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
Serplulimab (small cell lung cancer, in combination with carboplatin and etoposide, first-line)

of 16 October 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, 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 for 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, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. 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. According to Section 35a paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, subsection 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides 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 determines 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 threshold 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 serplulimab on 1 May 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 28 March 2025.

Serplulimab for the treatment of extensive-stage small cell lung cancer is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No 141/2000 of the European Parliament and the Council of 16 December 1999.

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

The G-BA carried out the benefit assessment and commissioned the IQWiG to assess 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 1 August 2025 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA adopted their resolution on the basis of the pharmaceutical company's dossier, the dossier assessment carried out by the G-BA, the IQWiG assessment of treatment costs and patient numbers (IQWiG G25-18) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

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

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Serplulimab (Hetronifly) in accordance with the product information

HETRONIFLY in combination with carboplatin and etoposide is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

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

Therapeutic indication of the resolution (resolution of 16 October 2025):

See the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

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

Adults with extensive-stage small cell lung cancer (ES-SCLC); first-line:

Hint for a non-quantifiable additional benefit

Justification:

The label-enabling study for serplulimab in this therapeutic indication is the phase III ASTRUM-005 RCT comparing serplulimab in combination with carboplatin and etoposide with carboplatin in combination with etoposide. In order to be able to depict the German healthcare context, the pharmaceutical company based the benefit assessment of serplulimab in the present therapeutic indication on an adjusted indirect comparison according to Bucher using the ASTRUM-005 approval study and the IMpower133 study. Thus, serplulimab in combination with carboplatin and etoposide (ASTRUM-005) can be compared to atezolizumab in combination with carboplatin and etoposide (IMpower133) using the bridge comparator carboplatin in combination with etoposide.

On the ASTRUM-005 and IMpower133 studies

The ASTRUM-005 and IMpower133 studies are completed, double-blind phase III RCTs, in which untreated patients with extensive-stage small cell lung cancer (ES-SCLC) were enrolled.

In the ASTRUM-005 study, 389 patients were randomised in a 2:1 ratio to the intervention arm with serplulimab in combination with carboplatin and etoposide and 196 patients to the control arm with carboplatin in combination with etoposide. The three pre-specified data cut-offs took place on 22.10.2021, 13.06.2022 and 07.05.2024.

In the IMpower133 study, a global main cohort and a China extension cohort were analysed. In the global cohort and the Chinese extension cohort, 201 and 57 patients respectively were examined in the intervention arm with atezolizumab in combination with carboplatin and etoposide and 202 and 53 patients respectively in the control arm with carboplatin in combination with etoposide. In addition to the pre-specified 1st data cut-off from 24.04.2018, the exploratory OS analysis as of 24.01.2019 required by the EMA existed for the global cohort. In addition to the pre-specified 1st data cut-off from 29.10.2018, the 2nd data cut-off from 24.01.2019 and the label-enabling (for China) 3rd data cut-off from 31.07.2019 existed for the China extension cohort.

On the adjusted indirect comparison according to Bucher

With regard to the study populations, there were differences between the two studies in terms of descent and never-smoker status: In the ASTRUM-005 study, the percentage of patients of Asian descent was higher (69% in ASTRUM-005 vs 35% in the pooled IMpower133 cohort) – as was the percentage of never smokers (20% in the ASTRUM-005 study vs 7% in the pooled IMpower133 cohort), with the percentage of never smokers being comparable between the ASTRUM-005 study and the China cohort of the IMpower133 study.

Analogous to the benefit assessment of atezolizumab (resolution of 2 April 2020), which was based on the IMpower133 study, the results of the global and Chinese cohorts from this study are considered as a pooled cohort in the present adjusted indirect comparison according to Bucher, since the descent characteristic did not show any effect modification in the subgroup analyses for the efficacy endpoints and the risk of bias for the two cohorts did not differ both at study level and at endpoint level.

Overall, the demographic and clinical characteristics of the study populations of ASTRUM-005 and the pooled IMpower133 cohort are estimated to be so sufficiently similar that they can be used as the basis for the adjusted indirect comparison according to Bucher.

In order to be able to base the adjusted indirect comparison according to Bucher on data cut-offs with comparable observation periods, the 2nd data cut-off for the endpoint of overall survival of the ASTRUM-005 study was compared to the pooled IMpower133 overall cohort, consisting of the 2nd data cut-off of the global cohort and the 3rd data cut-off of the China cohort. For the safety endpoints, the 2nd data cut-off of the ASTRUM-005 study was compared to the pooled IMpower133 overall cohort, consisting of the 1st data cut-off of the global cohort and the 3rd data cut-off of the China cohort, as only the hazard ratios (HR) at the 1st data cut-off are available for the safety endpoints from the global IMpower133 cohort and it is assumed that the duration of observation of these endpoints did not differ significantly between the 1st and the 2nd data cut-offs of the global IMpower133 cohort.

