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
Beremagene geperpavec (wound treatment for dystrophic epidermolysis bullosa, all age groups)

of 19 February 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 approved for novel therapies within the meaning of Section 4, paragraph 9 Medicinal Products Act, there is an obligation to submit evidence in accordance with Section 35a, paragraph 1, sentence 3 SGB V. Medical treatment with such a medicinal product is not subject to the assessment of examination and treatment methods according to Sections 135, 137c or 137h.

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, the additional medical benefit is considered to be proven through the grant of the marketing authorisation. 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 beremagen geperpavec on 15 August 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 14 August 2025.

Beremagene geperpavec for the treatment of wounds in patients with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene, from birth, 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.

Beremagene geperpavec concerns a gene therapy within the meaning of Section 4, paragraph 9 Medicinal Products Act.

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 17 November 2025 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 have adopted their resolution on the basis of the dossier of the pharmaceutical company, the dossier assessment carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G25-25) prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure.

In order to determine the extent of the additional benefit, the G-BA have 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 beremagene geperpavec.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Beremagene geperpavec (Vyjuvek) in accordance with the product information

Vyjuvek is indicated for the treatment of wounds in patients with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene, from birth.

Therapeutic indication of the resolution (resolution of 19 February 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 beremagene geperpavec is assessed as follows:

Patients with wounds due to dystrophic epidermolysis bullosa (DEB) with mutation in the collagen type VII alpha 1 chain (COL7A1) gene

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Justification:

For the benefit assessment of beremagene geperpavec for the treatment of patients with wounds due to dystrophic epidermolysis bullosa (DEB) with mutation in the collagen type VII alpha 1 chain (COL7A1) gene, the pharmaceutical company presented the results of the pivotal, multicentre, placebo-controlled, double-blind phase III GEM-3 study and the single-arm open-label (OLE) B-VEC-EX-02 extension study.

31 patients with a clinical diagnosis of DEB confirmed by genetic testing for COL7A1 and two comparable cutaneous wounds were enrolled in the GEM-3 study. 47 patients were enrolled in the B-VEC-EX-02 study, 24 of whom were continuing treatment from the GEM-3 study and 23 of whom were therapy naïve.

Almost all patients had the recessive subtype of the disease. In the GEM-3 study, only one subject had the dominant subtype, and in the B-VEC-EX-02 study, two subjects had it. Patients up to the age of 46 were enrolled. In the GEM-3 study, the majority of primary wounds had a wound area < 20 cm^2, with a median wound area of 10.6 cm^2 in the intervention arm and 10.4 cm^2 in the control arm. No data were available on how deep the treated primary wounds were or how long they had been present. Furthermore, it is unclear how many wounds the patients had in total or what percentage these wounds make up of the body surface area.

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

The comparative treatment duration in the GEM-3 study was 26 weeks, and the treatment duration in the single-arm OLE B-VEC-EX-02 study was 112 weeks.

The primary efficacy endpoint was the percentage of primary wounds with complete wound closure at month 6, confirmed 2 weeks later. In addition, other endpoints in the categories of morbidity, health-related quality of life and side effects were assessed.

The GEM-3 study was conducted using a split-body design. The study participants each had two comparable cutaneous wounds: One of these wounds was treated with beremagene geperpavec, while the other wound served as a control and received a placebo. This study design therefore does not allow for comparative statements between the intervention and the control for the endpoint categories of mortality, health-related quality of life and side effects. The data submitted for these endpoint categories are therefore not assessable for the present benefit assessment and do not allow quantification of the additional benefit. In contrast, for the morbidity endpoints "complete wound closure" and "pain during change of dressing", comparative statements are generally possible.

Mortality

Deaths were recorded in both studies as part of the safety assessment. No deaths occurred in the GEM-3 study or the B-VEC-EX-02 study.

Morbidity

Complete wound closure

Due to the existing genetic disposition in epidermolysis bullosa, the formation of collagen and thus, the connection of the skin layers of the patients is significantly disturbed. Due to this defect, the skin barrier is not fully intact and even minor trauma results in wounds that have a reduced clinical cure rate. Against this background, the complete closure of a wound represents a patient-relevant endpoint in the present therapeutic indication.

