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 (gastrointestinal stromal tumours))

of 16 April 2026

Contents

1. Legal basis

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

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

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

According to Section 35a paragraph 3 SGB V, the G-BA 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 gastrointestinal stromal tumours 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 21 April 2021, the G-BA decided on the benefit assessment of avapritinib in the therapeutic indication "Monotherapy for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation" 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 EUR 30 million turnover limit within the period from April 2024 to March 2025. Pursuant to Section 4, paragraph 3, No. 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 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 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

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 unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation.

Therapeutic indication of the resolution (resolution of 16 April 2026):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

Adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation

Appropriate comparator therapy for avapritinib as monotherapy:

- Best supportive care

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: For the present therapeutic indication, apart from avapritinib, no other therapy options are approved for the treatment of patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation.

The following active ingredients are also available for the treatment of patients with unresectable or metastatic GIST: Imatinib, sunitinib and ripretinib.

Furthermore, the active ingredient regorafenib is approved for this therapeutic indication, but is not available on the German market.

On 2. Non-medicinal treatment is not considered. This does not affect the use of resection and/or locally destructive procedures as palliative, patient-individual therapy options.

On 3. There is the following resolution of the G-BA on the use of medicinal products:

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

- Ripretinib, resolution of 16 June 2022
- Regorafenib: Resolution of 19 February 2015

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 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 current S3 Guideline on Soft Tissue Sarcomas recommends treatment with avapritinib for patients with metastatic or unresectable GIST harbouring a D842V mutation in the PDGFRA gene. According to the guideline, all tyrosine kinase inhibitors currently approved for the treatment of metastatic or unresectable GIST are ineffective in this type of mutation.

Overall, treatment with avapritinib therefore represents the therapy standard for patients with metastatic or unresectable GIST harbouring a D842V mutation in the PDGFRA gene.

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. For the benefit assessment according to Section 35a SGB V, a comparison with the assessed active ingredient itself, specifically a comparison of identical therapies, is thus ruled out - here: Avapritinib as monotherapy - with regard to the research question of the benefit assessment.

In summary, apart from avapritinib, no therapy standard for antineoplastic therapy has been established for the treatment of patients harbouring a D842V mutation in the PDGFRA gene. Taking into account the current stage of the disease, the appropriate comparator therapy is determined to be best supportive care (BSC).

Best supportive care (BSC) is defined as the therapy that provides the best possible, patient-individually optimised, supportive treatment to alleviate symptoms and improve quality of life.

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 is assessed as follows:

Adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation

An additional benefit is not proven.

Justification:

The pharmaceutical company did not identify any relevant studies, comparing avapritinib with the appropriate comparator therapy, to demonstrate the additional benefit of avapritinib as monotherapy in patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation. As the best available evidence, the pharmaceutical company presented the results of the label-enabling, single-arm NAVIGATOR study as well as data from the non-randomised CS3007-101 study (a Chinese bridge study for the NAVIGATOR study) in the dossier. It should also be noted that, when presenting the results, the pharmaceutical company refers, for comparison purposes, to the results of the data from the VOYAGER study, which were already presented in the initial assessment dossier as well as data of a propensity score (PS)-adjusted indirect comparison with the NAVIGATOR and BLU-285-1002 studies, and the retrospective study by Cassier et al., 2012[2]. Notwithstanding the fact that the data submitted for the comparison of individual arms from various studies were not processed in the present procedure, the pharmaceutical company did not explain to what extent the comparator

[2] Cassier PA, Fumagalli E, Rutkowski P et al. Outcome of patients with platelet-derived growth factor receptor alpha-mutated gastrointestinal stromal tumors in the tyrosine kinase inhibitor era. Clin Cancer Res 2012; 18(16): 4458-4464. https://doi.org/10.1158/1078-0432.CCR-11-3025

therapies used in these studies correspond to best supportive care. Overall, these analyses are unsuitable for the assessment of the additional benefit of avapritinib.

NAVIGATOR study

The NAVIGATOR study is a single-arm, multicentre phase I study of avapritinib, comprising a dose escalation phase (Part 1) and an extension phase (Part 2).

Adult patients with unresectable GIST or other advanced solid tumours were enrolled in the dose escalation phase. Patients with unresectable GIST must have previously been treated with at least 2 of the tyrosine kinase inhibitors specified in the study's inclusion criteria, including imatinib, and must have shown disease progression. Alternatively, the patients had to have a substitution mutation at position 842 from aspartic acid to valine (D842V) in the PDGFRA gene.

In the extension phase, adult patients with unresectable GIST were enrolled in 3 groups, which differed in terms of prior therapy and disease progression or the presence of the PDGFRA D842V mutation. The primary endpoints of the extension phase are the overall response rate and adverse events. Other secondary endpoints include endpoints in the categories of mortality and morbidity.

For the benefit assessment, the pharmaceutical company takes into account the sub-population of patients from the extension phase whose tumours harbour a PDGFRA D842V mutation and who have received a daily dose of 300 mg avapritinib in accordance with the requirements in the product information (n = 28).

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

CS3007-101 study

The CS3007-101 study is a non-randomised phase I/II study of avapritinib, which was conducted exclusively in China. The study consists of a dose escalation phase (Part 1) and an extension phase (Part 2). In the dose escalation phase, patients with unresectable or metastatic GIST, whose disease had progressed following treatment with imatinib and at least another tyrosine kinase inhibitor, or who were intolerant to standard therapy, or whose tumours harboured the PDGFRA D842V mutation, were enrolled.

In the extension phase, adult patients with unresectable GIST were enrolled into 2 groups, based on the presence of the PDGFRA D842 mutation and the line of therapy. The primary endpoint of the extension phase is the overall response rate. Other secondary endpoints include endpoints in the categories of mortality, morbidity, and side effects.

For the benefit assessment, the pharmaceutical company considers the sub-population of patients from both phases of the study whose tumours harbour a PDGFRA D842V mutation and who have received a daily dose of 300 mg of avapritinib (n = 28). In the absence of separate data for this sub-population, the pharmaceutical company reported the data for all patients who have received a daily dose of 300 mg avapritinib from both parts of the study (n = 59).

Due to its single-arm study design, the CS3007-101 study presented additionally by the pharmaceutical company did not allow a comparison with the appropriate comparator therapy.

Conclusion

The single-arm NAVIGATOR and CS3007-101 studies presented by the pharmaceutical company do not allow for comparison with the appropriate comparator therapy and are therefore unsuitable for the assessment of the additional benefit of avapritinib as monotherapy. The results of the data from the VOYAGER study, which were already presented in the initial assessment dossier and presented for comparison purposes in the presentation of findings, as well as data of a propensity score (PS)-adjusted indirect comparison with the NAVIGATOR and BLU-285-1002 studies, and the retrospective study by Cassier et al., 2012, were not processed in the present procedure and are therefore unsuitable for the assessment of the additional benefit.

Overall, no suitable data are therefore available for the assessment of the additional benefit of avapritinib. An additional benefit of avapritinib for patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation compared with the appropriate comparator 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 unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation."

The G-BA determined the appropriate comparator therapy to be best supportive care.

For the benefit assessment, the pharmaceutical company presented the results of the single-arm NAVIGATOR study as well as the CS3007-101 study. When presenting the results, the pharmaceutical company also refer, for comparison purposes, to the results of the data from the VOYAGER study, which were already presented in the initial assessment dossier, as well as data of a propensity score (PS)-adjusted indirect comparison with the NAVIGATOR and BLU-285-1002 studies, and the retrospective study by Cassier et al., 2012, which were however not processed in the present procedure and are therefore unsuitable for the assessment of the additional benefit.

Due to their single-arm design, the presented NAVIGATOR and CS3007-101 studies do not allow for comparison with the appropriate comparator therapy and are therefore unsuitable for the assessment of the additional benefit of avapritinib as monotherapy.

Overall, no suitable data are therefore available for the assessment of the additional benefit of avapritinib. An additional benefit of avapritinib for patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation compared with the appropriate comparator therapy 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 from the dossier submitted by the pharmaceutical company. The range of the SHI target population stated by the pharmaceutical company is plausible in terms of magnitude.

The difference in the number of patients in the SHI target population compared with the initial assessment of avapritinib in the present therapeutic indication is primarily due to the different GIST incidence figures reported. Given the Germany-specific incidence rate, the pharmaceutical company's current figure for the number of patients in the SHI target population should be given preference.

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: 16 December 2025):

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 patients with gastrointestinal stromal tumours as well as specialists in internal medicine and gastroenterology, and other specialists from other specialist groups participating in the Oncology Agreement.

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The EMA will assess new information on this medicinal product at least annually and update the product information as 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.

Treatment period:

Adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation

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	1 x daily, continuously	356	1.0	356
Best supportive care	Different from patient to patient			
Appropriate comparator therapy				
Best supportive care	Different from patient to patient			

Consumption:

Adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation

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	300 mg	300 mg	1 x 300 mg	365	365 x 300 mg
Best supportive care	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of

the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation

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 300 mg	30 FCT	€ 20,241.35	€ 1.77	€ 1,155.39	€ 19,084.19
Best supportive care	Not calculable				
Appropriate comparator therapy					
Best supportive care	Not calculable				
Abbreviations: FCT = film-coated tablets					

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.

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-apply unit are to be payable. These additional other costs are not added

to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

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

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

Basic principles of the assessed medicinal product

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

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

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

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

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

indication are specifically named.

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

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include 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:

Adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation

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 25 June 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. At their session on 28 October 2025, the Subcommittee on Medicinal Products newly 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 31 October 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 27 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	24 March 2020	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	28 October 2025	New 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