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
Asciminib (reassessment of an orphan drug > EUR 30 million turnover limit: chronic myeloid leukaemia, Ph+, after ≥ 2 prior therapies)

of 20 November 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 asciminib (Scemblix) was listed for the first time on 25 August 2022 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. Scemblix for the treatment of chronic myeloid leukaemia is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

At their session on 16 March 2023, the G-BA decided on the benefit assessment of asciminib in the therapeutic indication "Scemblix is indicated for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors." according to Section 35a SGB V.

If the sales of the orphan drug through the statutory health insurance at pharmacy sales prices and outside the scope of SHI-accredited medical care, including value-added tax, exceed an

amount of € 30 million in the last twelve calendar months, the pharmaceutical company must submit evidence in accordance with Chapter 5 Section 5, paragraphs 1 to 6 Rules of Procedure (VerfO) within three months of being requested to do so by the Federal Joint Committee, and must demonstrate the additional benefit compared to the appropriate comparator therapy in this evidence.

By letter dated 18 February 2025, the pharmaceutical company was requested to submit a dossier for the benefit assessment according to Section 35a SGB V by 1 June 2025, due to exceeding the € 30 million turnover limit within the period from January 2024 to December 2024. The pharmaceutical company submitted the final dossier in due time to the G-BA in accordance with Section 4, paragraph 3, number 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 6 VerfO on 26 May 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 September 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 asciminib compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA 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 asciminib.

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:

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

2.1.1 Approved therapeutic indication of Asciminib (Scemblix) in accordance with the product information

Scemblix is indicated for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors.

Therapeutic indication of the resolution (resolution of 20 November 2025):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors

Appropriate comparator therapy for asciminib:

Individualised therapy with selection of

- nilotinib,
- dasatinib,
- bosutinib and
- ponatinib

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.

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

On 1. The cytotoxic chemotherapies busulfan, cyclophosphamide, hydroxycarbamide, mitoxantrone and vindesine as well as the tyrosine kinase inhibitors bosutinib, ponatinib, dasatinib, imatinib und nilotinib are approved for the present therapeutic indication.

On 2. In principle, allogeneic stem cell transplantation is considered as non-medicinal treatment in the therapeutic indication for patients receiving pretreatment with tyrosine kinase inhibitors. For this therapeutic indication, it is assumed that patients are initially treated with BCR-ABL-TKIs as part of a remission-inducing therapy. Allogeneic stem cell transplantation can only be considered for some patients once they have achieved remission, and is therefore not part of the appropriate comparator therapy.

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

- Asciminib (resolution of 16 March 2023)
- Ponatinib (resolution of 20 November 2020)
- Bosutinib (resolution of 21 February 2019)

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic 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) as well as the AkdÄ is available.

According to the guidelines listed in the evidence synopsis and taking into account the authorisation status of the medicinal products, patients with Philadelphia chromosome-positive chronic myeloid leukaemia in the chronic phase (Ph+ CML-CP) who have already been treated with at least two TKIs can be treated with an alternative TKI or allogeneic stem cell transplantation, depending on the previous therapy, comorbidities and mutational status of the patients. In this regard, the TKIs nilotinib, dasatinib, imatinib, bosutinib and ponatinib are currently being considered. Once remission has been achieved, allogeneic stem cell transplantation may be considered for some patients. Allogeneic stem cell transplantation is not determined as a

component of the present appropriate comparator therapy since it is assumed with regard to the present therapeutic indication that the primary therapeutic goal is initially to achieve remission and that allogeneic stem cell transplantation is only considered for some of the patients who have achieved remission.

Patients with CP-CML who receive second-generation TKIs in the first and second lines of treatment and have to discontinue them due to toxicity can also switch to imatinib in the third line of treatment. However, it is to be assumed that this only affects very few patients in the therapeutic indication in the healthcare. Therefore, imatinib assumes minor significance in the present treatment setting and is not considered a treatment option in the appropriate comparator therapy for patients pretreated with at least two TKIs.

The available evidence shows that no treatment option that is considered for the entire patient population in the present therapeutic indication can be derived on the basis of the individual criteria. The treatment decision is made taking into account previous therapies as well as comorbidities and mutational status.