The endpoint of complete wound closure was predefined in the GEM-3 study as the percentage of primary wounds with confirmed complete wound closure from baseline to month 6 and as the percentage of primary wounds with confirmed complete wound closure from baseline to month 3. In addition, the pharmaceutical company presented the study report with the percentage of primary wounds that were completely closed in both month 3 and month 6. There is no information available on the closure of primary wounds between the evaluation time points at months 3 and 6.

Primary wounds were defined as two cutaneous wounds on one subject that were comparable in size, located in similar anatomical regions, and had a similar appearance. Complete wound closure was defined as complete re-epithelialisation of the skin without drainage and had to be confirmed two weeks later to be considered a responder. The assessment of wound closure should generally be performed on site by the principal investigator. In addition, the wounds were examined and compared using the Canfield photography quantification system.

For the endpoint of complete wound closure, the survey at month 3, month 6 and months 3 and 6 showed a statistically significant advantage of beremagene geperpavec over placebo in each case.

The differences shown in the endpoint of complete wound closure indicate a clearly pronounced effect in favour of treatment with beremagene geperpavec compared to a placebo control, which is not called into question despite the split-body design.

Pain during change of dressing

The endpoint of pain is generally considered patient-relevant in the therapeutic indication of epidermolysis bullosa. Here, patient relevance is independent of the type of pain, such as pain associated with new or existing wounds (background pain) or pain during change of dressings (procedural pain).

In the GEM-3 study, the endpoint of pain during change of dressing was assessed for patients aged < 6 years using the "Face, Legs, Activity, Cry, Consolability Behavioural Scale – Revised (FLACC-R) and for patients aged ≥ 6 years using a visual analogue scale (VAS).

There are uncertainties in the operationalisation of the endpoint, as it is unclear how much time elapsed between changes of dressing for the primary wounds, whether the pain assessment during change of dressing for the two primary wounds could be performed independently of each other, whether the assessment of the first primary wound influenced the assessment of the second primary wound, and how the care and pain assessment of wounds that had already closed was handled.

As part of the written statement procedure, further information on the assessment of pain during change of dressing was subsequently submitted. Even though the survey for the intervention and control groups was conducted successively, it is not possible to make a differentiated assessment of the intervention and control groups due to the systemically experienced pain event. The criterion of local measurability is therefore not met, and a valid survey is not possible due to the split-body design.

Overall, the results for the endpoint of pain during change of dressing are therefore only presented additionally.

General health status

General health status was assessed in the GEM-3 and B-VEC-EX-02 studies using the European Quality of Life 5-Dimension 5-Level (EQ-5D-5L) questionnaire. The pharmaceutical company presented the results of the visual analogue scale (EQ-5D-VAS). This is essentially a patient-relevant endpoint.

The EQ-5D-VAS result refers to a subject's overall condition and cannot be attributed to the intervention with beremagene geperpavec or the placebo control due to the split-body design. A comparator analysis is therefore not possible for this endpoint.

Symptoms using Skindex-29

In the GEM-3 study, the Skindex-29 questionnaire was used as a tool to collect symptoms and the effects of skin conditions on the health-related quality of life of adults. The Skindex-29, a shortened version of the original tool, comprises 29 items divided into three domains: "symptoms", "emotion" and "function". The domains "emotion" and "function" are assigned to the endpoint category of health-related quality of life, and the domain "symptoms" is assigned to the endpoint category of morbidity. The domain "symptoms" surveyed using Skindex-29 is patient-relevant.

The evaluation was based on the change in week 26 compared to baseline. The questionnaire was developed and validated exclusively for adults. Due to the reference points of some items and comprehensibility, it is not considered equally valid for younger age groups.

The assessment of symptoms using Skindex-29 refers to a subject's overall condition and, due to the split-body design, cannot be attributed to the intervention with beremagene geperpavec or the placebo control. A comparative statement is therefore not possible for this endpoint.

