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 Pirtobrutinib (mantle cell lymphoma, pretreated patients)

of 7 August 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess 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 studies the pharmaceutical company have 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

On 30 October 2023, pirtobrutinib received the marketing authorisation for the therapeutic indication as monotherapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor.

On 10 June 2024, the pharmaceutical company submitted an application for bundling two assessment procedures for the active ingredient pirtobrutinib in accordance with Section 35a paragraph 5b SGB V, as the marketing authorisation of at least one new therapeutic indication was expected within a period of six months from the relevant date for the start of the benefit assessment of the present therapeutic indication in accordance with Section 35a, paragraph 1, sentence 3 SGB V. At their session on 1 August 2024, the G-BA approved the application for bundling and postponed the relevant date for the start of the benefit assessment procedure

for the present therapeutic indication to four weeks post-authorisation of the other therapeutic indication, at the latest six months after the first relevant date.

The active ingredient pirtobrutinib (Jaypirca) was listed for the first time on 15 September 2024 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. The latest date for submitting the dossier as a result of the bundling was therefore six months after this date.

The bundling failed due to the notification by the pharmaceutical company on 21 January 2025 that the marketing authorisation procedure for the second therapeutic indication would probably be extended to such an extent that the latest date for submitting the dossier within the scope of the applied bundling could not be met. By letter dated 23 January 2025, the pharmaceutical company was therefore requested, pursuant to Chapter 5 Section 11, paragraph 3 of the Rules of Procedure (VerfO) of the G-BA, to submit a complete dossier to the G-BA in due time, i.e. within 4 weeks of receipt of the letter.

The pharmaceutical company submitted a dossier for the active ingredient pirtobrutinib in the present therapeutic indication in due time on 12 February 2025 pursuant to Section 4, paragraph 3, number 3 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 2 of the Rules of Procedure (VerfO) of the G-BA in conjunction with Nos. 3 and 4 of the resolution of 1 August 2024 on the application pursuant to Section 35a paragraph 5b SGB V (pirtobrutinib), according to which, if no further marketing authorisation of a therapeutic indication is granted within the six-month period and the benefit assessments commence within four weeks of the request by the G-BA.

The benefit assessment of pirtobrutinib in the present therapeutic indication as monotherapy for the treatment of adult patients with relapsed or refractory MCL who have previously been treated with a BTK inhibitor thus started on 15 February 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 May 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 pirtobrutinib 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. In order to determine the extent of the additional benefit, the G-BA have 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 pirtobrutinib.

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

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

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

2.1.1 Approved therapeutic indication of Pirtobrutinib (Jaypirca) in accordance with the product information

Jaypirca as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor.

Therapeutic indication of the resolution (resolution of 07.08.2025):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with relapsed or refractory mantle cell lymphoma who have who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor

Appropriate comparator therapy:

Individualised therapy with selection of

- bendamustine + rituximab,
- lenalidomide ± rituximab,
- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone),
- VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone),
- R-BAC (rituximab + bendamustine + cytarabine),
- R-FCM (fludarabine + cyclophosphamide + mitoxantrone + rituximab),
- ibrutinib,
- temsirolimus,
- brexucabtagene autoleucel (only for patients with at least two prior therapies),
- venetoclax,
- high-dose therapy with allogeneic stem cell transplantation and
- high-dose therapy with autologous stem cell transplantation

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):

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.

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 pirtobrutinib, the following active ingredients are approved for the treatment of relapsed or refractory mantle cell lymphoma: brexucabtagene autoleucel, ibrutinib, lenalidomide, temsirolimus. Bendamustine, bleomycin, carmustine, chlorambucil, cyclophosphamide, cytarabine, dexamethasone, doxorubicin, etoposide, ifosfamide, methotrexate, mitoxantrone, prednisone, prednisolone, trofosfamide, vinblastine, vincristine has the marketing authorisation for the treatment of non-Hodgkin lymphoma.

On 2. Allogeneic stem cell transplantation, autologous stem cell transplantation as well as radiotherapy are considered as non-medicinal therapy options in the present therapeutic indication.