Therefore, the G-BA determine the appropriate comparator therapy to be an individualised therapy with selection of nilotinib, dasatinib, bosutinib and ponatinib, taking into account previous therapies, comorbidities and mutational status.

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

When making the treatment decision, in particular the previous therapies, comorbidities and the mutational status must be considered, taking into account the available evidence.

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 asciminib is assessed as follows:

a) Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors

a1) Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom bosutinib is the appropriate individualised therapy

Indication of a minor additional benefit.

a2) Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom nilotinib, dasatinib or ponatinib is the appropriate individualised therapy

An additional benefit is not proven.

Justification:

For the benefit assessment, the pharmaceutical company submitted the results of the ASCEMBL study. This is a completed, multicentre, open-label RCT comparing asciminib with bosutinib.

Adult patients with chronic myeloid leukaemia (CML) in the chronic phase who had previously been treated with two or more TKIs were enrolled. The prerequisite for enrolment in the study was therapy failure or intolerance to the last TKI therapy administered.

Between 26 October 2017 and 4 December 2024, a total of 233 patients in 87 study sites in 25 countries in Asia, Europe, North and South America and Australia were enrolled in the ASCEMBL study and randomly assigned in a 2:1 ratio to treatment with asciminib (N = 157) or bosutinib (N = 76).

A total of five data cut-offs from the ASCEMBL study are available:

- 25.05.2020: analysis of the primary endpoint after 24 weeks of treatment
- 06.01.2021: required by the EMA, after 48 weeks of treatment,
- 06.10.2021: after 96 weeks of treatment
- 22.03.2023: 30 days after the end of the study treatment
- 04.12.2024: final analysis of overall survival and progression-free survival 5 years after the last patient has received the first dose of study medication

For the benefit assessment, the evaluations of the data cut-off from 22 March 2023, 30 days after the end of study treatment, and the final data cut-off from 4 December 2024 were submitted.

On the implementation of the individualised therapy

An individualised therapy with selection of nilotinib, dasatinib, bosutinib and ponatinib was determined as the appropriate comparator therapy. The pharmaceutical company presented the results of the ASCEMBL study comparing asciminib with bosutinib.

Since the appropriate comparator therapy includes other therapy options in addition to bosutinib, the ASCEMBL study does not allow any statements to be made on the additional benefit for patients, for whom a therapy other than bosutinib (nilotinib, dasatinib and ponatinib) is the appropriate individualised therapy.

Against this background, the G-BA consider it appropriate to divide the patient population accordingly and to make the statement on additional benefit separately for patients, for whom bosutinib is the appropriate individualised therapy (patient group a1), and patients, for whom nilotinib, dasatinib and ponatinib represent the appropriate individualised therapy (patient group a2).

<u>Extent and probability of the additional benefit</u>

a1) <u>Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom bosutinib is the appropriate individualised therapy</u>

Mortality

Overall survival is defined in the ASCEMBL study as the period between randomisation and death from any cause.
For the overall survival endpoint, there was no statistically significant difference between the treatment arms.

Morbidity

Progression to the blast phase

In the ASCEMBL study, blast phase was operationalised as a percentage of ≥ 30% blasts in the blood or bone marrow. For the endpoints on progression to the blast phase, there was no statistically significant difference.

Symptomatology and health status

For the endpoints of symptom severity and impairment of daily life due to symptoms, both assessed using MDASI-CML, there were statistically significant differences to the advantage of asciminib over bosutinib.

For the endpoint of impairment of everyday life, there was an effect modification by the sex characteristic. In this regard, there was a statistically significant difference to the advantage of asciminib only in the subgroup of women. The result for the total population was used for the assessment.

For the endpoints on symptomatology, assessed using PGIC, as well as health status, assessed using EQ-5D VAS, there were no statistically significant differences between the treatment arms.

Activity impairment (WPAI-CML question 6)

Results on question 6 of the WPAI-CML questionnaire are available. Question 6 of the WPAI-CML was assigned to the morbidity category. However, the WPAI-CML was not used for assessment as the MDASI-CML (impairment of daily life due to symptoms) adequately covers the patients' activity impairment.

Overall, there was an advantage of asciminib over bosutinib in the morbidity endpoint category.

Quality of life

Endpoints on health-related quality of life were not assessed in the study.

Side effects

Adverse events (AEs) in total

In the ASCEMBL study, almost all randomised patients experienced at least one adverse event. The results are only presented additionally.