The results of the Skindex-29 are only presented additionally due to uncertainties regarding the validity of the questionnaire for minor patients and the split-body design.

Quality of life

In the GEM-3 study, health-related quality of life was assessed using the Skindex-29 questionnaire. As described above, the domains "emotion" and "function" are assigned to the endpoint category of health-related quality of life. The domains "emotion" and "function" surveyed using Skindex-29 are patient-relevant.

As already explained, it is not possible to make a comparative statement for this endpoint due to uncertainties regarding the validity of the questionnaire for minor patients and the split-body design. The results of the Skindex-29 are therefore only presented additionally.

Side effects

Adverse events (AEs) were defined in the GEM-3 study as any adverse event that occurred in a subject who received the study medication. The event does not necessarily have to be directly related to the study medication.

In the GEM-3 study, 18 subjects experienced AE, 3 subjects experienced serious AE, 2 subjects experienced severe AE (CTCAE grade 3 or 4), and no subject discontinued (therapy) due to AE. In the B-VEC-EX-02 study, a total of 35 subjects experienced AE, 14 subjects experienced serious AE, 10 subjects experienced severe AE (CTCAE grade 3 or 4), and no subject discontinued (therapy) due to AE.

As the exact location of the AEs in relation to the skin and subcutaneous tissue (e.g. pruritus, erythema and eczema (rash)) was not recorded, the results in the side effects category refer to a subject's overall condition and cannot be attributed to the intervention with beremagene geperpavec or the placebo control due to the split-body design. A comparative statement is therefore not possible for this endpoint.

Overall assessment

Results from the placebo-controlled GEM-3 study and the open-label B-VEC-EX-02 extension study are available for the benefit assessment of beremagene geperpavec for the treatment of patients with wounds due to dystrophic epidermolysis bullosa with mutation in the collagen type VII alpha 1 chain (COL7A1) gene.

The placebo-controlled GEM-3 study was conducted with a split-body design. The study participants each had two comparable cutaneous wounds: One of these wounds was treated with beremagene geperpavec, while the other wound served as a control and received a placebo. Due to the split-body design, the results presented refer to a subject’s overall condition and, with the exception of the endpoint "complete wound closure", cannot be differentially attributed to the intervention with beremagene geperpavec or the placebo control. The study design therefore does not allow for comparative statements between the intervention and the control for the endpoint categories of mortality, health-related quality of life and side effects.

For the endpoint of complete wound closure, the survey at month 3, month 6 and months 3 and 6 showed a statistically significant advantage of beremagene geperpavec over placebo in each case. The differences shown in the endpoint of complete wound closure indicate a clearly pronounced effect in favour of treatment with beremagene geperpavec, which is not called into question despite the split-body design.

In the overall assessment, the endpoint of complete wound closure did show a statistically significant advantage of the active ingredient beremagene geperpavec compared to placebo.

However, a benefit-risk assessment based on the data presented is not possible due to the study design. The data presented are therefore unsuitable for quantifying the extent of the additional benefit.

A non-quantifiable additional benefit of beremagene geperpavec for the treatment of wounds in patients with dystrophic epidermolysis bullosa with mutation in the collagen type VII alpha 1 chain gene is identified, since the scientific data does not allow quantification.

Significance of the evidence

For the GEM-3 study presented, there is a low risk of bias at study level.

At endpoint level, there is a high risk of bias for all endpoints (except for the endpoint of complete wound closure) due to the split-body design. In contrast, the risk of bias is considered low for the endpoint of complete wound closure.

Due to the lack of control at both the study and endpoint levels, the open-label B-VEC-EX-02 extension study is considered to have a high risk of bias.

The reliability of data is therefore classified in the "hint" category.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Vyjuvek with the active ingredient beremagene geperpavec. Vyjuvek was approved as an orphan drug in the following therapeutic indication: "For the treatment of wounds in patients with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene, from birth."

