Gemeinsamer Bundesausschuss

Justification

to 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
Acalabrutinib (new therapeutic indication: mantle cell lymphoma, no prior BTKI therapy, relapsed or refractory, monotherapy)

of 18 December 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. requirement 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 pass a resolution 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 active ingredient acalabrutinib (Calquence) was listed for the first time on 1 December 2020 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 14 February 2025, the pharmaceutical company submitted an application for postponement of the date for the start of the benefit assessment procedure for acalabrutinib in the therapeutic indication "Monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) not previously treated with a BTK inhibitor" in accordance with Section 35a paragraph 5b SGB V.

The pharmaceutical company expected extensions of the marketing authorisation for the active ingredient acalabrutinib within the period specified in Section 35a paragraph 5b SGB V for multiple therapeutic indications at different times.

At their session on 3 April 2025, the G-BA approved the application pursuant to Section 35a paragraph 5b SGB V and postponed the relevant date for the start of the benefit assessment

and the submission of a dossier for the benefit assessment for the therapeutic indication in question to four weeks after the marketing authorisation of the other therapeutic indication of the therapeutic indication covered by the application, at the latest six months after the first relevant date. The marketing authorisation for the other therapeutic indication covered by the application according to Section 35a paragraph 5b SGB V was granted within the 6-month period.

On 2 May 2025, acalabrutinib received the extension of the marketing authorisation for the therapeutic indication "Monotherapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma not previously treated with a BTK inhibitor" and "In combination with bendamustine and rituximab (BR) for the treatment of adult patients with previously untreated mantle cell lymphoma who are not eligible for autologous stem cell transplant". The extension of the marketing authorisation for the therapeutic indication "In combination with venetoclax with or without obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL)" was granted on 2 June 2025. The mentioned extensions of the marketing authorisation are classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 27 June 2025, the pharmaceutical company submitted a dossier in due time in accordance with Section 4, paragraph 3, No. 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 of the G-BA (VerfO) for the active ingredient acalabrutinib with the therapeutic indication "Calquence as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) not previously treated with a BTK inhibitor".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 October 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 acalabrutinib 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 acalabrutinib.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made 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 Acalabrutinib (Calquence) in accordance with the product information

Calquence as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) not previously treated with a BTK inhibitor.

Therapeutic indication of the resolution (resolution of 18 December 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 not received pretreatment with a BTK inhibitor

Appropriate comparator therapy for acalabrutinib as monotherapy:

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) and
- ibrutinib

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 they determine 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. The following approved active ingredients are available for the treatment of relapsed or refractory mantle cell lymphoma not previously treated with a BTK inhibitor: Ibrutinib, lenalidomide and temsirolimus.

Mantle cell lymphoma is a type of B-cell non-Hodgkin lymphoma. Bendamustine, carmustine, chlorambucil, cyclophosphamide, cytarabine, doxorubicin, trofosfamide, prednisone, prednisolone, vinblastine, vincristine, bleomycin, etoposide, ifosfamide, mitoxantrone, methotrexate and dexamethasone are also approved for the treatment of B-cell non-Hodgkin lymphomas.

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:

- 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"). A written statement from the German Society for Haematology and Medical Oncology (DGHO) is 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 patients with relapsed or refractory mantle cell lymphoma who have not received pretreatment with 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 can be considered as the therapy standard for all patients in the present therapeutic indication.[2,3,4]

For adults with relapsed or refractory mantle cell lymphoma not previously treated with a Bruton's tyrosine kinase (BTK) inhibitor, the active ingredients ibrutinib, temsirolimus and lenalidomide as monotherapy 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.

The available guidelines and the statement by the clinical experts recommend, among others, the use of BTK inhibitors for patients with relapsed or refractory mantle cell lymphoma not previously treated with a BTK inhibitor. In Germany, ibrutinib is available for the present treatment setting.

By G-BA's resolution of 21 July 2016, an indication of a considerable additional benefit of ibrutinib compared to temsirolimus was found in adults with relapsed or refractory

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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; 2025. (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.

mantle cell lymphoma. Temsirolimus is therefore not determined to be a therapy option of the appropriate comparator therapy.

The joint written statement by the German Society for Haematology and Medical Oncology (DGHO) and German Lymphoma Alliance (GLA) indicates that other therapy options still assume significance in the present therapeutic indication.

