cycle From cycle 10 onwards: 1 x per 28-day cycle	28	1	28
Appropriate comparator therapy				
CAR-T cell therapies				
Axicabtagene ciloleucel	Single dose	1	1	1
Lisocabtagene maraleucel	Single dose	1	1	1
Tisagenlecleucel	Single dose	1	1	1
Induction chemotherapy followed by high-dose chemotherapy with autologous stem cell transplantation if there is a response to induction chemotherapy				
Induction chemotherapy				
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin)[9]				
Rituximab	1 x per 21-day cycle (day 1)	2 – 3	1	2 – 3
Gemcitabine	2 x per 21-day cycle (day 1 + 8)	2 – 3	2	4 – 6
Dexamethasone	4 x per 21-day cycle (day 1 - 4)	2 – 3	4	8 – 12

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Cisplatin	1 x per 21-day cycle (day 1)	2 – 3	1	2 – 3
R-ICE (rituximab + ifosfamide + carboplatin + etoposide)[10]				
Rituximab	1 x per 21-day cycle (day 1, additionally once on the day before the first cycle)	2 - 3	1	3 – 4
Ifosfamide	1 x per 21-day cycle (day 2)	2 - 3	1	2 – 3
Carboplatin	1 x per 21-day cycle (day 2)	2 - 3	1	2 – 3
Etoposide	3 x per 21-day cycle (day 1 - 3)	2 - 3	3	6 – 9
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin)[9,10]				
Rituximab	1 x per 21-day cycle (day 1; additionally once **optionally** on the day before the first cycle)	2 - 3	1	2 – 4
Dexamethasone	4 x per 21-day cycle (day 1 - 4)	2 - 3	4	8 – 12
Cytarabine	2 x on day 2 of a 21-day cycle	2 - 3	1	2 – 3
Cisplatin	1 x per 21-day cycle (day 1)	2 - 3	1	2 – 3
High-dose chemotherapy with autologous stem cell transplantation				

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Stem cell collection from autologous donors with chemotherapy or with most severe complications or comorbidities (CC), age > 15 years	once		15.9 (average length of stay)	15.9
Autologous stem cell transfusion	once		23.4 (average length of stay)	23.4
Induction chemotherapy followed by high-dose chemotherapy with allogeneic stem cell transplantation if there is a response to induction chemotherapy				
Induction therapy				
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin)[9]				
Rituximab	1 x per 21-day cycle (day -1)	2 – 3	1	2 – 3
Gemcitabine	2 x per 21-day cycle (day 1 + 8)	2 – 3	2	4 – 6
Dexamethasone	4 x per 21-day cycle (day 1 - 4)	2 – 3	4	8 – 12
Cisplatin	1 x per 21-day cycle (day 1)	2 – 3	1	2 – 3
R-ICE *(rituximab + ifosfamide + carboplatin + etoposide)*[10]				
Rituximab	1 x per 21-day cycle (day 1; additionally once on the day before the first cycle)	2 - 3	1	3 – 4
Ifosfamide	1 x per 21-day cycle (day 2)	2 - 3	1	2 – 3
Carboplatin	1 x per 21-day cycle (day 2)	2 - 3	1	2 – 3

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Etoposide	3 x per 21-day cycle (day 1 - 3)	2 - 3	3	6 – 9
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin)[9,10]				
Rituximab	1 x per 21-day cycle (day 1; additionally once **optionally** on the day before the first cycle)	2 - 3	1	2 – 4
Dexamethasone	4 x per 21-day cycle (day 1 - 4)	2 - 3	4	8 – 12
Cytarabine	2 x on day 2 of a 21-day cycle	2 - 3	1	2 – 3
Cisplatin	1 x per 21-day cycle (day 1)	2 - 3	1	2 – 3
High-dose chemotherapy with allogeneic stem cell transplantation				
Highly complex and intensive block chemotherapy	once		7.5 (average length of stay)	7.5
Allogeneic stem cell transfusion	once		35.0 (average length of stay)	35.0