On 3. The following resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Autologous anti-CD19-transduced CD3+ cells (resolution of 5 August 2021)
- Ibrutinib (resolution of 21 July 2016)
- Pixantrone (resolution of 16 May 2013)

Annex VI to Section K of the Pharmaceuticals Directive - Prescribability of approved medicinal products in non-approved therapeutic indications (so-called off-label use):

- Use of fludarabine in low or intermediate malignant B-non-Hodgkin lymphoma (B-NHL) other than chronic lymphocytic leukaemia (CLL) as specified in the marketing authorisation
- Rituximab in mantle cell lymphoma

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 indication according to Section 35a paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy"). Written statements from the German Society for Haematology and Medical Oncology (DGHO) as well as the AkdÄ are available.

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.

The evidence on the therapy standard for the treatment of relapsed or refractory mantle cell lymphoma after at least one prior therapy including a BTK inhibitor is extremely limited. Various therapy options are mentioned in the present guidelines, whereby reference is made to an individualised treatment decision depending, among others, on the response and duration of remission of the previous treatments as well as the general condition. It is not possible to derive a treatment option that is regularly considered as the therapy standard for all patients in the present therapeutic indication.[2][3][4]

[2] Eyre TA, Bishton MJ, McCulloch R, O'Reilly M, Sanderson R, Menon G, et al. Diagnosis and management of mantle cell lymphoma: a British Society for Haematology guideline. Br J Haematol 2024;204(1):108-126.

[3] Alberta Health Services (AHS). Lymphoma [online]. Edmonton (CAN): AHS; 2019. (Clinical practice guideline; volume LYHE-002 V20).

[4] National Comprehensive Cancer Network (NCCN). B-cell lymphoma. NCCN evidence blocks; version 3.2022 [online]. Plymouth Meeting (USA): NCCN; 2022.

In the present therapeutic indication, the active ingredients ibrutinib, temsirolimus, lenalidomide as monotherapy and brexucabtagene autoleucel are explicitly approved as well as rituximab in combination with fludarabine, cyclophosphamide and mitoxantrone (R-FCM), rituximab in combination with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) and rituximab in combination with bendamustine (R-bendamustine) can be prescribed in off-label use in accordance with Annex VI of the Pharmaceuticals Directive.

Since the patient population in the present therapeutic indication includes patients who have already received a BTK inhibitor, ibrutinib can only be considered as a therapy option for those patients who have not received prior ibrutinib therapy or in whom a relapse occurs after a longer treatment-free interval following prior ibrutinib therapy.

No clear therapy recommendation on lenalidomide as monotherapy and temsirolimus can be derived from the available guidelines and further literature. By G-BA's resolution of 21 July 2016, an indication of a considerable additional benefit of ibrutinib compared to temsirolimus in adults with relapsed or refractory mantle cell lymphoma was found. Temsirolimus and lenalidomide monotherapy are considered as therapy options according to the German healthcare context.[5]

Brexucabtagene autoleucel is only approved after two prior therapies and is only considered for patients with a sufficiently good general condition.

According to the available evidence, a repeat immunochemotherapy in the form of R-FCM, R-CHOP or R-bendamustine is only indicated for adults with a late relapse. R-FCM is also an intensive therapy which, among others, due to myelotoxicity, can only be considered as a therapy option for patients with a sufficiently good general condition. R-bendamustine is a treatment option for adults with a reduced general condition.

The above-mentioned limitations on the use of approved therapy options or therapy options that can be prescribed in off-label use in accordance with Annex VI to the Pharmaceuticals Directive mean that these therapy options cannot be used to provide individualised therapy for all patients covered by this therapeutic indication after at least one prior therapy including a BTK inhibitor, or that these therapy options cannot be considered for relevant patient groups. In addition, the above-mentioned treatment options are no longer considered for adults with more than one prior therapy if they have already been used in an earlier line of therapy.

The present guidelines, the written statements of the AkdÄ and the DGHO and further literature recommend the following further individualised treatment options, which are put to off-label use and for which there is significant evidence from single-arm studies:

- Lenalidomide + rituximab[6]

[5] Onkopedia guideline of the DGHO, Mantle cell lymphoma, last revised June 2023 [online].

[6] Wang M et al. Lenalidomide in combination with rituximab for patients with relapsed or refractory mantle-cell lymphoma: a phase 1/2 clinical trial. Lancet Oncol. 2012 Jul;13(7):716-23. doi: 10.1016/S1470-2045(12)70200-0. Epub 2012 Jun 6. PMID: 22677155.

- VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)[7,8]
- R-BAC (rituximab + bendamustine + cytarabine)[9]
- Venetoclax.[10]

The available evidence shows that lenalidomide is also a relevant treatment option in combination with rituximab on a patient-individual basis due to higher response rates.

According to the German healthcare context, venetoclax monotherapy is generally suitable for patients who have already received a BTK inhibitor.[5]

In accordance with the generally recognised state of medical knowledge, it can be determined in the overall assessment that the off-label use of the above-mentioned therapy options for relevant patient groups of the present therapeutic indication as part of individualised therapy is generally preferable to the medicinal products, which were previously approved in the therapeutic indication; Section 6, paragraph 2, sentence 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV).

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 pirtobrutinib is assessed as follows:

An additional benefit is not proven.

Justification:

For the benefit assessment of pirtobrutinib, the pharmaceutical company submitted the single-arm, ongoing phase 1/2 BRUIN study to investigate the efficacy, safety and pharmacokinetic properties of pirtobrutinib in adult patients with B-cell neoplasms.

The BRUIN study has been conducted in North America, Europe, Asia and Australia since 2018. Pretreated patients with chronic lymphocytic leukaemia (CLL) and small cell lymphocytic lymphoma (SLL) as well as non-Hodgkin lymphoma, including mantle cell lymphoma (MCL), and an Eastern Cooperative Oncolgy Group (ECOG) performance status of 0-2 were enrolled

---

7 Robak T et al; LYM-3002 investigators. Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: final overall survival results of a randomised, open-label, phase 3 study. Lancet Oncol. 2018 Nov;19(11):1449-1458.

8 Fisher RI et al. Multicentre phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. J Clin Oncol. 2006 Oct 20;24(30):4867-74. doi: 10.1200/JCO.2006.07.9665. Epub 2006 Sep 25. PMID: 17001068.

9 McCulloch R et al. Efficacy of R-BAC in relapsed, refractory mantle cell lymphoma post BTK inhibitor therapy; Br J Haematol. 2020 May;189(4):684-688. doi: 10.1111/bjh.16416. Epub 2020 Feb 3.

10 Eyre, T.A. et al. Efficacy of venetoclax monotherapy in patients with relapsed, refractory mantle cell lymphoma after Bruton tyrosine kinase inhibitor therapy. Haematologica 2018, 104, 68–71.

in the total of seven cohorts. Patients with MCL were enrolled in cohorts 1 (non-blastoid MCL) and 7 (including blastoid MCL). A total of 152 patients with MCL who have been previously treated with a BTK inhibitor were enrolled in cohorts 1 and 7 (cohort 1: N = 124, cohort 7: N = 28).

The study is divided into a phase 1 (dose escalation phase) and a phase 2 (pirtobrutinib monotherapy with the recommended phase 2 dose). The primary endpoint of phase 1 is the determination of the maximum tolerated dose and the recommended phase 2 dose. Further endpoints are the characterisation of the safety profile, the determination of pharmacokinetic parameters and the overall response rate. The primary endpoint of phase 2 for patients with MCL is the overall response rate. Other endpoints include the best overall response, the duration of the treatment response and overall survival.

The pharmaceutical company presented the evaluations of the data cut-offs from 31 January 2022 and 29 July 2022 in the dossier.

In addition, the pharmaceutical company presented the result of a Matching-Adjusted Indirect Comparison (MAIC) analysis without a bridge comparator based on the BRUIN study and the retrospective observational study SCHOLAR-2 for the endpoint of overall survival.

Assessment:

As the BRUIN study is a single-arm study, it does not allow an assessment of the additional benefit of pirtobrutinib compared with the appropriate comparator therapy and is therefore unsuitable for the benefit assessment of pirtobrutinib.

MAIC analyses against aggregated study arms are generally considered inappropriate in the context of benefit assessments.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Jaypirca with the active ingredient pirtobrutinib.

Pirtobrutinib is approved for the treatment of adults with relapsed or refractory mantle cell lymphoma (MCL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor.