No clear therapy recommendation on lenalidomide as monotherapy can be derived from the available guidelines and further literature. However, lenalidomide monotherapy is considered as a therapy option in the German healthcare context.[5]

According to the available evidence, a repeat immunochemotherapy in the form of R-FCM, R-CHOP or R-bendamustine may be indicated for adults with a late relapse after prior therapy. 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 who are covered by this therapeutic indication and have not received pretreatment with 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 available guidelines 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]
- VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)[7,8]
- R-BAC (rituximab + bendamustine + cytarabine)[9]

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.

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5 Onkopedia guideline of the DGHO, Mantle cell lymphoma, last revised June 2023, https://www.onkopedia.com/de/onkopedia/guidelines/mantelzell-lymphom/

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.

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.

9 Visco C 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;31(11):1442–9.

In accordance with the generally recognised state of medical knowledge, it is to 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).

In summary, an individualised therapy with selection of the aforementioned therapy options is determined as the appropriate comparator therapy. The treatment decision is made in particular taking into account the previous therapy, the response and the duration of remission of the previous therapies and the general condition.

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 acalabrutinib is assessed as follows:

Adults with relapsed or refractory mantle cell lymphoma who have not received pretreatment with a BTK inhibitor

An additional benefit is not proven.

Justification:

No relevant studies for comparison with the appropriate comparator therapy could be identified by the pharmaceutical company to demonstrate the additional benefit of acalabrutinib as monotherapy for the treatment of adults with relapsed or refractory mantle cell lymphoma who have not received pretreatment with a BTK inhibitor.

For reasons of clinical relevance, the pharmaceutical company presented the results of the uncontrolled approval study ACE-LY-004 in the dossier.

ACE-LY-004 study

The ACE-LY-004 study is a single-arm, completed phase II study that was conducted in North America, Europe and Australia between 2 March 2015 and 4 December 2020. 124 adults with relapsed and refractory mantle cell lymphoma who had received between one and five prior therapies were enrolled in the study. Patients must not have previously received therapy with a B-cell receptor inhibitor (BTK, PI3K or SYK inhibitor) or a BCL-2 inhibitor. The evaluations of the final data cut-off from 4 December 2020 were presented in the dossier.

Conclusion:

Due to its single-arm study design, the ACE-LY-004 study does not allow a comparison with the appropriate comparator therapy and is therefore unsuitable for the assessment of the additional benefit of acalabrutinib as monotherapy. An additional benefit of acalabrutinib as

monotherapy for the treatment of adults with relapsed or refractory mantle cell lymphoma who have not received pretreatment with a BTK inhibitor is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient acalabrutinib.

The therapeutic indication assessed here is as follows: Calquence as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) not previously treated with a BTK inhibitor.

The G-BA determined the appropriate comparator therapy to be an individualised therapy with selection of various rituximab-containing immunochemotherapies, lenalidomide (with or without rituximab) and ibrutinib as monotherapy.

The pharmaceutical company presented the ACE-LY-004 study for the benefit assessment.

Due to its single-arm study design, the ACE-LY-004 study does not allow a comparison with the appropriate comparator therapy and is therefore unsuitable for the assessment of the additional benefit of acalabrutinib as monotherapy. An additional benefit of acalabrutinib as monotherapy for the treatment of adults with relapsed or refractory mantle cell lymphoma who have not received pretreatment 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 patient numbers stated by the pharmaceutical company in the written statement procedure. The patient number determined by the pharmaceutical company is subject to uncertainties.

The main uncertainties result from presumably missing progression events in the data to determine the patients receiving at least one second line of therapy and the limited observation period of the data. The data relates exclusively to the period from 2020 to 2023. Furthermore, the use of BTK inhibitors in the first line of therapy has increased in recent years, which means that a decreasing percentage of patients in the second line of therapy not previously treated with a BTK inhibitor can be expected.

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 Calquence (active ingredient: acalabrutinib) at the following publicly accessible link (last access: 12 November 2025):

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

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

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 October 2025).

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

The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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.