On the results

Mortality

With regard to the "overall survival" endpoint, the adjusted indirect comparison did not show any statistically significant difference between serplulimab and atezolizumab for comparable observation periods between the ASTRUM-005 study (2nd data cut-off from 13 June 2022) and the overall cohort of the IMpower133 study (2nd data cut-off of the global cohort from 24 January 2019 and the 3rd data cut-off of the China cohort from 31 July 2019).

Morbidity

No usable data are available for the endpoint "General health status using EQ-5D-VAS" for the adjusted indirect comparison.

Quality of life

No usable data are available from the survey with EORTC QLQ-C30 for this endpoint for the adjusted indirect comparison.

Side effects

Serious adverse events (SAEs), severe adverse events (CTCAE grade 3 or 4)

For the serious adverse events (SAEs) and the severe adverse events, data are available for comparable observation periods between the ASTRUM-005 study (2nd data cut-off from 13 June 2022) and the overall cohort of the IMpower133 study (1st data cut-off of the global cohort from 24 April 2018 and the 3rd data cut-off of the China cohort from 31 July 2019).

For SAEs, the adjusted indirect comparison between serplulimab and atezolizumab did not show any significant difference.

For the severe adverse events, the pharmaceutical company subsequently submitted the data in an operationalisation with severity grade CTCAE 3 or 4 to enable a comparison between the two studies. Due to the different treatment duration between the study arms of the ASTRUM-005 study, it can be assumed that the observation time for the safety endpoints linked to the

treatment duration was also different. In addition, in the IMpower133 study, "severe AEs" were collected up to maximum 30 days after the end of treatment, whereas in the ASTRUM-005 study they were collected until maximum day 90. The subsequently submitted effect estimator for the adjusted indirect comparison was presented as a relative risk and is therefore unusable due to the different observation periods.

Discontinuation due to AEs

For this endpoint, data are available for comparable observation periods between the ASTRUM-005 study (2nd data cut-off from 13 June 2022) and the global IMpower133 cohort (1st data cut-off from 24 April 2018).

The event rates for this endpoint were comparable in the intervention arms of the two studies, but significantly fewer events occurred in the placebo arm of the IMpower133 study than in the ASTRUM-005 study. This results in additional uncertainty in the interpretation of the result from the adjusted indirect comparison. Overall, the statistically significant effect from the adjusted indirect comparison is assessed to be inadequately reliable to allow conclusions to be drawn.

Conclusion

The present assessment is based on the adjusted indirect comparison according to Bucher of the phase III ASTRUM-005 (serplulimab + chemotherapy vs chemotherapy) and IMpower133 (atezolizumab + chemotherapy vs chemotherapy) studies, which compared serplulimab with atezolizumab via the chemotherapy bridge comparator. Results on mortality and side effects are available from the adjusted indirect comparison.

For the endpoint of overall survival, there was no statistically significant difference between serplulimab and atezolizumab.

For the side effects, no advantages or disadvantages can be identified owing to the limited data basis with limited interpretability of the effect estimators from the adjusted indirect comparison.

In the overall assessment, the G-BA classified the extent of the additional benefit of serplulimab in combination with carboplatin and etoposide for the treatment of extensive-stage small cell lung cancer (ES-SCLC) as non-quantifiable since the scientific data does not allow quantification.

Significance of the evidence

Per se relevant uncertainties with regard to the reliability of data occur as the present assessment is based on an adjusted indirect comparison according to Bucher. Overall, the data are subject to considerable uncertainty, which is why the reliability of data regarding the additional benefit identified is classified as hint.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "Hetronifly" with the active ingredient serplulimab. Serplulimab in combination with carboplatin and etoposide is approved for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC). Hetronifly was approved as an orphan drug.

The present assessment is based on the adjusted indirect comparison according to Bucher of the phase III ASTRUM-005 (serplulimab + chemotherapy vs chemotherapy) and IMpower133 (atezolizumab + chemotherapy vs chemotherapy) studies, which compared serplulimab with atezolizumab via the chemotherapy bridge comparator. Results on mortality and side effects are available from the adjusted indirect comparison.

