Gemeinsamer Bundesausschuss

Justification

for 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
Avapritinib
(reassessment of an orphan drug after exceeding the EUR 30 million turnover limit: advanced systemic mastocytosis, after at least 1 prior therapy)

of 16 April 2026

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1. Legal basis

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

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

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

According to Section 35a paragraph 3 SGB V, the G-BA decide 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 avapritinib (Ayvakyt) was listed for the first time on 1 November 2020 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. Ayvakyt for the treatment of advanced systemic mastocytosis is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999.

At their session on 15 September 2022, the G-BA decided on the benefit assessment of avapritinib in the therapeutic indication:

"Monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy" 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 in this evidence, must demonstrate the additional benefit compared to the appropriate comparator therapy.

By letter dated 16 July 2025, the pharmaceutical company was requested to submit a dossier for the benefit assessment according to Section 35a SGB V by 1 November 2025, due to exceeding the EUR 30 million turnover limit. Pursuant to Section 4, paragraph 3, No. 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 8, Paragraph 1, No. 6 Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 30 October 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 February 2026 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 avapritinib compared to 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 avapritinib.

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:

2.1.1 Approved therapeutic indication of Avapritinib (Ayvakyt) in accordance with the product information

Ayvakyt is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy.

Therapeutic indication of the resolution (resolution of 16.04.2026):

See the approved therapeutic indication.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy

Appropriate comparator therapy for avapritinib as monotherapy:

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Individualised therapy with selection of

- Midostaurin,
- cladribine (only for subjects who have been pretreated with midostaurin) and
- imatinib (only for subjects pretreated with midostaurin, without KIT D816V mutation or with unknown KIT mutational status and for subjects pretreated with midostaurin, with existing eosinophilia with FIP1L1-PDGFRA fusion gene).

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 according to 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. Apart from avapritinib, the active ingredient midostaurin is approved in this therapeutic indication.

On 2. In principle, implementation of allogeneic stem cell transplantation is a non-medicinal treatment option in this therapeutic indication. When determining the appropriate comparator therapy, it was however assumed that allogeneic stem cell transplantation was not an option at the time of treatment with avapritinib.

On 3. Annex VI to Section K of the Pharmaceuticals Directive - Prescribability of approved medicinal products in unapproved therapeutic indications (so-called off-label use); Part A:

- IV. Disodium cromoglycate (DNCG)-containing medicinal products (oral) for systemic mastocytosis

Annex I to Section F of the Pharmaceuticals Directive Statutory exclusions from prescription in the supply of medicinal products and approved exceptions; approved exceptions to the statutory exclusion from prescription pursuant to Section 34, paragraph 1, sentence 2 SGB V (OTC overview):

- 15. Disodium cromoglycate (DNCG)-containing medicinal products (oral) only for the symptomatic treatment of systemic mastocytosis

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

- Midostaurin: Resolution of 02.05.2024

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"). In this regard, an opinion passed by the German Society for Haematology and Medical Oncology (DGHO) (hereinafter: scientific-medical society) is available.

Overall, the evidence on treatment options in this therapeutic indication is extremely limited. No methodologically sound reviews or guidelines could be identified during the systematic search. Consequently, the National Comprehensive Cancer Network (NCCN) guideline was additionally used.

When determining the appropriate comparator therapy, it is assumed that cytoreductive therapy is indicated for patients in this therapeutic indication. In this context, the NCCN guideline recommends the active ingredients midostaurin and avapritinib as the preferred options. The scientific-medical society also mention avapritinib and, for midostaurin naïve patients, midostaurin as the standard second-line therapy.

In the benefit assessment, it was determined in the reassessment of midostaurin as an orphan drug after exceeding the EUR 30 million turnover limit by resolution of 02.05.2024 that an additional benefit of midostaurin is not proven as no suitable data were available to enable an assessment of the additional benefit.

Avapritinib is approved for patients after at least one systemic therapy. In contrast, the marketing authorisation for midostaurin also covers initial treatment. In addition to midostaurin and avapritinib, the NCCN guideline also recommends the active ingredients cladribine, peginterferon alfa-2a +/- prednisone and imatinib, which are not approved for this therapeutic indication. The latter only for subjects without KIT D816V mutation or with unknown KIT mutational status and for subjects with existing eosinophilia with FIP1L1-PDGFRA fusion gene.