Treatment period:

Adults with relapsed or refractory mantle cell lymphoma who have not received pretreatment with a 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				
Acalabrutinib	Continuously, 2 x daily	365	1	365
Appropriate comparator therapy				
Individualised therapy with selection of				
Bendamustine + rituximab[10,11]				
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 From cycle 8 (if applicable, maintenance):	6.0 3.0	1	9.0

[10] 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

[11] Rummel et al.; Two years Rituximab maintenance vs. observation after first line treatment with bendamustine plus rituximab (B-R) in patients with marginal zone lymphoma (MZL): results of a prospective, randomized, multicenter phase 2 study (the StiL NHL7-2008 MAINTAIN trial); Meeting Abstract: 2018 ASCO Annual Meeting I; https://ascopubs.org/doi/10.1200/JCO.2018.36.15_suppl.7515

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	1 x every 56 days			
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]	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	8.0	1	8.0
	From cycle 9 onwards: if applicable, maintenance every 56 days	3.5	1	3.5
Cyclophosphamide	1 x on day 1 of a 21-day cycle	8.0	1	8.0
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

[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: 29 August 2025)

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Prednisone	1 x on day 1-5 of a 21-day cycle	8.0	5	40.0
VR-CAP (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	1 x on day 0 of a 21-day cycle	6.0 - 8.0	1	6.0 - 8.0
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 of a 21-day cycle	6.0 - 8.0	1	6.0 - 8.0
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]				
Rituximab	Cycle 1: 1 x on day 1 of a 28-day cycle	Cycle 1: 1.0	Cycle 1: 4	Cycle 1: 4
	From cycle 2 for cycles 4-6: 1 x on day 2 of a 28-day cycle[18]	Cycle 2 - 5: 4.0	Cycle 2 - 5: 1	Cycle 2 - 5: 4.0
Bendamustine	2 x on day 2 and 3[18] or day	4.0 – 6.0	2	8.0 – 12.0

[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. Multicenter 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
	1 and 2[17] of a 28-day cycle			
Cytarabine	3 x on day 2, 3, 4[18] or day 1, 2 and 3[17] of a 28-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

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).[19]

Adults with relapsed or refractory mantle cell lymphoma who have received at least one prior therapy with a Bruton's tyrosine kinase (BTK) inhibitor

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

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					
Acalabrutinib	100 mg	200 mg	2 x 100 mg	365	730 x 100 mg
Appropriate comparator therapy					
Individualised therapy with selection of					
Bendamustine + rituximab [10,11]					
Bendamustine	90 mg/m² = 171.9 mg	171.9 mg	1 x 100 mg + 3 x 25 mg	12.0	12 x 100 mg + 36 x 25 mg
Rituximab	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	6.0 – 9.0	6 x 500 mg + 18 x 100 mg - 9.0 x 500 mg + 27 x 100 mg
Lenalidomide					
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Lenalidomide + rituximab [12,13]					
Lenalidomide	20 mg	20 mg	1 x 20 mg	252.0	252 x 20 mg
Rituximab	375 mg/m² = 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/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	8.0	8 x 500 mg + 24 x 100 mg
				11.5	11.5 x 500 mg + 34.5 x 100 mg
Cyclophosphamide	750 mg/m² = 1,432.5 mg	1,432.5 mg	1 x 2,000 mg	8.0	8.0 x 2,000 mg
Doxorubicin	50 mg/m² = 95.5 mg	95.5 mg	1 x 100 mg	8.0	8.0 x 100 mg
Vincristine	1.4 mg/m² = 2.7 mg (max. 2 mg)[14]	2.0 mg	1 x 2 mg	8.0	8.0 x 2 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
Prednisone (PO)	100 mg	100 mg	2 x 50 mg	40.0	80.0 x 50 mg
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone) [15,16]					
Bortezomib	1.3 mg/m² = 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	375 mg/m² = 716.3 mg	716.3 mg	1 x 500 mg + 3 x 100 mg	6.0 - 8.0	6.0 x 500 mg + 18.0 x 100 mg - 8.0 x 500 mg 24.0 x 100 mg
Cyclophosphamide	750 mg/m² = 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/m² = 95.5 mg	95.5 mg	1 x 100 mg	6.0 - 8.0	6.0 x 100 mg - 8.0 x 100 mg
Prednisone (PO)	100 mg/m² = 191.0 mg	191.0 mg	3 x 50 mg + 2 x 20 mg	30.0 - 40.0	90.0 x 50 mg + 60 x 20 mg - 120.0 x 50 mg + 80 x 20 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	4.0 – 6.0	4.0 x 500 mg + 12.0 x 100 mg - 6.0 x 500 mg + 18.0 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	500[17] mg/m² = 1,528 mg - 800[18] mg/m² = 1,528 mg	955 mg - 1,528 mg	1 x 1,000 mg - 1 x 2,000 mg	12.0 – 18.0	12.0 x 1,000 mg - 18.0 x 1,000 mg – 12.0 x 2,000 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
					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

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.

