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
Nirogacestat (progressing desmoid tumour)

of 2 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.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit of an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, Nos. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seqq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. In accordance with Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company shall provide evidence - within three months of being requested to do so by the G-BA - in accordance with Chapter 5 Section 5, paragraphs 1 to 6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy specified by the G-BA in accordance with Chapter 5 Section 6 VerfO, and in this evidence, demonstrate the additional benefit over the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decide whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation, the G-BA modified the procedure for the benefit assessment of orphan drugs at their session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determine an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at their session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover limit according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a paragraph 2 SGB V, the assessment by the G-BA 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 relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient nirogacestat on 15 October 2025 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO). Pursuant to Section 4, paragraph 3, No. 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, No. 1 Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 13 October 2025.

Nirogacestat for the treatment of adult patients with progressing desmoid 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.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the approval studies by the G-BA.

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 15 January 2026 together with the IQWiG assessment 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 adopted their resolution on the basis of the pharmaceutical company's dossier, the dossier assessment carried out by the G-BA, the IQWiG assessment of treatment costs and patient numbers (IQWiG G25-29) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA have assessed the studies relevant to the marketing authorisation on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7, sentence 1, numbers 1 to 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of nirogacestat.

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

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Nirogacestat (Ogsiveo) in accordance with the product information

Ogsiveo as monotherapy is indicated for the treatment of adult patients with progressing desmoid tumours who require systemic treatment.

Therapeutic indication of the resolution (resolution of 2 April 2026):

See the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

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

Adults with progressing desmoid tumours who require systemic treatment

Hint for a minor additional benefit

Justification:

The pharmaceutical company submitted the results of the DeFi study for the benefit assessment of nirogacestat for the treatment of adult patients with progressing desmoid tumours who require systemic treatment.

The DeFi study is a randomised, multicentre, double-blind, controlled phase III study comparing nirogacestat with placebo. Following the double-blind phase, patients were able to move on to the open-label phase.

The study that commenced in May 2019 was completed in October 2024. It was conducted at 52 study sites across 7 countries (North America and Europe).

Adults with progressing desmoid tumours who had shown a tumour progression ≥ 20% according to RECIST v1.1 within 12 months prior to the screening visit were enrolled in the study.

The 142 patients enrolled in the study were randomised in a 1:1 ratio to the nirogacestat arm (N = 72) and the placebo arm (N = 70). It was stratified according to target tumour localisation (intra-abdominal vs extra-abdominal).

In addition to the primary endpoint of progression-free survival, endpoints in the categories of mortality, morbidity, health-related quality of life and side effects were collected.

For the DeFi study, data from the final data cut-off of the double-blind phase on 07.04.2022 is available, with the data cut-off being used for the benefit assessment.

Mortality

Deaths

For the mortality endpoint, deaths from any cause were continuously recorded as part of the side effects. Overall survival in the DeFi study was operationalised as the time from randomisation to death.

There was one death in the placebo arm.

For mortality, there was no significant difference.

Morbidity

Progression-free survival

In the DeFi study, progression-free survival (PFS) was defined as the time from randomisation to the date of finding radiograpic progression or death, whichever occurred first, based on the time of the imaging documentation of disease progression in accordance with the RECIST (Response Evaluation Criteria in Solid Tumours, version 1.1) criteria.

The fifth amendment to the protocol (09.02.2021) added clinical progression to radiographic progression. The onset or deterioration of symptoms that led to an overall deterioration in health status, thus resulting in the discontinuation of the study treatment and the initiation of subsequent therapy, was classified as progression. However, specific criteria that the investigators should use to definitively determine this clinical progression were not detailed. Furthermore, it is unclear to what extent all subjects were assessed for clinical progression, as the amendment was introduced approximately 21 months after the first subject was enrolled.

The present PFS endpoint is a composite endpoint consisting of endpoints from the mortality and morbidity categories. The mortality endpoint component is already assessed via the overall survival endpoint as an independent endpoint. The morbidity component of disease progression is assessed according to RECIST criteria, on the one hand, and thus by means of imaging procedures. On the other, disease progression was assessed as clinical progression; however, its present operationalisation and the associated significance remain unclear.

Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient relevance of the PFS endpoint.

The overall statement on the extent of the additional benefit remains unaffected.

Tumour volume, presented additionally

The endpoint of change in tumour volume was pre-specified as a secondary endpoint for the Defi study and was later changed to an exploratory endpoint. The endpoint was operationalised as the change in volume of the largest target tumour compared with baseline, as measured by volumetric MRI. The Defi study showed a reduction in tumour volume by cycle 7 with nirogacestat compared with placebo.