Serious adverse events (SAEs), severe AEs (CTCAE grade ≥ 3)

For the endpoints of serious adverse events (SAEs) and severe AEs (CTCAE grade ≥ 3), there was a statistically significant difference between the treatment arms to the advantage of asciminib in each case.

Therapy discontinuation due to AEs

For the endpoint of discontinuation due to side effects, there was a statistically significant difference to the advantage of asciminib over bosutinib.

Specific adverse events

In detail, there were advantages for the severe AEs of respiratory, thoracic and mediastinal disorders, gastrointestinal disorders, skin and subcutaneous tissue disorders, alanine aminotransferase elevated and aspartate aminotransferase elevated.
In the severe AE of thrombocytopenia, there was a statistically significant difference to the disadvantage of asciminib.

Overall assessment/ conclusion

The ASCEMBL RCT, which compared asciminib with bosutinib, was presented for the assessment of the additional benefit of asciminib for the treatment of adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors. The study is suitable for the assessment of the additional benefit for patients in the therapeutic indication, for whom bosutinib is the appropriate individualised therapy. Results on mortality, morbidity and side effects are available.

The results for the overall survival endpoint showed no statistically significant difference between the treatment groups.

For the endpoints of progression to blast phase, symptomatology (assessed using PGIC) and health status (assessed using EQ-5D VAS) in the morbidity endpoint category, there were no statistically significant differences between the treatment groups. There were advantages - rated as moderate - in the endpoints of symptom severity and impairment of daily life due to symptoms (assessed using MDASI-CML).

For serious adverse events (SAEs), severe adverse events (severe AEs) and discontinuation due to adverse events in the endpoint category of side effects, an advantage of asciminib was observed. In detail, there were advantages for the severe AEs of respiratory, thoracic and mediastinal disorders, gastrointestinal disorders, skin and subcutaneous tissue disorders, alanine aminotransferase elevated and aspartate aminotransferase elevated, as well as a disadvantage for the endpoint of thrombocytopenia (severe AEs). Overall, the results for side effects are considered as significant improvement.

In a weighted decision, the G-BA came to the overall conclusion that there was a minor additional benefit of asciminib over bosutinib for the treatment of adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, and for whom bosutinib is the appropriate individualised therapy.

Reliability of data (probability of additional benefit)

The present assessment is based on the results of the open-label, randomised, multicentre phase III ASCEMBL study.

The risk of bias at study level is rated as high due to the open-label study design.

The risk of bias for the results on patient-reported endpoints (PGIC, MDASI-CML, EQ-5D VAS) and for the results on the endpoint of discontinuation due to AEs is also rated as high due to the open-label study design.

The reliability of data for the endpoint of discontinuation due to AEs is additionally limited by the fact that premature therapy discontinuation can also occur for reasons other than AEs. These reasons represent a competing event for the assessed endpoint of discontinuation due to AEs.

Since the results for the further endpoints on side effects, from which the additional benefit is largely derived, predominantly show high significance, an indication of an additional benefit can be derived overall on the available data basis despite the limitations described.

a2) Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom nilotinib, dasatinib or ponatinib is the appropriate individualised therapy

No data were presented for comparison with nilotinib, dasatinib or ponatinib.

An additional benefit of asciminib over the appropriate comparator therapy for the treatment of adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom nilotinib, dasatinib or ponatinib is the appropriate individualised therapy, was not proven.

2.1.4 Summary of the assessment

The present assessment is the new benefit assessment of the active ingredient asciminib due to the exceeding of the € 30 million turnover limit.

Asciminib was approved as an orphan drug for the treatment of adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors.

The appropriate comparator therapy was determined to be the individualised therapy with selection of nilotinib, dasatinib, bosutinib and ponatinib, taking into account previous therapies as well as comorbidities and mutational status.

For the benefit assessment, the pharmaceutical company submitted the results of the ASCEMBL study.

The G-BA conducted a separate assessment of the additional benefit depending on the appropriate individualised therapy:

a1) Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom bosutinib is the appropriate individualised therapy

The data from the ASCEMBL study submitted by the pharmaceutical company are used for patients, for whom bosutinib is the appropriate individualised therapy.

The results for the overall survival endpoint showed no statistically significant difference between the treatment groups.