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Per se relevant uncertainties with regard to the reliability of data occur as the present assessment is based on an adjusted indirect comparison according to Bucher. Overall, the data are subject to considerable uncertainty, which is why the reliability of data regarding the additional benefit identified is classified as hint.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The G-BA base their resolution on the information from the pharmaceutical company's dossier for the upper limit and the information from the resolution on durvalumab from 1 April 2021 for the lower limit.

It should be taken into account that the lower limit from the pharmaceutical company’s dossier is likely to be an overestimaton, as the target population was not narrowed down according to suitability for platinum therapy. In order to narrow down the target population to patients who have received platinum-based chemotherapy with etoposide , the resolution was based on the lower limit from the resolution on durvalumab from 1 April 2021.

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 Hetronifly (active ingredient: serplulimab) at the following publicly accessible link (last access: 17 July 2025):

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

Treatment with serplulimab should only be initiated and monitored by specialists in internal medicine, haematology and oncology who are experienced in the treatment of patients with small cell lung cancer, as well as specialists in internal medicine and pulmonology or specialists in pulmonary medicine and other doctors from other specialist groups participating in the Oncology Agreement.

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 August 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 varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and the maximum treatment duration, if specified in the product information.

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

Treatment period:

Adults with extensive-stage small cell lung cancer (ES-SCLC); first-line:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Serplulimab	1 x every 21 days	17.4	1	17.4
Carboplatin	1 x every 28 days	13.0	1	13.0
Etoposide	1 x on day 1, 3 and 5 of a 21 or 28-day cycle	13.0 - 17.4	3	39.0 - 52.2

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.

For dosages depending on body weight (BW) or body surface area (BSA) of the adult patients, the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg). This results in a body surface area of 1.91 m² (calculated according to Du Bois 1916)[2].

The dosage regimen of the concomitant active ingredients etoposide and carboplatin is based on the respective underlying product information. Accordingly, carboplatin is administered at a dose of 400 mg/m² in the 28-day cycle and etoposide at a dose of 100 mg/m² – 120 mg/m² on days 1, 3 and 5 of a 21 or 28-day cycle.

Adults with extensive-stage small cell lung cancer (ES-SCLC); first-line

[2] Federal health reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

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					
Serplulimab	4.5 mg/kg = 349.7 mg	349.7 mg	4 x 100 mg	17.4	69.6 x 100 mg
Carboplatin	400 mg/m² = 764 mg	764 mg	2 x 450 mg	13.0	26.0 x 450 mg
Etoposide	100 mg/m² = 191 mg – 120 mg/m² = 229.2 mg	191 mg – 229.2 mg	2 x 100 mg – 1 x 200 mg + 1 x 50 mg	39.0 or 52.2	78.0 x 100 mg or 104.4 x 100 mg – 39.0 x 200 mg + 39.0 x 50 mg or 52.2 x 200 mg + 52.2 x 50 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Serplulimab 100 mg	1 CIS	€ 1,402.45	€ 1.77	€ 77.02	€ 1,323.66
Carboplatin 450 mg	1 CIS	€ 228.24	€ 1.77	€ 10.29	€ 216.18
Etoposide 200 mg	1 CIS	€ 81.90	€ 1.77	€ 3.35	€ 76.78
Etoposide 100 mg	10 CIS	€ 403.89	€ 1.77	€ 18.63	€ 383.49
Etoposide 50 mg	1 CIS	€ 28.73	€ 1.77	€ 0.96	€ 26.00
Abbreviations: CIS = concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 15 August 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.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

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

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

Basic principles of the assessed medicinal product

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

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered

due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

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

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

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

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

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

Adults with extensive-stage small cell lung cancer (ES-SCLC); first-line

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 serplulimab (Hetronifly); HETRONIFLY 10 mg/ml concentrate for the preparation of an infusion solution; last revised: July 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 serplulimab (Hetronifly) is a medicinal product placed on the market from 1 January 2025.

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.

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 28 March 2025, the pharmaceutical company submitted a dossier for the benefit assessment of serplulimab 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 1 August 2025 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting statements was 22 August 2025.

The oral hearing was held on 8 September 2025.

An amendment to the benefit assessment with a supplementary assessment was submitted on 25 September 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 7 October 2025, and the draft resolution was approved.
At their session on 17 October 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	29 July 2025	Information of the benefit assessment of the G-BA
Working group Section 35a	3 September 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on	8 September 2025	Conduct of the oral hearing

Medicinal Products		
Working group Section 35a	17 September 2025 1 October 2025	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee on Medicinal Products	7 October 2025	Concluding discussion of the draft resolution
Plenum	16 October 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 16 October 2025

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

Prof. Hecken