According to the guideline, peginterferon alfa-2a +/- prednisone is a treatment option only for patients with slowly progressive disease. Against this background, peginterferon alfa-2a +/- prednisone assumes secondary significance in this therapeutic indication.

Avapritinib is therefore the only approved active ingredient in the subsequent therapy for patients, who have initially been pretreated with midostaurin, with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL).

According to Section 6, paragraph 2, sentence 2 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. In this regard, it should be considered in the current treatment setting (after at least one systemic therapy) that midostaurin has already been administered to a significant extent during the initial treatment. Since avapritinib itself is therefore not considered as an appropriate comparator therapy for patients who have initially been pretreated with midostaurin, but in the present case we are dealing with advanced forms of mastocytosis for which cytoreductive treatment is indicated, it is necessary to consider unapproved therapy options for the determination of the appropriate comparator therapy. According to the generally recognised state of medical knowledge in the therapeutic indication to be assessed, the off-label use is considered to be the therapy standard as it would be without avapritinib (Section 6, paragraph 2, sentence 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV)).

In the overall assessment, the G-BA therefore determine individualised treatment with selection of cladribine, midostaurin and imatinib as the appropriate comparator therapy. For the reasons mentioned above and given the absence of the marketing

authorisation, cladribine and imatinib are an option only for specific sub-populations (details in brackets).

The treatment decision is made, in particular, taking into account the KIT mutational status and prior therapy.

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

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

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

An additional benefit is not proven.

Justification:

In the dossier, the pharmaceutical company did not identify any studies for direct comparison of avapritinib with the appropriate comparator therapy. They presented the two single-arm PATHFINDER and EXPLORER studies, and stated their intention to use the PATHFINDER study for the assessment of the additional therapeutic benefit. The pharmaceutical company did not derive an additional benefit compared with the appropriate comparator therapy. They additionally presented the results of the single-arm EXPLORER study, as well as the pooled results from the PATHFINDER and EXPLORER studies.

PATHFINDER study

The PATHFINDER study is an open-label, multicentre, single-arm phase II study of avapritinib for the treatment of adults with advanced systemic mastocytosis. Patients with ASM, SM-AHN or MCL were enrolled in this study in accordance with the criteria of the World Health Organization (WHO). The population was divided into 2 cohorts: One cohort of patients with ASM or SM-AHN without C-findings and another cohort of patients with ASM or SM-AHN and ≥ 1 C-finding or with MCL regardless of C-findings (in each case according to the modified International Working Group - Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis criteria).

The primary endpoint of the study was the overall response rate. Secondary endpoints were endpoints in the categories of mortality, morbidity, health-related quality of life and side effects.

In the dossier, the pharmaceutical company presented results from the final data cut-off from 13.03.2025 for a sub-population of patients (n = 67) who received prior systemic therapy and a dose of avapritinib in accordance with the product information.

EXPLORER study

The EXPLORER study is an open-label, multicentre, single-arm phase I study of avapritinib for the treatment of adult patients with advanced systemic mastocytosis, comprising a dose escalation phase (Part 1) and an extension phase (Part 2). Adult patients with ASM, SM-AHN, MCL or a relapsed or refractory myeloid malignancy were enrolled in the study in accordance with the WHO criteria. All patients (N = 86) received avapritinib.

The primary endpoints of the study were the maximum tolerated dose, the recommended phase II dose, and side effects. Secondary endpoints were endpoints in the categories of mortality, morbidity and health-related quality of life.

In the dossier, the pharmaceutical company presented data at the final data cut-off from 19.01.2023 on a sub-population of patients (n = 12) who received prior systemic therapy and a dose of avapritinib in accordance with the product information.

Conclusion

The single-arm PATHFINDER and EXPLORER studies presented by the pharmaceutical company do not allow for a comparison with the appropriate comparator therapy. No data are therefore available to allow an assessment of the additional benefit. An additional benefit of avapritinib for the treatment of adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy, is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is a new benefit assessment of the medicinal product Ayvakyt with the active ingredient avapritinib due to exceeding the EUR 30 million turnover limit. Ayvakyt was approved as an orphan drug. The therapeutic indication assessed here is as follows:

"Ayvakyt is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy."

The appropriate comparator therapy was determined to be individualised therapy with selection of midostaurin, cladribine (only for subjects pretreated with midostaurin) and imatinib (only for subjects pretreated with midostaurin, without KIT D816V mutation, or with unknown KIT mutational status, as well as for subjects pretreated with midostaurin, with existing eosinophilia, with the FIP1L1-PDGFRA fusion gene).