In this disease, the tumours are visible in isolated areas. However, in terms of patient-relevant benefit, the focus here is not so much on the change in tumour volume per se, but on clinical changes, particularly functional improvements and pain relief. This is also evident from the relevant statements made by clinical experts. A change in tumour volume alone is not patient-relevant per se. The results for the endpoint of change in tumour volume were only presented additionally.

Symptomatology

GODDESS-DTSS/-DTIS

The GOunder/DTRF Desmoid Symptom/Impact Scale (GODDESS) is a disease-specific tool developed for quantification of the symptoms of desmoid tumours and their impact on patients.

For the GODDESS-DTSS, the "weighted DTSS total score" and the "intra-abdominal symptoms" domain score were taken into account in the benefit assessment.

The responder analyses of time to first deterioration for the weighted DTSS total score show a statistically significant difference to the advantage of nirogacestat.

For the GODDESS-DTIS, the 3 domain scores "Physical functioning", "Sleep" and "Emotion" were taken into account. No analysis of the individual items "Body image", "Self-awareness" and "Everyday practical challenges" was available.

For the domain scores "Physical functioning" and "Sleep", the responder analysis of time to first deterioration showed a statistically significant difference between the two treatment arms in favour of nirogacestat.

In the subgroup analysis of physical functioning, an effect modification was observed for the "Tumour localisation" and "Any prior therapy" characteristics. In subjects with extra-abdominal symptom, there was an advantage of nirogacestat, whereas no difference was observed in those with intra-abdominal symptom. There was an advantage in subjects who had received any prior treatment, whereas no difference was observed in those who had not received any prior treatment. These effect modifications were not observed for other patient-relevant endpoints. These characteristics were not taken into account any further in the overall assessment.

Brief Pain Inventory Short Form (BPI-SF)

Pain was assessed in the DeFi study using the BPI-SF questionnaire. For the benefit assessment, the responder analyses operationalised as time to first deterioration on the two scales "Pain interference" and "Pain intensity" were taken into account.

A statistically significant difference in favour of nirogacestat was observed on the "Pain interference" subscale.

EORTC QLQ-C30

Symptomatology was assessed using the EORTC QLQ-C30 questionnaire. The time to first deterioration by ≥ 10 points was used for the benefit assessment.

The responder analysis showed a statistically significant disadvantage of nirogacestat on each of the symptom scales "Nausea and vomiting", "Appetite loss" and "Diarrhoea". A statistically significant advantage of nirogacestat was observed on the "Constipation" symptom scale.

Desmoid tumour-related disease symptoms (assessed using the PGIS)

For desmoid tumour-related disease symptoms assessed using the PGIS, there was a statistically significant difference between the treatment groups in favour of nirogacestat in terms of the time to first improvement.

General health status (assessed using the PGIC)

For health status assessed using the PGIC, there was a statistically significant difference to the advantage of nirogacestat.

The subgroup analysis showed an effect modification for the "Age" characteristic (< 35 years and ≥ 35 years). There was an advantage of nirogacestat in subjects < 35 years, whereas no difference was observed in subjects ≥ 35 years. This effect modification is not evident in other patient-relevant endpoints. This characteristic is not taken into account any further in the overall assessment.

In summary, in the morbidity endpoint category, there were positive effects with a partly significant extent on most of the endpoints assessed. It should however be noted that some symptoms were collected twice across several survey tools. The disadvantages observed on the symptom scales are also evident in the analyses of safety endpoints and may therefore reflect side effects of nirogacestat. In summary, an advantage of treatment with nirogacestat

in terms of morbidity can be identified, the extent of which is estimated to be a significant improvement overall.

Quality of life

EORTC QLQ-C30

Health-related quality of life was assessed using the EORTC QLQ-C30 questionnaire. The time to first deterioration by ≥ 10 points was used for the benefit assessment.

The responder analysis showed a statistically significant difference with an advantage of nirogacestat on the "Physical functioning" functional scale.

Overall, there was an advantage of treatment with nirogacestat in terms of health-related quality of life.

Side effects

Adverse events (AEs) in total

In the DeFi study, an AE occurred in almost all patients in the control arm and in all patients in the intervention arm. The results are only presented additionally.

Serious AEs (SAEs)

With regard to SAEs, there was no significant difference.

Severe AEs (CTCAE grade ≥ 3) and discontinuation due to AEs

For the endpoints of severe AEs and discontinuation due to AEs, there was a statistically significant disadvantage.

