Gemeinsamer Bundesausschuss

Justification

of 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 Sipavibart (COVID-19, pre-exposure prophylaxis, ≥ 12 years)

of 7 August 2025

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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.
7. Number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

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 decides 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 eligibility for reimbursement of prescription-only medicinal products for pre-exposure prophylaxis against COVID-19 for a restricted group of insured persons is based on Section 2 of the Ordinance on the Entitlement to Vaccination and Pre-Exposure Prophylaxis against COVID-19 (COVID-19 Prevention Ordinance).

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient sipavibart on 15 February 2025 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit

Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 1 VerfO on 13 February 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 May 2025 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of sipavibart compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of sipavibart.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have come to the following assessment:

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

2.1.1 Approved therapeutic indication of Sipavibart (Kavigale) in accordance with the product information

KAVIGALE is indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments.

Therapeutic indication of the resolution (resolution of 07.08.2025):

Pre-exposure prophylaxis of COVID-19 in adults and adolescents 12 years of age and older weighing at least 40 kg, who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments and are entitled to a supply of this medicinal product in accordance with Section 2 paragraph 1 of the COVID-19 Prevention Ordinance.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults and adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

Appropriate comparator therapy for sipavibart:

Monitoring wait-and-see approach

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

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines 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. In addition to sipavibart, the combinations of active ingredients tixagevimab/ cilgavimab and casirivimab/ imdevimab are approved for pre-exposure prophylaxis of COVID-19.[2]

On 2. In the therapeutic indication of pre-exposure prophylaxis of COVID-19, no non-medicinal treatments that are covered by statutory health insurance are indicated.

On 3. There is a resolution from 2 November 2023 on the benefit assessment according to Section 35a SGB V in the therapeutic indication of pre-exposure prophylaxis of COVID-19 for the combination of active ingredients tixagevimab/ cilgavimab.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V (see “Information on Appropriate Comparator Therapy”).

Pre-exposure prophylaxis of COVID-19 for subjects 12 years and older is carried out in Germany as a rule in accordance with the Standing Committee on Vaccination of the Robert Koch Institute (STIKO) with approved vaccines (active immunisation) and by observing generally recognised hygiene measures (e.g. keeping a distance, observing hygiene measures).

Approved medicinal products for pre-exposure prophylaxis against COVID-19[2] are the combinations of active ingredients casirivimab/ imdevimab and tixagevimab/ cilgavimab. The combination of active ingredients casirivimab/ imdevimab is currently not sold in Germany. The combination of active ingredients tixagevimab/ cilgavimab does not show sufficient neutralisation activity against the omicron viral variants primarily circulating at the time of the resolution. No additional benefit of the combination of active ingredients tixagevimab/ cilgavimab was derived in the early benefit assessment. Significance for clinical medical treatment practice cannot be derived at the present time.

Furthermore, no non-medicinal treatments that can be provided under SHI are indicated in the therapeutic indication to be assessed.

Currently, measures to prevent COVID-19 disease are therefore limited to reducing the likelihood of exposure through generally accepted hygiene measures, as well as the use of the approved SARS-CoV-2 vaccines.

In the overall assessment of the evidence and clinical practice, the G-BA therefore considers "monitoring wait-and-see approach" to be an appropriate comparator therapy for sipavibart at the current time in the indication of pre-exposure prophylaxis of COVID-19.

[2] According to Section 2 of the COVID-19 Prevention Ordinance, only a restricted group of insured persons are eligible for reimbursement of prescription-only medicinal products for pre-exposure prophylaxis against COVID-19.

The generally recognised hygiene rules for reducing the risk of infection must be observed here. As soon as a symptomatic disease is present, treatment according to the generally recognised state of medical knowledge is indicated.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

a) Adults, who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

An additional benefit is not proven.

b) Adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

An additional benefit is not proven.

Justification:

For the benefit assessment, the pharmaceutical company presented the SUPERNOVA study.

The SUPERNOVA study is a phase I/III study on COVID-19 pre-exposure prophylaxis. The double-blind, randomised, controlled phase III study investigates the comparison of sipavibart with tixagevimab/ cilgavimab or placebo for COVID-19 pre-exposure prophylaxis in immunocompromised adults and adolescents 12 years of age and older. Adults and adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments were enrolled. In the SUPERNOVA study, two-time treatment (day 1 and day 181) with the study medication was planned. A total of 3,349 subjects were randomised to the treatment arms in a 1:1 ratio. At the start of the study, the participants in the control arm initially received the combination of antibodies tixagevimab/ cilgavimab. With a global amendment to the study protocol (amendment 6 dated 14 June 2023), the study design was adjusted and placebo was specified as the study medication in the control group instead of tixagevimab/ cilgavimab. At this point in time, no subject had received a 2nd dose. The co-primary endpoints of the SUPERNOVA study were confirmed symptomatic COVID-19 until day 361 – once for infection with any SARS-CoV-2 variant and once for infection with viral variants without an F456L mutation in the spike protein.