For this therapeutic indication, an individualised therapy with selection of bendamustine + rituximab, lenalidomide ± rituximab, R-CHOP, VRCAP, R-BAC, R-FCM, ibrutinib, temsirolimus, brexucabtagene autoleucel (only for patients with at least two prior therapies), venetoclax, high-dose therapy with allogeneic stem cell transplantation and high-dose therapy with autologous stem cell transplantation was determined as the appropriate comparator therapy.

The pharmaceutical company submitted the single-arm BRUIN study for the benefit assessment. Furthermore, the pharmaceutical company presented the result of a Matching-Adjusted Indirect Comparison (MAIC) analysis. The BRUIN study is unsuitable for the benefit assessment as it does not allow a comparison with the appropriate comparator therapy. MAIC analyses against aggregated study arms are generally considered inappropriate in the context of benefit assessments.

There are therefore no appropriate data for the benefit assessment.

An additional benefit of pirtobrutinib for the treatment of adults with relapsed or refractory MCL who have been previously treated with a BTK inhibitor 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 resolution is based on the information from the resolution on the benefit assessment of autologous anti-CD19-transduced CD3+ cells (resolution of 5 August 2021), which relates to patients after two or more systemic therapies. The number of patients derived by the pharmaceutical company in the dossier for the patient population from the second line of therapy onwards is assessed as underestimated overall due to the methodological procedure used to select the patient population. This could not be dispelled by the analyses submitted by the pharmaceutical company as part of the written statement procedure.

The number of patients identified in the resolution on the benefit assessment of autologous anti-CD19-transduced CD3+ cells is considered to be the better estimate, despite the different therapeutic indication with regard to the line of therapy as well as the existing uncertainties.

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 Jaypirca (active ingredient: pirtobrutinib) at the following publicly accessible link (last access: 16 April 2025):

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

Treatment with pirtobrutinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with mantle cell lymphoma.

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 will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 July 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 comorbidities) are not taken into account when calculating the annual treatment costs.

CAR-T cell therapies

Brexucabtagene autoleucel concerns 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 this active ingredient as the treatment option of the medicinal product to be assessed.

Brexucabtagene autoleucel is listed on LAUER-TAXE®, but is only dispensed to appropriate qualified inpatient treatment facilities, and administered there. Accordingly, the active ingredient is 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.

Brexucabtagene autoleucel is administered as a single intravenous infusion according to the requirements in the underlying product information.

Inpatient treatments

Some treatment options 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 2025 (€ 4,394.22). Furthermore, the nursing revenue is included in the inpatient costs. This is calculated from the average length of stay of the concerned DRG multiplied by the nursing fee according to Section 15 para. 2a KHEntgG (Act on Fees for Full and Semi-inpatient Hospital Services) (from 28 March 2024: € 250) and the treatment-specific nursing revenue valuation ratio.

High-dose chemotherapy for conditioning prior to autologous or allogeneic stem cell transplantation is included in the revenue from the diagnosis-related groups (DRG).

Treatment period:

Adults with relapsed or refractory mantle cell lymphoma who have who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Pirtobrutinib	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Brexucabtagene autoleucel (only for patients with at least two prior therapies)				
Brexucabtagene autoleucel	Single dose	1	1	1
High-dose chemotherapy with autologous stem cell transplantation				
Highly complex and intensive block chemotherapy	once		7.9 (average length of stay)	7.9
Stem cell collection from autologous donors with chemotherapy or with most severe complications or comorbidities (CC), age > 15 years	once		16.0 (average length of stay)	16.0
Autologous stem cell transfusion	once		22.3 (average length of stay)	22.3
High-dose chemotherapy with allogeneic stem cell transplantation				
Highly complex and intensive block chemotherapy	once		7.9 (average length of stay)	7.9
Allogeneic stem cell transfusion	once		33.6 (average length of stay)	33.6
Bendamustine + rituximab[11]				

[11] Rummel et al.; Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial. Lancet. 2013 Apr 6;381(9873):1203-10