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b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Epcoritamab	Cycle 1 – 3: 4 x per 28-day cycle Cycle 4 – 9: 2 x per 28-day cycle From cycle 10 onwards: 1 x per 28-day cycle	28	1	28
Appropriate comparator therapy				
Polatuzumab vedotin + bendamustine + rituximab				
Polatuzumab vedotin	1 x per 21-day cycle	6.0	1	6.0
Bendamustine	2 x per 21-day cycle	6.0	2	12.0
Rituximab	1 x per 21-day cycle	6.0	1	6.0
Tafasitamab + lenalidomide				
Tafasitamab	Cycle 1: Day 1, 4, 8, 15 and 22 (28-day cycle)	13.0	Cycle 1: 5	33.0
	Cycle 2 + 3: Day 1, 8, 15, 22 (28-day cycle)		Cycle 2 + 3: 4	
	Cycle 4 until disease progression: Day 1 and 15 (28-day cycle)		From cycle 4 onwards: 2	
Lenalidomide	Day 1 – 21 of a 28-day cycle	12.0	21	252.0
radiotherapy				

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
radiotherapy	Different from patient to patient			

Consumption:

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg). This results in a body surface area of 1.91 m² (calculated according to Du Bois 1916).[11]

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are eligible for CAR-T cell therapy or stem cell transplantation

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Epcoritamab	Cycle 1: Day 1: 0.16 mg	0.16 mg	1 x 4 mg	28	2 x 4 mg
	Cycle 1: Day 8: 0.8 mg	0.8 mg	1 x 4 mg		
	Cycle 1: Day 15 and 22: 48 mg	48 mg	1 x 48 mg		26 x 48 mg
	Cycle 2 - 3: Day 1, 8, 15 and 22: 48 mg	48 mg			
	Cycle 4 – 9: Day 1 and 15: 48 mg	48 mg			
	From cycle 10 onwards: Day 1:	48 mg			

[11] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	48 mg				
Appropriate comparator therapy					
CAR-T cell therapies					
Axicabtagene ciloleucel	< 100 kg: 1 - 2 x 10^6 viable CAR+ T cells/kg	1 - 2 x 10^6/kg CAR+ T cells	1 single infusion bag	1	1 single infusion bag
	≥ 100 kg: 2 x 10^8 Viable CAR+ T cells (from 100 kg regardless of body weight)	2 x 10^8 CAR+ T cells			
Lisocabtagene maraleucel	100 × 10^6 viable CAR+ T cells	100 × 10^6 viable CAR+ T cells	1 single infusion bag	1	1 single infusion bag
Tisagenlecleucel	0.6 - 6 × 10^8 CAR-positive viable T cells (regardless of the body weight)	0.6 - 6 × 10^8 CAR-positive T cells	1 single infusion bag	1	1 single infusion bag
Induction chemotherapy followed by high-dose chemotherapy with autologous stem cell transplantation if there is a response to induction chemotherapy					
Induction chemotherapy					
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin)[9]					
Rituximab	375 mg/m^2 = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	2 – 3	2.0 x 500 mg + 6.0 x 100 mg – 3.0 x 500 mg + 9.0 x 100 mg
Gemcitabine	1,000 mg/m^2 = 1,910 mg	1,910 mg	2 x 1,000 mg	4 – 6	8.0 x 1,000 mg – 12.0 x 1,000 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	8 – 12	8.0 x 40 mg – 12.0 x 40 mg

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Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 100 mg + 1 x 50 mg	2 – 3	2.0 x 100 mg + 2.0 x 50 mg – 3.0 x 100 mg + 3.0 x 50 mg
R-ICE *(rituximab + ifosfamide + carboplatin + etoposide)*[10]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	3 – 4	3.0 x 500 mg + 9.0 x 100 mg – 4.0 x 500 mg + 12.0 x 100 mg
Ifosfamide	5,000 mg/m² = 9,550 mg	9,550 mg	2 x 5000 mg	2 – 3	4.0 x 5000 mg – 6.0 x 5000 mg
Carboplatin	AUC = 5 (= 641.4 mg); max. 800 mg	641.4 mg – 800 mg	1 x 600 mg + 1 x 50 mg – 1 x 600 mg + 4 x 50 mg	2 – 3	2.0 x 600 mg + 2.0 x 50 mg - 3.0 x 600 mg + 3.0 x 50 mg – 2.0 x 600 mg + 8.0 x 50 mg - 3.0 x 600 mg + 12.0 x 50 mg
Etoposide	100 mg/m² = 191 mg	191 mg	1 x 200 mg	6 – 9	6.0 x 200 mg – 9.0 x 200 mg
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin)[9,10]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	2 – 4	2.0 x 500 mg + 6.0 x 100 mg – 4.0 x 500 mg + 12.0 x 100 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	8 – 12	8.0 x 40 mg – 12.0 x 40 mg
Cytarabine	2 x daily 2,000 mg/m² = 2 x 3,820 mg	7,640 mg	4 x 2,000 mg	2 – 3	8.0 x 2,000 mg – 12.0 x 2,000 mg
Cisplatin	100 mg/m²	191 mg	2 x 100 mg	2 – 3	4.0 x 100 mg