AE of special interest

Gastrointestinal disorders, diarrhoea

For the endpoints "Gastrointestinal disorders" and "Diarrhoea", there were statistically significant disadvantages.

In the overall analysis of the endpoints on side effects, treatment with nirogacestat showed negative effects. These are characterised by disadvantages in terms of severe AEs (CTCAE grade ≥ 3) and therapy discontinuation due to AEs. Detailed analysis also showed disadvantages for the endpoints "Gastrointestinal disorders" and "Diarrhoea".

Overall assessment

Results on mortality, morbidity, quality of life and side effects from the double-blind DeFi RCT, which compared nirogacestat with placebo, are available for the benefit assessment of nirogacestat for the treatment of patients with progressing desmoid tumours who require systemic therapy.

For mortality, there was no significant difference.

Morbidity was assessed using the GODDESS-DTSS, GODDESS-DTIS, BPI-SF, PGIC, PGIS and EORTC QLQ-C30 questionnaires. There were advantages in most of the morbidity endpoints assessed. It should however be noted that some symptoms were collected twice across several survey tools. The disadvantages observed on the symptom scales are also evident in the analyses of safety endpoints and may therefore reflect side effects of nirogacestat. Given the positive effects with a partly significant extent, an advantage of treatment with

nirogacestat in terms of morbidity can be identified, the extent of which is estimated to be a significant improvement overall.

Treatment with nirogacestat showed an advantage in physical functioning in terms of health-related quality of life.

In terms of side effects, severe AEs (CTCAE grade ≥ 3) and therapy discontinuation due to AEs occurred during treatment with nirogacestat. Detailed analysis showed disadvantages for the endpoints "Gastrointestinal disorders" and "Diarrhoea". Overall analysis of the endpoints on side effects showed a disadvantage.

Overall analysis of the available results on patient-relevant endpoints show partly significant advantages in the morbidity endpoint category, as well as an advantage in health-related quality of life. In contrast, there were disadvantages in terms of side effects. In a weighted decision on the extent of the additional benefit, the G-BA concluded a minor additional benefit of nirogacestat over placebo for the treatment of patients with progressing desmoid tumours who require systemic treatment.

A hint for a minor additional benefit of nirogacestat was identified for the treatment of patients with progressing desmoid tumours who require systemic treatment.

Significance of the evidence

The randomised, double-blind DeFi study forms the basis of the present benefit assessment.

Overall, the risk of bias at the study level is rated as low.

For the endpoint of overall survival, there is a low risk of bias.

The endpoint-specific risk of bias for the results of the patient-reported endpoints on morbidity and health-related quality of life is rated as high in each case due to the declining return rates of the questionnaires early on. Only the short- and medium-term effects of nirogacestat can therefore be assessed.

Furthermore, limited transferability of the results to the German healthcare context is assumed. The DeFi study involved a comparison with a placebo. As part of the written statement procedure, the scientific-medical societies state that patients are treated with multikinase inhibitors in the German healthcare context. In addition, the active ingredient sorafenib can be prescribed for off-label use since August 2024 for the treatment of adults with progressing desmoid tumours who have demonstrated disease progression and require treatment (see Annex VI to the Pharmaceuticals Directive).

In summary, the G-BA derive a hint for the identified additional benefit with regard to the significance.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Ogsiveo with the active ingredient nirogacestat.

Ogsiveo was approved as an orphan drug.

The active ingredient nirogacestat as monotherapy is indicated for the treatment of adult patients with progressing desmoid tumours who require systemic treatment.

Results on mortality, morbidity, quality of life and side effects from the DeFi RCT are available for the benefit assessment of nirogacestat.

For mortality, there was no significant difference.

Morbidity was assessed using the GODDESS-DTSS, GODDESS-DTIS, BPI-SF, PGIC, PGIS and EORTC QLQ-C30 questionnaires. There were advantages in most of the endpoints assessed. It should however be noted that some symptoms were collected twice across several survey tools. The disadvantages observed on the symptom scales are also evident in the analyses of safety endpoints and may therefore reflect side effects of nirogacestat. Given the positive effects with a partly significant extent, an advantage of treatment with nirogacestat in terms of morbidity can be identified, the extent of which is estimated to be a significant improvement overall.

There was an advantage in physical functioning in terms of health-related quality of life.

During treatment with nirogacestat, severe AEs (CTCAE grade ≥ 3), therapy discontinuation due to AEs and, in detail, AE of special interest occurred. A disadvantage was observed in terms of side effects.