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Bendamustine	1 x on day 1 and 2 of a 28-day cycle	6.0	2	12.0
Rituximab	1 x on day 1 of a 28-day cycle	6.0	1	6.0
Lenalidomide				
Lenalidomide	1 x on day 1-21 of a 28-day cycle	13.0	21	273
Lenalidomide + rituximab[12,13]				
Lenalidomide	1 x on day 1-21 of a 28-day cycle	12.0[13]	21	252
Rituximab	Cycle 1[12] 1 x on day 1, 8, 15, 22 of a 28-day cycle - Cycles 2-5[13] 1 x on day 1 of a 28-day cycle	1.0 – 5.0	1-4	4.0 – 8.0
R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)[14]				
Rituximab	Cycle 1–8: 1 x on day 0 of a 21-day cycle From cycle 9 onwards: 1 x every 56 days	11.5	1	11.5
Cyclophosphamide	1 x on day 1 of a 21-day cycle	8.0	1	8.0

12 Wang et al.; Lenalidomide in combination with rituximab for patients with relapsed or refractory mantle-cell lymphoma: a phase 1/2 clinical trial. Lancet Oncol. 2012 Jul;13(7):716-23

13 Leonard et al.; AUGMENT: A Phase III Study of Lenalidomide Plus Rituximab Versus Placebo Plus Rituximab in Relapsed or Refractory Indolent Lymphoma. J Clin Oncol. 2019 May 10;37(14):1188-1199

14 Annex VI to Section K of the Pharmaceuticals Directive (last revised: 07.05.2025)

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Doxorubicin	1 x on day 1 of a 21-day cycle	8.0	1	8.0
Vincristine	1 x on day 1 of a 21-day cycle	8.0	1	8.0
Prednisone	1 x on day 1-5 of a 21-day cycle	8.0	5	40.0
VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)[15,16]				
Bortezomib	4 x on day 1, 4, 8, 11 of a 21-day cycle	6.0 - 8.0	4	24.0 - 32.0
Rituximab	6-8 cycles: 1 x on day 0 of a 21-day cycle From cycle 7-9 onwards: 1 x every 56 days	10.3 - 11.5	1	10.3 - 11.5
Cyclophosphamide	1 x on day 1 of a 21-day cycle	6.0 - 8.0	1	6.0 - 8.0
Doxorubicin	1 x on day 1-5 of a 21-day cycle	6.0 - 8.0	5	30.0 - 40.0
Prednisone	1 x on day 1-5 of a 21-day cycle	6.0 - 8.0	5	30.0 - 40.0
R-BAC (rituximab + bendamustine + cytarabine)[17,18]				

15 Robak et al; LYM-3002 investigators. Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: final overall survival results of a randomised, open-label, phase 3 study. Lancet Oncol. 2018 Nov;19(11):1449-1458.

16 Fisher et al. Multicentre phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. J Clin Oncol. 2006 Oct 20;24(30):4867-74. doi: 10.1200/JCO.2006.07.9665. Epub 2006 Sep 25. PMID: 17001068.

17 McCulloch R et al. Efficacy of R-BAC in relapsed, refractory mantle cell lymphoma post BTK inhibitor therapy; Br J Haematol. 2020 May;189(4):684-688

18 Visco et al.; Combination of rituximab, bendamustine, and cytarabine for patients with mantle-cell non-Hodgkin lymphoma ineligible for intensive regimens or autologous transplantation. J Clin Oncol. 2013 Apr 10;31(11):1442-9

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Rituximab	Cycle 1: 1 x on day 1 of a 21-day cycle From cycle 2 onwards for cycles 4-6: 1 x on day 2 of a 21-day cycle From cycle 5-7 onwards: 1 x every 56 days	9.0 – 10.3	1	9.0 – 10.3
Bendamustine	2 x on day 2 and 3 of a 21-day cycle	4.0 – 6.0	2	8.0 – 12.0
Cytarabine	3 x on day 2, 3, 4 of a 21-day cycle	4.0 – 6.0	3	12.0 – 18.0
R-FCM (fludarabine + cyclophosphamide + mitoxantrone + rituximab)[14]				
Fludarabine	3 x on day 1, 2, 3 of a 28-day cycle	4.0	3	12.0
Cyclophosphamide	3 x on day 1, 2, 3 of a 28-day cycle	4.0	3	12.0
Mitoxantrone	1 x on day 1 of a 28-day cycle	4.0	1	4.0
Rituximab	1 x on day 0 of a 28-day cycle	4.0	1	4.0
Ibrutinib				
Ibrutinib	Continuously, 1 x daily	365	1	365
Temsirolimus				
Temsirolimus	Continuously, 1 x every 7 days	52.1	1	52.1