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	= 191 mg				– 6.0 x 100 mg
Induction chemotherapy followed by high-dose chemotherapy with allogeneic stem cell transplantation if there is a response to induction chemotherapy					
Induction therapy					
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin)[9]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	2 – 3	2.0 x 500 mg + 6.0 x 100 mg – 3.0 x 500 mg + 9.0 x 100 mg
Gemcitabine	1,000 mg/m² = 1,910 mg	1,910 mg	2 x 1,000 mg	4 – 6	8.0 x 1,000 mg – 12.0 x 1,000 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	8 – 12	8.0 x 40 mg – 12.0 x 40 mg
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 100 mg + 1 x 50 mg	2 – 3	2.0 x 100 mg + 2.0 x 50 mg – 3.0 x 100 mg + 3.0 x 50 mg
R-ICE (rituximab + ifosfamide + carboplatin + etoposide)[9, 10]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	3 – 4	3.0 x 500 mg + 9.0 x 100 mg – 4.0 x 500 mg + 12.0 x 100 mg
Ifosfamide	5,000 mg/m² = 9,550 mg	9,550 mg	2 x 5000 mg	2 – 3	4.0 x 5000 mg – 6.0 x 5000 mg
Carboplatin	AUC = 5 (= 641.4 mg); max. 800 mg	641.4 mg – 800 mg	1 x 600 mg + 1 x 50 mg – 1 x 600 mg + 4 x 50 mg	2 – 3	2.0 x 600 mg + 2.0 x 50 mg - 3.0 x 600 mg + 3.0 x 50 mg – 2.0 x 600 mg + 8.0 x 50 mg -

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
					3.0 x 600 mg + 12.0 x 50 mg
Etoposide	100 mg/m² = 191 mg	191 mg	1 x 200 mg	6 – 9	6.0 x 200 mg – 9.0 x 200 mg
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin) [9,10]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	2 – 4	2.0 x 500 mg + 6.0 x 100 mg – 4.0 x 500 mg + 12.0 x 100 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	8 – 12	8.0 x 40 mg – 12.0 x 40 mg
Cytarabine	2 x daily 2,000 mg/m² = 2 x 3,820 mg	7,640 mg	4 x 2,000 mg	2 – 3	8.0 x 2,000 mg – 12.0 x 2,000 mg
Cisplatin	100 mg/m² = 191 mg	191 mg	2 x 100 mg	2 – 3	4.0 x 100 mg – 6.0 x 100 mg

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b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Epcoritamab	Cycle 1: Day 1: 0.16 mg	0.16 mg	1 x 4 mg	28	2 x 4 mg
	Cycle 1: Day 8: 0.8 mg	0.8 mg	1 x 4 mg		
	Cycle 1: Day 15 and 22: 48 mg	48 mg	1 x 48 mg		26 x 48 mg
	Cycle 2 - 3: Day 1, 8, 15 and 22: 48 mg	48 mg			
	Cycle 4 – 9: Day 1 and 15: 48 mg	48 mg			
	From cycle 10 onwards: Day 1: 48 mg	48 mg			
Appropriate comparator therapy					
Polatuzumab vedotin + bendamustine + rituximab					
Polatuzumab vedotin	1.8 mg/kg = 139.9 mg	139.9 mg	1 x 140 mg	6.0	6.0 x 140 mg
Bendamustine	90 mg/m^2 = 171.9 mg	171.9 mg	1 x 100 mg + 3 x 25 mg	12.0	12.0 x 100 mg + 36.0 x 25 mg
Rituximab	375 mg/m^2 = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	6.0	6.0 x 500 mg + 18.0 x 100 mg
Tafasitamab + lenalidomide					
Tafasitamab	12 mg/kg = 932.4 mg	932.4 mg	5 x 200 mg	33.0	165.0 x 200 mg