The pharmaceutical company submitted data from the double-blind, randomised, placebo-controlled phase III GEM-3 study and the open-label B-VEC-EX-02 extension study for the benefit assessment.

Due to the split-body design of the GEM-3 study, the results presented refer to a subject's overall condition and, with the exception of the endpoint "complete wound closure", cannot be differentially attributed to the intervention with beremagene geperpavec or the placebo control. The study design therefore does not allow for comparative statements between the intervention and the control for the endpoint categories of mortality, health-related quality of life and side effects.

For the endpoint of complete wound closure, the survey at month 3, month 6 and months 3 and 6 showed a statistically significant advantage of beremagene geperpavec over placebo in each case. The differences shown in the endpoint of complete wound closure indicate a clearly pronounced effect in favour of treatment with beremagene geperpavec.

In the overall assessment, the endpoint of complete wound closure did show a statistically significant advantage of the active ingredient beremagene geperpavec compared to placebo. However, a benefit-risk assessment based on the data presented is not possible due to the study design. The data presented are therefore unsuitable for quantifying the extent of the additional benefit.

A non-quantifiable additional benefit of beremagene geperpavec is identified, since the scientific data does not allow quantification.

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 overall uncertainties due to the limited epidemiological data basis on the incidence and prevalence of epidermolysis bullosa in the German healthcare context. Overall, the number of patients determined by the pharmaceutical company is largely plausible on the basis of the literature presented.

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 Vyjuvek (active ingredient: beremagene geperpavec) at the following publicly accessible link (last access: 10 February 2026):

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

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (if applicable incl. patient identification card).

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 December 2025).

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

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is 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 for the maximum treatment duration, if specified in the product information.

As topical application is carried out locally on the affected wound, the calculation of annual treatment costs is based on the assumption that wounds requiring treatment are present.

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				
Beremagene geperpavec	Continuously, 1 x every 7 days	52.1	1.0	52.1

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 co-morbidities) are not taken into account when calculating the annual treatment costs.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration. The dosages recommended in the product information for the maximum weekly total dose based on wound area were used as the basis for calculation.

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					
Beremagene geperpavec	20 cm^2 wound area: 0.2 ml (4×10^8 PFU)	0.2 ml	1 x 2 ml	52.1	52.1 x 2 ml
	200 cm^2 wound area: 2 ml (4×10^9 PFU)	2 ml	1 x 2 ml	52.1	52.1 x 2 ml

Costs:

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

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Beremagene geperpavec 5 x 10^9 plaque-forming units/ml suspension and gel for the preparation of a gel	1 SUS	€ 30,301.80	€ 1.77	€ 1,727.25	€ 28,572.78
Abbreviations: PFU = plaque-forming units; SUS = suspension					

LAUER-TAXE® last revised: 15 December 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.

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 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:

Patients with wounds due to dystrophic epidermolysis bullosa (DEB) with mutation in the collagen type VII alpha 1 chain (COL7A1) gene

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

References:
Product information for beremagene geperpavec (Vyjuvek); Vyjuvek 5 × 10^9 plaque-forming units/ml suspension and gel for preparation of a gel; 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 Vyjuvek 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% (0.0%) of the total number of study participants according to the information provided by the pharmaceutical company.

The pharmaceutical company provides information on a total of 3 studies. They state that the percentage of study participants at study sites within the scope of SGB V is 0% for all relevant studies. This information is comprehensible.

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

On 14 August 2025, the pharmaceutical company submitted a dossier for the benefit assessment of beremagene geperpavec 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 17 November 2025 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 8 December 2025.

The oral hearing was held on 13 January 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 session on 10 February 2026, and the draft resolution was approved.

At their session on 19 February 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 November 2025	Information of the benefit assessment of the G-BA
Working group Section 35a	6 January 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	13 January 2026	Conduct of the oral hearing
Working group Section 35a	20 January 2026 3 February 2026	Consultation on the dossier evaluation 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	10 February 2026	Concluding discussion of the draft resolution
Plenum	19 February 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 19 February 2026

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

Prof. Hecken