For the benefit assessment in accordance with Section 35a SGB V, only the patient population for which reimbursability is given at the time of adoption of the resolution is taken into account. In accordance with Section 2 COVID-19 Prevention Ordinance, insured persons are only entitled to the provision of prescription-only medicinal products for pre-exposure prophylaxis against COVID-19 at the expense of the SHI if

1. for medical reasons, no or insufficient immune protection against COVID-19 can be achieved through vaccination, or
2. they cannot be vaccinated against the SARS-CoV-2 coronavirus due to a contraindication and they have risk factors for a severe course of COVID-19.

Medical reasons within the meaning of sentence 1 number 1 may include, in particular, congenital or acquired immunodeficiencies, underlying diseases or a significant impairment of the immune response due to immunosuppressive therapy.

For the benefit assessment, the pharmaceutical company therefore submits the results of a sub-population for which, from the pharmaceutical company's point of view, there is an entitlement to the provision of prescription-only medicinal products for preventive use to protect against COVID-19 at the expense of the SHI according to the criteria of the COVID-19 Prevention Ordinance. They derive the sub-population on the basis of the following criteria, at least one of which must apply:

- after autologous or allogeneic stem cell transplantation before immunological reconstitution,
- under or after therapy with anti-B-cell antibodies, if no reconstitution of the B-cell capacities has taken place,
- under CAR-T cell therapy,
- under strong immunosuppression, e.g. after transplantation of a solid organ or under ongoing chemotherapy,
- with genetically determined immunodeficiencies that impair antiviral immunity.

Taking the above criteria into account, the sub-population evaluated by the pharmaceutical company in the dossier comprises 1,072 (32.0%) of the 3,349 subjects randomised in the SUPERNOVA study (sipavibart arm N = 548; control arm N = 524). The sub-population presented by the pharmaceutical company in the dossier is nevertheless not suitable for the present research question of the benefit assessment, as the evaluations also include the comparison with tixagevimab/ cilgavimab. The use of tixagevimab/ cilgavimab in the comparator arm does not correspond to the implementation of the appropriate comparator therapy "monitoring wait-and-see approach".

In the written statement procedure, the pharmaceutical company submitted evaluations of the sub-population of the SUPERNOVA study comparing sipavibart with placebo in accordance with the COVID-19 Prevention Ordinance. This evaluated sub-population comprises 389 study participants (sipavibart arm N = 221; control arm N = 168), who were randomised after implementation of protocol amendment 6. The following results relate to the sub-population, in which the appropriate comparator therapy "monitoring wait-and-see approach" was implemented by means of a placebo comparison and there is an entitlement to care in accordance with the COVID-19 Prevention Ordinance. As the relevant evaluation period, the survey conducted immediately prior to administration of the 2nd dose (day 181) is used, as there is no information available as to whether the criteria for pre-exposure prophylaxis in accordance with Section 2 COVID-19 Prevention Ordinance still existed on day 181.

For adolescents from 12 to under 18 years of age weighing at least 40 kg, no data compared to the appropriate comparator therapy are available for pre-exposure prophylaxis of COVID-19. Furthermore, no sufficient justification is provided for the transferability of the results from adults to adolescents 12 years of age and older.

Extent and probability of the additional benefit

Mortality

For the endpoint of overall mortality, there was no statistically significant difference between the treatment groups.

Morbidity

For the endpoints on morbidity, evaluations are available until day 91 and until day 181 as well as for SARS-CoV-2 infections with any viral variant and infections without F456L mutation. The evaluations of all viral variants with the longest duration of observation (day 181) are used for the benefit assessment.

Confirmed symptomatic COVID-19

In the SUPERNOVA study, confirmed symptomatic COVID-19 was defined as the presence of a positive SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) test with concomitant symptomatology. Operationalised based on the World Health Organization (WHO) COVID-19 case definition, this included the following clinical criteria:

- two of the following criteria: acute onset of fever, cough, positive COVID-19 test (rapid antigen test or RT-PCR)

or

- acute occurrence of 3 or more of the following criteria: Fever, cough, general weakness/ fatigue, headache, myalgia, sore throat, rhinitis, dyspnoea, nausea/ diarrhoea/ anorexia, conjunctivitis, positive COVID-19 test, symptom associated with COVID-19 according to the principal investigator's assessment.

For the endpoint "confirmed symptomatic COVID-19", there was no statistically significant difference between the treatment groups.