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Lenalidomide	25 mg	25 mg	1 x 25 mg	252.0	252.0 x 25 mg
radiotherapy					
radiotherapy	Different from patient to patient				

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Inpatient treatments:

Calculation year	DRG	Average length of stay [d]	DRG valuation ratio (main department)	Federal base case value	Nursing revenue valuation ratio	Nursing fee	Case flat fee revenue	Nursing revenue	Total case flat fee revenue and nursing revenue
Appropriate comparator therapy									
High-dose chemotherapy with allogeneic stem cell transplantation									
2025	R61G	7.6	1.005	€ 4,210.59	0.7749	€ 250	€ 4,231.64	€ 1,472.31	€ 5,703.95
2025	A04E	34.4	8.985	€ 4,210.59	1.9317	€ 250	€ 37,832.15	€ 16,612.62	€ 54,444.77
High-dose chemotherapy with autologous stem cell transplantation									
2025	A42A	16.1	1.986	€ 4,210.59	0.7507	€ 250	€ 8,362.23	€ 3,021.57	€ 11,383.80
2025	A15C	23.8	5.303	€ 4,210.59	1.241	€ 250	€ 22,328.76	€ 7,383.95	€ 29,712.71

Courtesy translation – only the German version is legally binding.

Costs of the medicinal products:

Medicinal product to be assessed					
Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Epcoritamab 4 mg	1 CII	€ 559.35	€ 1.77	€ 30.34	€ 527.24
Epcoritamab 48 mg	1 SFI	€ 6,433.14	€ 1.77	€ 364.11	€ 6,067.26

Appropriate comparator therapy				
Designation of the therapy	Packaging size	Costs (purchase price clinic pack plus value added tax)	Value added tax (19%)	Costs of the medicinal product
CAR-T cell therapies				
Axicabtagene ciloleucel	1 single infusion bag	€ 230,621.00	€ 0[12]	€ 230,621.00
Lisocabtagene maraleucel	1 single infusion bag	€ 227,500.00	€ 0[12]	€ 227,500.00
Tisagenlecleucel	1 single infusion bag	€ 239,000.00	€ 0[12]	€ 239,000.00

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Bendamustine 100 mg	5 PIC	€ 1,465.28	€ 1.77	€ 69.00	€ 1,394.51
Bendamustine 25 mg	5 PIC	€ 374.81	€ 1.77	€ 17.25	€ 355.79
Carboplatin 600 mg	1 CIS	€ 300.84	€ 1.77	€ 13.74	€ 285.33
Carboplatin 50 mg	1 CIS	€ 34.66	€ 1.77	€ 1.11	€ 31.78
Cisplatin 100 mg	1 CIS	€ 76.59	€ 1.77	€ 3.10	€ 71.72
Cisplatin 50 mg	1 CIS	€ 47.71	€ 1.77	€ 1.73	€ 44.21
Cytarabine 2,000 mg	1 SII	€ 77.06	€ 1.77	€ 3.12	€ 72.17
Dexamethasone 40 mg	10 TAB	€ 46.29	€ 1.77	€ 0.00	€ 44.52
Dexamethasone 40 mg	20 TAB	€ 81.59	€ 1.77	€ 0.00	€ 79.82
Etoposide 200 mg	1 CIS	€ 81.90	€ 1.77	€ 3.35	€ 76.78
Gemcitabine 1000 mg	1 PIS	€ 102.35	€ 1.77	€ 10.62	€ 89.96
Ifosfamide 5 g	1 CIS	€ 177.77	€ 1.77	€ 7.90	€ 168.10
Lenalidomide 25 mg	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Polatuzumab vedotin 140 mg	1 PIC	€ 10,680.39	€ 1.77	€ 0.00	€ 10,678.62

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates

[12] The medicinal product is exempt from value added tax at the applied LAUER-TAXE® last revised.

Courtesy translation – only the German version is legally binding.