Overall analysis of the available results on patient-relevant endpoints show partly significant advantages in the morbidity endpoint category, as well as an advantage in health-related quality of life. In contrast, there were disadvantages in terms of side effects. In a weighted decision on the extent of the additional benefit, the G-BA concluded a minor additional benefit of nirogacestat over placebo.

The significance of the evidence is classified in the hint category.

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 takes into account the patient numbers stated in the pharmaceutical company's dossier, which are, however, subject to uncertainty overall. There were methodological limitations and uncertainty regarding the percentages of desmoid tumours, which also relate exclusively to inpatients, under ICD-10 code D48.1. Furthermore, patients who had been ill for more than 5 years were not considered.

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 Ogsiveo (active ingredient: nirogacestat) at the following publicly accessible link (last access: 9 January 2026):

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

Therapy with nirogacestat should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with desmoid tumours and other doctors from other specialist groups participating in the Oncology Agreement.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide information material for medical professionals and patients (including patient identification card).

The information material contains, in particular, information and warnings of the potential risk of embryo-foetal toxicity.

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: 1 February 2026).

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

Treatment period:

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 different from patient to patient 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 the maximum treatment duration, if specified in the product information.

The annual treatment costs shown refer to the first year of treatment.

The (daily) doses recommended in the product information or in the labelled publications were used as the basis for calculation.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Nirogacestat	Continuously, 2 x daily	365.0	1	365.0

Consumption:

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.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Nirogacestat	150 mg	300 mg	2 x 150 mg	365.0	730 x 300 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:

Adults with progressing desmoid tumours who require systemic treatment

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					
Nirogacestat 150 mg	56 FCT	€ 21,213.56	€ 1.77	€ 1,208.22	€ 20,003.57
Abbreviations: FCT = film-coated tablets					

LAUER-TAXE® last revised: 1 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.

No additionally required SHI services are taken into account for the cost representation.

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 progressing desmoid tumours who require systemic treatment

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.

2.6 Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Ogsiveo is a medicinal product placed on the market from 1 January 2025. In accordance with Section 35a, paragraph 3, sentence 5 SGB V, the G-BA must determine whether a relevant percentage of the clinical studies on the medicinal product were conducted within the scope of SGB V. This is the case if the percentage of study participants who have participated in the clinical studies on the medicinal product to be assessed in the therapeutic indication to be assessed at study sites within the scope of SGB V is at least five per cent of the total number of study participants.

The calculation is based on all studies that were submitted as part of the benefit assessment dossier in the therapeutic indication to be assessed in accordance with Section 35a, paragraph 1, sentence 3 SGB V in conjunction with Section 4, paragraph 6 AM-NutzenV.

Approval studies include all studies submitted to the regulatory authority in section 2.7.3 (Summary of Clinical Efficacy) and 2.7.4 (Summary of Clinical Safety) of the authorisation dossier in the therapeutic indication for which marketing authorisation has been applied for. In addition, studies, which were conducted in whole or in part within the therapeutic indication described in this document, and in which the company was a sponsor or is otherwise financially involved, must also be indicated.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5% (4.3%) of the total number of study participants according to the information provided by the pharmaceutical company.

In the dossier, the pharmaceutical company provided information on a total of 3 studies in the present therapeutic indication, with a total percentage of 4.3% study participants at German study sites.

With regard to one of the studies (14-C-0007 study), it is uncertain whether the pharmaceutical company was involved in the study. In a comparison with the CTD, further studies, which were submitted to the regulatory authority for the assessment of the medicinal product's clinical efficacy and safety, were also identified.

Taking into account the studies for which data are already available, the percentage of study participants at study sites within the scope of SGB V is less than 5%.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant percentage within the scope of SGB V.

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

On 13 October 2025, the pharmaceutical company submitted a dossier for the benefit assessment of nirogacestat to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 15 January 2026 together with the IQWiG assessment of treatment costs and patient numbers on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 5 February 2026.

The oral hearing took place on 23 February 2026.

An amendment to the benefit assessment with a supplementary assessment was submitted on 13 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 was discussed at the Subcommittee's session on 24 March 2026, and the draft resolution was approved.

At their session on 2 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	13 January 2026	Information of the benefit assessment of the G-BA
Working group Section 35a	18 February 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	23 February 2026	Conduct of the oral hearing
Working group Section 35a	4 March 2026; 18 March 2026	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee on Medicinal Products	24 March 2026	Concluding discussion of the draft resolution
Plenum	2 April 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 2 April 2026

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

Prof. Hecken