For the endpoints of progression to blast phase, symptomatology and health status in the morbidity endpoint category, there were no statistically significant differences. For the endpoints of symptom severity and impairment of daily life due to symptoms (assessed using MDASI-CML), there were statistically significant differences - assessed as moderate - to the advantage of asciminib over bosutinib.

For serious adverse events (SAEs), severe adverse events (severe AEs) and discontinuation due to adverse events in the endpoint category of side effects, an advantage of asciminib was observed. In detail, there were advantages and one disadvantage for specific AEs. Overall, the results for side effects are considered as significant improvement.

Overall, a minor additional benefit was identified.

The reliability of data of the additional benefit identified is classified in the "indication" category.

a2) Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors, for whom nilotinib, dasatinib or ponatinib is the appropriate individualised therapy

No data are available from the ASCEMBL study for patients, for whom nilotinib, dasatinib or ponatinib is the appropriate individualised therapy. The additional benefit is therefore not proven for this sub-population.

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 provided by the pharmaceutical company. Uncertainties exist in particular for the following reasons:

- When calculating the prevalence, it cannot be ruled out that some patients were included solely on the basis of secondary diagnoses.
- When calculating the percentage of patients with ≥ 2 prior TKI therapies, additional patients may be eligible for this therapeutic indication.

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 Scemblix (active ingredient: asciminib) at the following publicly accessible link (last access: 07 August 2025):

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

Treatment with asciminib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with chronic myeloid leukaemia.

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 September 2025). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

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 to adults (average body height: 1.72 m; average body weight: 77.7 kg). This results in a BSA of 1.91 m² (calculated according to Du Bois 1916)[2].

Treatment period:

Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Asciminib	Continuously 2 x daily	730	1	365
Appropriate comparator therapy				
Nilotinib	Continuously 2 x daily	730	1	365
Dasatinib	Continuously 1 x daily	365	1	365
Bosutinib	Continuously 1 x daily	365	1	365
Ponatinib	Continuously 1 x daily	365	1	365

Consumption:

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

Adults with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors

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					
Asciminib	40 mg	80 mg	2 x 40 mg	365	730 x 40 mg
Appropriate comparator therapy					
Nilotinib	400 mg	800 mg	4 x 200 mg	365	1,460 x 200 mg
Dasatinib	100 mg	100 mg	1 x 100 mg	365	365 x 100 mg
Bosutinib	500 mg	500 mg	1 x 500 mg	365	365 x 500 mg
Ponatinib	45 mg	45 mg	1 x 45 mg	365	365 x 45 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.

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					
Asciminib 40 mg	180 FCT	€ 15,780.78	€ 1.77	€ 897.95	€ 14,881.06
Appropriate comparator therapy					
Bosutinib 500 mg	28 FCT	€ 1,979.55	€ 1.77	€ 94.08	€ 1,883.70
Dasatinib 100 mg	30 FCT	€ 822.56	€ 1.77	€ 38.50	€ 782.29
Nilotinib 200 mg	112 HC	€ 3,857.33	€ 1.77	€ 186.00	€ 3,669.56
Ponatinib 45 mg	30 FCT	€ 6,694.06	€ 1.77	€ 379.01	€ 6,313.28
Abbreviations: FCT = film-coated tablets; HC = hard capsules					

LAUER-TAXE® last revised: 15 September 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.

Because there are no 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, no costs for additionally required SHI services had to be taken into account.

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 Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:

Product information for asciminib (Scemblix); Scemblix 20 mg film-coated tablets, Scemblix 40 mg film-coated tablets; last revised: 3 September 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 11 February 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 26 May 2025 the pharmaceutical company submitted a dossier for the benefit assessment of asciminib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 6 VerfO.

By letter dated 28 May 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 asciminib.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 August 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 September 2025. The deadline for submitting statements was 22 September 2025.

The oral hearing was held on 6 October 2025.

By letter dated 7 October 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 31 October 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 11 November 2025, and the proposed draft resolution was approved.

At their session on 20 November 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 February 2025	Determination of the appropriate comparator therapy
Working group Section 35a	1 October 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	6 October 2025	Conduct of the oral hearing commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	15 October 2025 5 November 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 November 2025	Concluding discussion of the draft resolution
Plenum	20 November 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 November 2025

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

Prof. Hecken