Tafasitamab 200 mg	1 PIC	€ 654.48	€ 1.77	€ 35.61	€ 617.10
Rituximab 500 mg	1 CIS	€ 782.56	€ 1.77	€ 36.60	€ 744.19
Rituximab 100 mg	2 CIS	€ 321.07	€ 1.77	€ 14.70	€ 304.60
Abbreviations: HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SII = solution for injection/infusion; CII = concentrate for injection or infusion solution; PIS = powder for the preparation of an infusion solution, PIC = powder for the preparation of an infusion solution concentrate; TAB = tablets					

LAUER-TAXE® last revised: 1 April 2025

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5aSGB V, when a non-prescription medicinal product is dispensed and invoiced in accordance with Section 300, a medicinal product dispensing price in the amount of the dispensing price of the pharmaceutical company plus the surcharges in accordance with Sections 2 and 3 of the Pharmaceutical Price Ordinance in the version valid on 31 December 2003 applies to the insured.

Prophylactic premedication

Antipyretic and antihistamine premedication is only recommended in the product information for axicabtagene ciloleucel, tisagenlecleucel and lisocabtagene maraleucel.

Mesna is given in combination with ifosfamide for the prophylaxis of haemorrhagic cystitis.

Conditioning chemotherapy for lymphocyte depletion under CAR-T cell therapy

Axicabtagene ciloleucel is an autologous cell product produced from the patient's own T cells. Therefore, a leukapheresis is usually necessary to obtain the cell material. Since leukapheresis is part of the manufacture of the medicinal product pursuant to Section 4, paragraph 14 Medicinal Products Act, no further costs are incurred in this respect for axicabtagene ciloleucel.

For axicabtagene ciloleucel, a treatment regimen for lymphocyte depletion, consisting of intravenous administration of cyclophosphamide (500 mg/m^2 = 955 mg) and fludarabine (30 mg/m^2 = 57.3 mg), is given daily for 3 days, with infusion administered 3 to 5 days after the start of lymphocyte depletion.

For tisagenlecleucel, provided the white blood cell count is not below ≤ 1,000 cells/µl one week prior to infusion, a treatment regimen for lymphocyte depletion, consisting of intravenous administration of fludarabine (25 mg/m^2 = 47.75 mg) and cyclophosphamide (250 mg/m^2 = 477.5 mg) daily over 3 days starting with the first fludarabine dose, with tisagenlecleucel infusion administered 2 to 14 days after the start of lymphocyte depletion.

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For lisocabtagene maraleucel, a treatment regimen for lymphocyte depletion, consisting of intravenous administration of cyclophosphamide (500 mg/m^2 = 950 mg) and fludarabine (30 mg/m^2 = 57 mg), is given daily for 3 days, with infusion administered 3 to 5 days after the start of lymphocyte depletion.

Screening for hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) under CAR-T cell therapy

Patients should be tested for hepatitis B, hepatitis C and HIV infection prior to starting treatment with axicabtagene ciloleucel. This test is not required for all therapy options of the appropriate comparator therapy. Since there is a regular difference between the medicinal product to be assessed and the appropriate comparator therapy with regard to the tests for hepatitis B, hepatitis C and HIV, the costs of additionally required SHI services are presented in the resolution.

Diagnostics to rule out chronic hepatitis B requires sensibly coordinated steps. A step-by-step serological diagnosis initially consists of the examination of HBs antigen and anti-HBc antibodies. If both are negative, a past HBV infection can be excluded. In certain case constellations, further steps may be necessary in accordance with current guideline recommendations.[13]

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient / year
Medicinal product to be assessed							
Epcoritamab							
Prednisolone [14] 100 mg	100 TAB at 20 mg	€ 21.62	€ 1.77	€ 0.82	€ 19.03	16	€ 19.03
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 SFI at 4 mg	€ 26.24	€ 1.77	€ 7.02	€ 17.45	4	€ 34.90
Paracetamol 500 mg – 1,000 mg	10 TAB at 500 mg 10 TAB at 1,000 mg	€ 2.96 € 3.32	€ 0.15 € 0.17	€ 0.13 € 0.14	€ 2.68 € 3.01	4	€ 2.68 - € 3.01
Appropriate comparator therapy							
CAR-T cell therapies							
Screening for HBV, HCV and HIV							
HBV test	-	-	-	-	€ 5.06	1.0	€ 5.06

[13] S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011 https://register.awmf.org/assets/guidelines/021-011l_S3_Prophylaxe-Diagnostik-Therapie-der-Hepatitis-B-Virusinfektion_2021-07.pdf].