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Venetoclax[19]				
Venetoclax	Continuously, 1 x daily	365	1	365

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).[20]

Adults with relapsed or refractory mantle cell lymphoma who have who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor

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					
Pirtobrutinib	200 mg	200 mg	2 x 100 mg	365	730 x 100 mg
Appropriate comparator therapy					
Brexucabtagene autoleucel *(only for patients with at least two prior therapies)*					
Brexucabtagene autoleucel	1 - 2 x 10^6 viable CAR+ T cells/kg[21]	1 - 2 x 10^6/kg	1 single infusion bag	1	1 single infusion bag
Bendamustine + rituximab[11]					
Bendamustine	90 mg/m² = 171.9 mg	171.9 mg	1 x 100 mg + 3 x 25 mg	12.0	12 x 100 mg + 18 x 25 mg
Rituximab	375 mg/m²	716.3 mg	1 x 500 mg +	6.0	6 x 500 mg +

19 Eyre et al.; Efficacy of venetoclax monotherapy in patients with relapsed, refractory mantle cell lymphoma after Bruton tyrosine kinase inhibitor therapy. Haematologica. 2019 Feb;104(2): e68-e71

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

21 For patients over 100 kg, the maximum dose is 2 × 10^8 viable CAR+ T cells.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	= 716.3 mg		3 x 100 mg		36 x 100 mg
Lenalidomide					
Lenalidomide	20 mg	20 mg	1 x 20 mg	273.0	273 x 20 mg
Lenalidomide + rituximab[12,13]					
Lenalidomide	20 mg	20 mg	1 x 20 mg	252.0	252 x 20 mg
Rituximab	375 mg/m^2 = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	4.0 – 8.0	4 x 500 mg + 12 x 100 mg - 8 x 500 mg + 24 x 100 mg
R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)[14]					
Rituximab	375 mg/m^2 = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	11.5	11.5 x 500 mg + 34.5 x 100 mg
Cyclophosphamide	750 mg/m^2 = 1,432.5 mg	1,432.5 mg	1 x 2,000 mg	8.0	8.0 x 2,000 mg
Doxorubicin	50 mg/m^2 = 95.5 mg	95.5 mg	2 x 50 mg	8.0	16.0 x 50 mg
Vincristine	1.4 mg/m^2 = 2.7 mg	2.7 mg	2 x 2 mg	8.0	16.0 x 2 mg
Prednisone (PO)	100 mg	100 mg	2 x 50 mg	40.0	80.0 x 50 mg
VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)[15,16]					
Bortezomib	1.3 mg/m^2 = 2.5 mg	2.5 mg	1 x 2.5 mg	24.0 – 32.0	24.0 x 2.5 mg - 32.0 x 2.5 mg
Rituximab	750 mg/m^2 = 1,432.5 mg	1,432.5 mg	3 x 500 mg	10.3 – 11.5	30.9 x 500 mg - 34.5 x 500 mg
Cyclophosphamide	750 mg/m^2 = 1,432.5 mg	1,432.5 mg	1 x 2,000 mg	6.0 - 8.0	6.0 x 2,000 mg - 8.0 x 2,000 mg
Doxorubicin	50 mg/m^2 = 95.5 mg	95.5 mg	2 x 50 mg	6.0 - 8.0	12.0 x 50 mg - 16.0 x 50 mg
Prednisone (PO)	100 mg	100 mg	2 x 50 mg	30.0 - 40.0	60.0 x 50 mg -