Costs of the medicinal products:

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
Medicinal product to be assessed					
Acalabrutinib 100 mg	60 FCT	€ 6,181.12	€ 1.77	€ 0.00	€ 6,179.35
Appropriate comparator therapy					
Bendamustine 100 mg	5 PIC	€ 1,653.78	€ 1.77	€ 208.35	€ 1,443.66
Bendamustine 100 mg	1 PIC	€ 337.73	€ 1.77	€ 41.31	€ 294.65
Bendamustine 25 mg	5 PIC	€ 422.90	€ 1.77	€ 52.08	€ 369.05
Bendamustine 25 mg	1 PIC	€ 101.23	€ 1.77	€ 11.38	€ 88.08
Bortezomib 2.5 g	1 PSI	€ 185.37	€ 1.77	€ 8.26	€ 175.34
Cyclophosphamide 2,000 mg	1 CII	€ 70.38	€ 1.77	€ 2.80	€ 65.81

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
Medicinal product to be assessed					
Acalabrutinib 100 mg	60 FCT	€ 6,181.12	€ 1.77	€ 0.00	€ 6,179.35
Appropriate comparator therapy					
Cyclophosphamide 500 mg	6 PSI	€ 85.98	€ 1.77	€ 9.45	€ 74.76
Cytarabine 2,000 mg	1 IIS	€ 77.06	€ 1.77	€ 3.12	€ 72.17
Cytarabine 1,000 mg	1 IIS	€ 44.21	€ 1.77	€ 1.56	€ 40.88
Doxorubicin 100 mg[20]	1 CIS	€ 285.79	€ 1.77	€ 21.71	€ 262.31
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 25 mg[20]	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Lenalidomide 20 mg[20]	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[20]	50 TAB	€ 68.06	€ 1.77	€ 4.49	€ 61.80
Prednisone 50 mg[20]	10 TAB	€ 23.19	€ 1.77	€ 0.94	€ 20.48
Prednisone 20 mg[20]	100 TAB	€ 29.29	€ 1.77	€ 1.42	€ 26.10
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
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
Vincristine 2 mg	1 VIA	€ 39.04	€ 1.77	€ 2.23	€ 35.04
Abbreviations: VIA = vial; FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SII = solution for injection/infusion; CII = concentrate for injection or 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 October 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

[20] Fixed reimbursement rate

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.

The calculation of the additionally required SHI services is based on packs in distribution with the LAUER-TAXE® last revised on 15 September 2025 and fee structure items (FSI) - last revised in the 3rd quarter of 2025 - of the uniform value scale (UVS 2025/Q3).

Premedication with an analgesic/ antipyretic and an antihistamine should always be administered prior to each application of rituximab. The costs of this premedication cannot be quantified as there is no dosage information that allows cost representation.

Screening for hepatitis B virus (HBV)

Patients should be tested for hepatitis B infection prior to starting treatment.

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.[21]

The costs of HBV testing are not presented as there is no regular difference between the medicinal product to be assessed and the appropriate comparator therapy.

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.

[21] 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].

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 not received pretreatment with a 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.

References:
Product information for acalabrutinib (Calquence); Calquence® 100 mg film-coated tablets; last revised: July 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 26 November 2024, 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 8 April 2025.

On 27 June 2025 the pharmaceutical company submitted a dossier for the benefit assessment of acalabrutinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 1 July 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits 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 acalabrutinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 September 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 October 2025. The deadline for submitting statements was 22 October 2025.

The oral hearing was held on 10 November 2025.

By letter dated 11 November 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 27 November 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 9 December 2025, and the proposed draft resolution was approved.

At their session on 18 December 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	26 November 2024	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	4 April 2025	New determination of the appropriate comparator therapy
Working group Section 35a	5 November 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 November 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	19 November 2025 3 December 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	9 December 2025	Concluding discussion of the draft resolution
Plenum	18 December 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 18 December 2025

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

Prof. Hecken