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Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient / year
Hepatitis B surface antigen status (GOP 32781)							
Anti-HBc antibody (GOP 32614)	-	-	-	-	€ 5.43	1.0	€ 5.43
Hepatitis C HCV antibody status (GOP 32618)	-	-	-	-	€ 9.02	1.0	€ 9.02
HIV HIV-1 and HIV-2 antibody status (GOP: 32575)	-	-	-	-	€ 4.09	1.0	€ 4.09
Axicabtagene ciloleucel							
Conditioning chemotherapy for lymphocyte depletion							
Cyclophosphamide 500 mg/m² = 955 mg	6 PSI each 500 mg	€ 84.44	€ 1.77	€ 9.25	€ 73.42	3.0	€ 73.42
Fludarabine 30 mg/m² = 57.3 mg	1 KII at 50 mg	€ 118.54	€ 1.77	€ 5.09	€ 111.68	3.0	€ 670.08
Tisagenlecleucel							
Conditioning chemotherapy for lymphocyte depletion							
Cyclophosphamide 250 mg/m² = 477.5 mg	10 PIJ at 200 mg	€ 69.60	€ 1.77	€ 3.23	€ 64.60	3.0	€ 64.60
Fludarabine 25 mg/m² = 47.75 mg	1 KII at 50 mg	€ 118.54	€ 1.77	€ 5.09	€ 111.68	3.0	€ 670.08
Lisocabtagene maraleucel							
Conditioning chemotherapy for lymphocyte depletion							
Cyclophosphamide 300 mg/m² = 573 mg	6 PSI each 500 mg	€ 84.44	€ 1.77	€ 9.25	€ 73.42	3.0	€ 73.42
Fludarabine 30 mg/m² = 57.3 mg	1 KII at 50 mg	€ 118.54	€ 1.77	€ 5.09	€ 111.68	3.0	€ 670.08
Polatuzumab vedotin + bendamustine + rituximab							
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 SFI at 4 mg	€ 26.24	€ 1.77	€ 7.02	€ 17.45	6.0	€ 52.35
Paracetamol[14] (500 mg - 1,000 mg, PO)	10 TAB 500 mg –	€ 2.96 – € 3.32	€ 0.15 – € 0.17	€ 0.13 – € 0.14	€ 2.68 – € 3.01	6.0	€ 2.68 – € 3.01

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Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient / year
	10 TAB 1,000 mg						
HBV test Hepatitis B surface antigen status (GOP 32781)	-	-	-	-	€ 5.06	1.0	€ 5.06
Anti-HBc antibody (GOP 32614)	-	-	-	-	€ 5.43	1.0	€ 5.43
Induction chemotherapies (R-GDP, R-DHAP, R-ICE) prior to autologous or allogeneic stem cell transplantation							
Rituximab (R-GDP, R-DHAP, R-ICE)							
HBV diagnostics							
HBV test Hepatitis B surface antigen status (GOP 32781)	-	-	-	-	€ 5.06	1.0	€ 5.06
Anti-HBc antibody (GOP 32614)	-	-	-	-	€ 5.43	1.0	€ 5.43
Premedication (R-GDP)							
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 SFI at 4 mg	€ 26.24	€ 1.77	€ 7.02	€ 17.45	2.0 – 3.0	€ 17.45 – € 34.90
Paracetamol[14] (500 mg - 1,000 mg, PO)	10 TAB 500 mg – 10 TAB 1,000 mg	€ 2.96 – € 3.32	€ 0.15 – € 0.17	€ 0.13 – € 0.14	€ 2.68 – € 3.01	2.0 – 3.0	€ 2.68 – € 3.01
Premedication (R-DHAP)							
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 SFI at 4 mg	€ 26.24	€ 1.77	€ 7.02	€ 17.45	2.0 – 3.0	€ 17.45 – € 34.90
Paracetamol[14] (500 mg - 1,000 mg, PO)	10 TAB 500 mg – 10 TAB 1,000 mg	€ 2.96 – € 3.32	€ 0.15 – € 0.17	€ 0.13 – € 0.14	€ 2.68 – € 3.01	2.0 – 4.0	€ 2.68 – € 3.01