Severe COVID-19

In the SUPERNOVA study, severe COVID-19 was defined as a combination of a score ≥ 5 on the WHO Clinical Progression Scale for COVID-19 and the presence of at least one of the following two events: Pneumonia (fever ≥ 38°C, cough, tachypnoea or dyspnoea and pulmonary infiltrates) or hypoxaemia (blood oxygen saturation [SpO_2] < 90% in room air and/or severe dyspnoea).

For the endpoint "severe COVID-19", there was no statistically significant difference between the treatment groups.

Quality of life

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

Side effects

The pharmaceutical company presented overall rates both including and excluding events assessed as potentially COVID-19 related. Their results are comparable and it was possible to exclude with sufficient certainty that neither advantages nor disadvantages were overlooked in these endpoints. The overall rates excluding potentially COVID-19-related events are used for the benefit assessment.

In the SUPERNOVA study, SAEs were observed over the entire study period. In the SUPERNOVA study, AEs and severe AEs were collected in full for 90 days after administration of the study medication. In the subsequent period between day 91 and the administration of the 2nd dose of the study medication on day 181, only those AEs that were associated with COVID-19 or the study medication according to the principal investigator's estimate were collected. The selective collection of AEs after day 91 is not relevant for the benefit assessment, therefore the evaluation until day 91 is used for the endpoint of severe AEs. For the endpoints of SAEs (until day 181) and severe AEs (until day 91), there was no statistically significant difference between the treatment groups.

The endpoint of discontinuation due to AEs was assessed as immediate hypersensitivity reactions after administration of the 1st dose of the study medication, which led to the 2nd dose of the study medication not being administered. This definition is not suitable for the benefit assessment, as it does not include all AEs that can lead to therapy discontinuation up to the administration of the 2nd dose of the study medication. No suitable data are thus available for the benefit assessment for the endpoint of discontinuation due to AEs.

Overall assessment

The results of the pivotal double-blind, randomised, controlled SUPERNOVA study are available for the present benefit assessment. The G-BA determined the "monitoring wait-and-see approach" as the appropriate comparator therapy. Only the sub-population, for which eligibility for reimbursement is given at the time of adoption of the resolution according to the COVID-19 Prevention Ordinance and in which the appropriate comparator therapy was appropriately implemented by means of a placebo comparison is taken into account for the benefit assessment according to Section 35a SGB V.

Results on mortality, morbidity and side effects are available for the patient population of adults.

For the endpoint of overall mortality, there was no statistically significant difference between the treatment arms of the study.

For the morbidity endpoint category, there were no statistically significant differences between the treatment groups for the endpoints "confirmed symptomatic COVID-19" and "severe COVID-19".

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

In terms of side effects, there were no statistically significant differences between the treatment groups in the overall rates for the endpoints of SAEs (until day 181) and severe AEs (until day 91). No suitable data are available for the benefit assessment for the endpoint of discontinuation due to AEs.

Overall, there were neither advantages nor disadvantages of sipavibart compared to placebo for adults for pre-exposure prophylaxis of COVID-19 in the endpoint categories of mortality,

morbidity and side effects. No data on health-related quality of life are available. An additional benefit of sipavibart compared with the appropriate comparator therapy "monitoring wait-and-see approach" is therefore not proven for this patient population.

For adolescents from 12 to under 18 years of age weighing at least 40 kg, no data compared to the appropriate comparator therapy are available. For this age group, the additional benefit of sipavibart is therefore not proven.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Kavigale with the active ingredient sipavibart. Sipavibart is approved for the pre-exposure prophylaxis of COVID-19 in adults and adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to due to a medical condition or receipt of immunosuppressive treatments. For the benefit assessment in accordance with Section 35a SGB V, only the patient population for which reimbursability is given at the time of adoption of the resolution is considered. In accordance with Section 2 COVID-19 Prevention Ordinance, there is an entitlement to the provision of prescription-only medicinal products for pre-exposure prophylaxis against COVID-19 at the expense of the SHI if no or insufficient immune protection against COVID-19 can be achieved by vaccination for medical reasons or vaccinations cannot be carried out due to a contraindication and there are risk factors for a severe course of COVID-19.

The G-BA determined the "monitoring wait-and-see approach" as the appropriate comparator therapy.

a) Adults, who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

The results of the sub-population of the pivotal double-blind, randomised, controlled SUPERNOVA study, for which reimbursability is given according to the COVID-19 Prevention Ordinance and in which the appropriate comparator therapy was appropriately implemented by means of a placebo comparison, are available for the present benefit assessment.