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
					80.0 x 50 mg
R-BAC (rituximab + bendamustine + cytarabine)[17,18]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	9.0 – 10.3	9.0 x 500 mg + 27.0 x 100 mg - 10.3 x 500 mg + 30.9 x 100 mg
Bendamustine	70 mg/m² = 133.7 mg	133.7 mg	1 x 100 mg + 2 x 25 mg	8.0 – 12.0	8.0 x 100 mg + 16.0 x 25 mg - 12.0 x 100 mg + 24.0 x 25 mg
Cytarabine	800 mg/m² = 1,528 mg	1,528 mg	1 x 2,000 mg	12.0 – 18.0	12.0 x 2,000 mg - 18.0 x 2,000 mg
R-FCM (fludarabine + cyclophosphamide + mitoxantrone + rituximab)[14]					
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	4.0	4.0 x 500 mg + 12.0 x 100 mg
Fludarabine	25 mg/m² = 47.8 mg	47.8 mg	1 x 50 mg	12.0	12.0 x 50 mg
Cyclophosphamide	200 mg/m² = 382 mg	382 mg	1 x 500 mg	12.0	12.0 x 500 mg
Mitoxantrone	8 mg/m² = 15.3 mg	15.3 mg	1 x 20 mg	4.0	4 x 20 mg
Ibrutinib					
Ibrutinib	560 mg	560 mg	1 x 560 mg	365	365 x 560 mg
Temsirolimus					
Temsirolimus	Week 1 - 3: 175 mg From week 3: 75 mg	Week 1 - 3: 175 mg From week 3: 75 mg	Week 1 - 3: 18 x 30 mg From week 3: 3 x 30 mg	52.1	165.3 x 30 mg
Venetoclax[19]					
Venetoclax	Week 1: 20 mg	Week 1: 20 mg	Week 1: 2 x 10 mg	365	14 x 10 mg +

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	Week 2: 50 mg Week 3: 100 mg Week 4: 200 mg Week 5: 400 mg Week 6: 800 mg From week 7: 1,200 mg	Week 2: 50 mg Week 3: 100 mg Week 4: 200 mg Week 5: 400 mg Week 6: 800 mg From week 7: 1,200 mg	Week 2: 1 x 50 mg Week 3: 1 x 100 mg Week 4: 2 x 100 mg Week 5: 4 x 100 mg Week 6: 8 x 100 mg From week 7: 12 x 100 mg		7 x 50 mg + 3,981 x 100 mg

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	7.9	1.061	€ 4,394.22	0.7864	€ 250	€ 4,662.27	€ 1,553.14	€ 6,215.41
2025	A04E	33.6	9.004	€ 4,394.22	1.7706	€ 250	€ 39,565.56	€ 14,873.04	€ 54,438.60
High-dose chemotherapy with autologous stem cell transplantation									
2025	R61G	7.9	1.061	€ 4,394.22	0.7864	€ 250	€ 4,662.27	€ 1,553.14	€ 6,215.41
2025	A42A	16.1	2.095	€ 4,394.22	0.7016	€ 250	€ 9,205.89	€ 2,823.94	€ 12,029.83
2025	A15C	22.3	4.918	€ 4,394.22	1.2007	€ 250	€ 21,610.77	€ 6,693.90	€ 28,304.67

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
Pirtobrutinib 100 mg	168 FCT	€ 34,990.11	€ 1.77	€ 1,995.00	€ 32,993.34

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 therapy					
Brexucabtagene autoleucel	1 single infusion bag	€ 271,000.00		€ 0[22]	€ 271,000.00
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	€ 1,620.96	€ 1.77	€ 204.07	€ 1,415.12
Bendamustine 100 mg	1 PIC	€ 331.03	€ 1.77	€ 40.46	€ 288.80
Bendamustine 25 mg	1 PIC	€ 99.39	€ 1.77	€ 11.15	€ 86.47
Bortezomib 2.5 mg	1 PSI	€ 185.37	€ 1.77	€ 8.26	€ 175.34
Cyclophosphamide 2,000 mg	1 CII	€ 70.38	€ 1.77	€ 2.80	€ 65.81
Cyclophosphamide 500 mg	1 CII	€ 26.19	€ 1.77	€ 0.71	€ 23.71
Cytarabine 2,000 mg	1 IIS	€ 77.06	€ 1.77	€ 3.12	€ 72.17
Doxorubicin 50 mg[23]	1 INF	€ 151.26	€ 1.77	€ 11.07	€ 138.42
Fludarabine 50 mg	5 CII	€ 550.85	€ 1.77	€ 25.60	€ 523.48
Fludarabine 50 mg	1 CII	€ 118.54	€ 1.77	€ 5.09	€ 111.68
Ibrutinib 560 mg	28 FCT	€ 7,670.29	€ 1.77	€ 0.00	€ 7,668.52
Lenalidomide 20 mg[23]	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Mitoxantrone 20 mg	1 CIS	€ 235.57	€ 1.77	€ 10.64	€ 223.16
Prednisone 50 mg[23]	50 TAB	€ 68.06	€ 1.77	€ 4.49	€ 61.80
Prednisone 50 mg[23]	10 TAB	€ 23.19	€ 1.77	€ 0.94	€ 20.48
Rituximab 500 mg[14]	1 CIS	€ 1,777.34	€ 1.77	€ 84.18	€ 1,691.39
Rituximab 100 mg[14]	2 CIS	€ 717.21	€ 1.77	€ 33.50	€ 681.94
Rituximab 500 mg	1 CIS	€ 1,777.34	€ 1.77	€ 98.21	€ 1,677.36
Rituximab 100 mg	2 CIS	€ 717.21	€ 1.77	€ 39.08	€ 676.36
Temsirolimus 30 mg	1 CIS	€ 1,435.77	€ 1.77	€ 78.87	€ 1,355.13
Venetoclax 10 mg	14 FCT	€ 86.99	€ 1.77	€ 0.00	€ 85.22
Venetoclax 50 mg	7 FCT	€ 200.49	€ 1.77	€ 0.00	€ 198.72