[14] Fixed reimbursement rate

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Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient / year
Premedication (R-ICE)							
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 SFI at 4 mg	€ 26.24	€ 1.77	€ 7.02	€ 17.45	2.0 – 3.0	€ 17.45 – € 34.90
Paracetamol[14] (500 mg - 1,000 mg, PO)	10 TAB 500 mg – 10 TAB 1,000 mg	€ 2.96 – € 3.32	€ 0.15 – € 0.17	€ 0.13 – € 0.14	€ 2.68 – € 3.01	3.0 – 4.0	€ 2.68 – € 3.01
Cisplatin (R-GDP, R-DHAP)							
Antiemetic treatment: In clinical practice, an appropriate antiemetic treatment is established before and/or after administration of cisplatin. The product information for cisplatin does not provide any specific information on this, which is why the necessary costs cannot be quantified.							
Mannitol 10% Inf. Sol., 37.5 g/day	10 x 250 ml INF	€ 87.05	€ 4.35	€ 7.94	€ 74.76	2.0 – 3.0	€ 74.76
Sodium chloride 0.9% Inf. Sol., 3 l - 4.4 l/day	20 x 500 ml INF	€ 5.51	€ 0.28	€ 0.38	€ 4.85	2.0 – 3.0	€ 9.70 – € 19.40
Mesna (R-ICE)							
Mesna (Bolus with 1,900 mg mesna (= 20% of the ifosfamide dose), followed by 24-hour continuous infusion with at least 1,900 mg up to 9,500 mg (= 20% - 100% of the ifosfamide dose), followed by subsequent infusion with up to 4,750 mg mesna (= 0% - 50% of the ifosfamide dose) for 6 - 12 hours	Bolus with 1,900 mg followed by 24-hour continuous infusion with 1,900 mg						
	5 SFI x 1,000 mg	€ 66.24	€ 1.77	€ 6.95	€ 57.52	2.0 – 3.0	€ 115.04 – € 172.56
	Bolus of 1,900 mg followed by 24-hour continuous infusion of 9,500 mg followed by subsequent infusion of 4,750 mg						
	50 AMP x 400 mg	€ 148.19	€ 1.77	€ 17.33	€ 129.09	2.0 – 3.0	€ 301.65 - € 373.22
	5 SFI x 1,000 mg	€ 66.24	€ 1.77	€ 6.95	€ 57.52		
Abbreviations: AMP = ampoules; SFI = solution for injection, INF = infusion solution; CII = concentrate for injection or infusion solution, PSI = powder for solution for injection, TAB = tablets							

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Other SHI services:

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The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

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2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or

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- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

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If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are eligible for CAR-T cell therapy or stem cell transplantation

   No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

   References:
   Product information for epcoritamab (Tepkinly); Tepkinly 48 mg solution for injection; last revised: January 2025

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b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

References:
Product information for epcoritamab (Tepkinly); Tepkinly 48 mg solution for injection; last revised: January 2025

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At their session on 8 November 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 29 October 2024.

On 31 October 2024, the pharmaceutical company submitted a dossier for the benefit assessment of epcoritamab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 6 and Section 12, number 2 VerfO.

By letter dated 1 November 2024 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient epcoritamab.

The dossier assessment by the IQWiG was submitted to the G-BA on 30 January 2025, and the written statement procedure was initiated with publication on the G-BA website on 3 February 2025. The deadline for submitting statements was 24 February 2025.

The oral hearing was held on 10 March 2025.

By letter dated 25 March 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 4 April 2025.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 8 April 2025, and the proposed draft resolution was approved.

At their session on 17 April 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

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Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	8 November 2022	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	29 October 2024	New determination of the appropriate comparator therapy
Working group Section 35a	4 March 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 March 2025	Conduct of the oral hearing
Subcommittee on Medicinal Products	25 March 2025	Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	18 March 2025 1 April 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	8 April 2025	Concluding discussion of the draft resolution
Plenum	17 April 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 17 April 2025

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken

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