For the patient population of adults, there were neither advantages nor disadvantages of sipavibart compared to placebo for pre-exposure prophylaxis of COVID-19 in the endpoint categories of mortality, morbidity and side effects. No data are available for the endpoint category of health-related quality of life. In the overall assessment, there was therefore no additional benefit of sipavibart compared with the appropriate comparator therapy "monitoring wait-and-see approach" for adults for pre-exposure prophylaxis of COVID-19.

b) Adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

No data compared with the appropriate comparator therapy are available for the patient population of adolescents from 12 to under 18 years of age weighing at least 40 kg. The additional benefit of sipavibart compared with the appropriate comparator therapy for pre-exposure prophylaxis of COVID-19 is therefore not proven for adolescents from 12 to under 18 years of age.

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 pre-exposure prophylaxis using sipavibart for the pre-exposure prophylaxis of COVID-19 shall take into account the findings on the characteristics of the circulating SARS CoV-2 viruses, including regional or geographical differences, and the available information on their sensitivity patterns to sipavibart.

Due to the lack of in vitro neutralisation activity, it cannot be assumed that sipavibart offers protection against symptomatic COVID-19 in viral variants with F456L mutations in the spike protein. According to current information from the Robert Koch Institute for weeks 8 to 24 of the year 2025, all samples analysed show an F456L mutation in the spike protein – with the exception of 8.33% for the BA.3.2.2 variant in week 18.[3] The viral variants predominantly circulating in Germany at the time of adoption of the resolution thus show F456L mutations in the spike protein. Taking into account the circulating SARS-CoV-2 viruses, an indication for pre-exposure prophylaxis of COVID-19 with sipavibart therefore does not appear to be indicated as a rule at the time of adoption of the resolution, even for the vulnerable patient population in accordance with Section 2 of the COVID-19 Prevention Ordinance. The SHI target population therefore tends to be zero at the present time. Only in individual cases may pre-exposure prophylaxis of COVID-19 with sipavibart still be indicated based on medical assessment.

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 Kavigale (active ingredient: sipavibart) at the following publicly accessible link (last access: 23 June 2025):

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

The viral variants predominantly circulating in Germany at the time of adoption of the resolution show F456L mutations in the spike protein.

Due to the lack of in vitro neutralisation activity, it cannot be assumed that sipavibart offers protection against symptomatic COVID-19 in viral variants with F456L mutations in the spike protein.

[3] Robert Koch Institute. Overview of the circulating SARS-CoV-2 sublines [online]. 2025 [accessed: 25.06.2025]. URL: https://public.data.rki.de/t/public/views/IGS_Dashboard/DashboardSublineages?%3Aembed=y&%3AisGuestRedirectFromVizportal=y

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 July 2025).

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				
Sipavibart	Single dose[4]	1	1	1
Appropriate comparator therapy				
Monitoring wait-and-see approach	Not calculable			

Consumption:

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					
Sipavibart	300 mg	300 mg	1 x 300 mg	1	1 x 300 mg
Appropriate comparator therapy					
Monitoring wait-and-see approach	Not calculable				

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.

[4] Repeated use within one year may be indicated.

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					
Sipavibart	1 SII	€ 2,388.78	€ 1.77	€ 133.13	€ 2,253.88
Appropriate comparator therapy					
Monitoring wait-and-see approach	Not calculable				
Abbreviations: SII = solution for injection/infusion					

LAUER-TAXE® last revised: 15 July 2025

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

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

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

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed

therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

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

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

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

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

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

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

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the

date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA have decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the

preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

a) Adults, who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.
References:
Product information for sipavibart (Kavigale); KAVIGALE® 300 mg solution for injection/infusion; last revised: April 2025

b) Adolescents 12 years of age and older weighing at least 40 kg and who are immunocompromised due to a medical condition or receipt of immunosuppressive treatments, with an indication for pre-exposure prophylaxis of COVID-19 disease

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.
References:
Product information for sipavibart (Kavigale); KAVIGALE® 300 mg solution for injection/infusion; last revised: April 2025

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 Kavigale 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 the authorisation dossier for the assessment of the clinical efficacy and safety of the medicinal product in the therapeutic indication to be assessed.

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 per cent (3.6%) of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant extent 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

At their session on 28 November 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

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

By letter dated 13 February 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit 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 sipavibart.

The dossier assessment by the IQWiG was submitted to the G-BA on 12 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 15 May 2025. The deadline for submitting statements was 5 June 2025.

The oral hearing was held on 23 June 2025.

By letter dated 24 June 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 11 July 2025.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the Subcommittee on 29 July 2025, and the proposed draft resolution was approved.

At their session on 7 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	28 November 2023	Determination of the appropriate comparator therapy
Working group Section 35a	18 June 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	23 June 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	1 July 2025 15 July 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	29 July 2025	Concluding discussion of the draft resolution
Plenum	7 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 August 2025

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

Prof. Hecken