[22] The medicinal product is exempt from value added tax at the applied LAUER-TAXE® last revised.
[23] Fixed reimbursement rate

Venetoclax 100 mg	360	FCT	€ 18,921.18	€ 1.77	€ 0.00	€ 18,919.41
Vincristine 2 mg	1	SFI	€ 37.66	€ 1.77	€ 1.25	€ 34.64
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SII = solution for injection/infusion; SFI = solution for injection; CII = concentrate for injection or infusion solution; PIF = powder for the preparation of an infusion solution; PSI = powder for solution for injection; PIC = powder for the preparation of an infusion solution concentrate; TAB = tablets						

LAUER-TAXE® last revised: 15 July 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.

CAR-T cell therapy

Antipyretic and antihistamine premedication is only recommended in the product information for brexucabtagene autoleucel.

Conditioning chemotherapy for lymphocyte depletion under CAR-T cell therapy

Brexucabtagene autoleucel 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 brexucabtagene autoleucel, 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.

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 brexucabtagene autoleucel. 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. [24]

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
Appropriate comparator therapy							
Brexucabtagene autoleucel							
Screening for HBV, HCV and HIV							
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
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
Conditioning chemotherapy for lymphocyte depletion							
Cyclophosphamide 500 mg/m² = 955 mg	2 CII each 500 mg	€ 550.85	€ 1.77	€ 25.60	€ 523.48	3.0	€ 1570.44
Fludarabine 30 mg/m² = 57.3 mg	1 KII at 50 mg	€ 118.54	€ 1.77	€ 5.09	€ 111.68	3.0	€ 670.08
Lenalidomide, rituximab							
Screening for HBV							
HBV test	-	-	-	-	€ 5.06	1.0	€ 5.06

[24] 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].

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
Abbreviations: CII = concentrate for injection or infusion solution; PSI = powder for solution for injection							

LAUER-TAXE® last revised: 15 July 2025

Other SHI services:

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.

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 designate 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 have 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 have 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
- 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 have 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.

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:

Adults with relapsed or refractory mantle cell lymphoma who have who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor

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.

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 27 July 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 26 September 2023.

On 12 February 2025, the pharmaceutical company submitted a dossier for the benefit assessment of pirtobrutinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 2 in conjunction with Nos. 3 and 4 of the resolution of 1 August 2024 on the application in accordance with Section 35a, paragraph 5b SGB V (pirtobrutinib).

By letter dated 13 February 2025 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 pirtobrutinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 12 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 15 May 2025. The deadline for submitting statements was 5 June 2025.

The oral hearing was held on 23 June 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 29 July 2025, and the proposed draft resolution was approved.

At their session on 7 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	27 July 2021	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	26 September 2023	New determination of the appropriate comparator therapy
Working group Section 35a	17 June 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	23 June 2025	Conduct of the oral hearing
Working group Section 35a	2 July 2025 16 July 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	29 July 2025	Concluding discussion of the draft resolution
Plenum	7 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 August 2025

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

Prof. Hecken