In the dossier, the pharmaceutical company presented the two single-arm PATHFINDER and EXPLORER studies, and stated their intention to use the PATHFINDER study for the assessment of the additional therapeutic benefit. The pharmaceutical company did not derive an additional benefit compared with the appropriate comparator therapy. They additionally presented the results of the single-arm EXPLORER study, as well as the pooled results from the PATHFINDER and EXPLORER studies.

The single-arm studies presented by the pharmaceutical company do not allow for a comparison with the appropriate comparator therapy. No data are therefore available to allow an assessment of the additional benefit. An additional benefit of avapritinib 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 G-BA base their resolution on the patient numbers indicated by the pharmaceutical company in the dossier, which are based on a more recent data basis compared with the initial assessment of avapritinib in this therapeutic indication. The pharmaceutical company’s approach to determining patient numbers is mostly plausible. Although individual steps in the

calculation are subject to uncertainty, it is generally assumed that the number of patients in the SHI target population is likely to fall within the specified range.

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 Ayvakyt (active ingredient: avapritinib) at the following publicly accessible link (last access: 10 March 2026):

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

Treatment with avapritinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of aggressive systemic mastocytosis, systemic mastocytosis with an associated haematological neoplasm or mast cell leukaemia.

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency (EMA) will assess new information on this medicinal product at least annually and update the product information where necessary.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 February 2026).

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

For the cost representation, one year is assumed for all medicinal products. The (daily) doses recommended in the product information or in the labelled publications were used as the basis for calculation.

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

There are no marketing authorisations for cladribine and imatinib for this therapeutic indication. The G-BA use the therapy protocols from the recommendations of the German Society for Haematology and Medical Oncology (DGHO) as the basis for cost calculation in the context of the off-label use of this therapy.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Avapritinib	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Midostaurin	Continuously, 2 x daily	730	1	365
Cladribine	On day 1 – 5 of a 28-day cycle	13	5	65
Imatinib	Continuously, 1 x daily	365	1	365

Consumption:

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were used as a basis (average body weight of adults: 77.7 kg).[2]

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					
Avapritinib	200 mg	200 mg	1 x 200 mg	365	365 x 200 mg
Appropriate comparator therapy					
Midostaurin	100 mg	200 mg	8 x 25 mg	365	2,920 x 25 mg
Cladribine	0.14 mg/kg	10.78 mg	2 x 10 mg	65	130 x 10 mg
Imatinib	400 mg	400 mg	1 x 400 mg	365	365 x 400 mg

[2] Federal Health Reporting. Average body measurements of the population (2021), www.gbe bund.de

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					
Avapritinib 200 mg	30 FCT	€ 20,241.35	€ 1.77	€ 1,155.39	€ 19,084.19
appropriate comparator therapy					
Midostaurin 25 mg	112 SC	€ 14,424.69	€ 1.77	€ 820.51	€ 13,602.41
Cladribine 10 mg	5 SFI	€ 2,006.52	€ 1.77	€ 254.40	€ 1,750.35
Imatinib 400 mg[3]	90 FCT	€ 538.33	€ 1.77	€ 41.68	€ 494.88
Abbreviations: FCT = film-coated tablets; SFI = solution for injection; SC = soft capsules					

LAUER-TAXE® last revised: 15 February 2026

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.

[3] Fixed reimbursement rate

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 data from the product 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 statutory 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 aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy

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 approved in monotherapy.

3. Bureaucratic costs calculation

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

4. Process sequence

At their session on 27 May 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 30 October 2025, the pharmaceutical company submitted a dossier for the benefit assessment of avapritinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 6 VerfO.

By letter dated 3 November 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 avapritinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 January 2026, and the written statement procedure was initiated with publication on the G-BA website on 2 February 2026. The deadline for submitting written statements was 23 February 2026.

The oral hearing took place on 9 March 2026.

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 were discussed at the Subcommittee's session on 8 April 2026, and the draft resolution was approved.

At its session on 16 April 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	27 May 2025	Determination of the appropriate comparator therapy
Working group Section 35a	4 March 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	9 March 2026	Conduct of the oral hearing

Working group Section 35a	18 March 2026 1 April 2026	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	8 April 2026	Concluding discussion of the draft resolution
Plenum	16 April 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 16 April 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken