Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee 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

At their session on 16 October 2025, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient Serplulimab as follows:

Serplulimab

Resolution of: 16 October 2025
Entry into force on: 16 October 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 3 February 2025):

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).

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

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Serplulimab is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with 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.

The G-BA determine the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

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

Extent of the additional benefit and significance of the evidence of serplulimab:

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

Study results according to endpoints:[1]

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

[1] Data from the dossier assessment of the G-BA (published on 1. August 2025), and from the amendment to the dossier assessment from 24 September 2025, unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	↔	No relevant difference for the benefit assessment.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference
∅: No data available.
n.a.: not assessable

<u>Adjusted indirect comparison according to Bucher from the ASTRUM-005 and IMpower133 studies</u>

ASTRUM-005 study:
Serplulimab + carboplatin + etoposide vs carboplatin + etoposide

IMpower133 study:
Serplulimab + carboplatin + etoposide vs carboplatin + etoposide

Bridge comparator:
Carboplatin + etoposide (CE)

Mortality

Endpoint	Serplulimab + CE or atezolizumab + CE		CE		Group difference
	N[a]	Median survival time in months [95% CI][b] Patients with event n (%)	*N*[a]	Median survival time in months [95% CI][b] Patients with event n (%)	*Hazard ratio [95% CI][d]* *p value*[e]
Overall survival					
Second data cut-off[c]					
Serplulimab + CE vs placebo + CE ASTRUM-005	389	15.8 [14.1; 17.6] 223 (57.3)	196	11.1 [9.96; 12.4] 140 (71.4)	0.62 [0.50; 0.76] < 0.001
Atezolizumab + CE vs placebo + CE	258	n.d. 183 (70.9)	255	n.d. 201 (78.8)	0.79 [0.65; 0.97][f]

Endpoint	Serplulimab + CE or atezolizumab + CE		CE		Group difference
	N[a]	Median survival time in months [95% CI][b] Patients with event n (%)	*N*[a]	Median survival time in months [95% CI][b] Patients with event n (%)	*Hazard ratio [95% CI][d] p value*[e]
IMpower133					< 0.03
Indirect comparison via bridge comparator: Serplulimab + CE vs atezolizumab + CE[g] HR [95% CI] p value	0.78 [0.58; 1.04] 0.10				

Morbidity

Endpoint	Serplulimab + CE or atezolizumab + CE		CE		Group difference
	N[a]	Median survival time in months [95% CI] Patients with event n (%)	*N*[a]	Median survival time in months [95% CI] Patients with event n (%)	*Hazard ratio [95% CI] p value*
General health status using EQ-5D-VAS					
Second data cut-off[b]					
Indirect comparison via bridge comparator: Serplulimab + CE vs atezolizumab + CE	No usable data available[h]				

Health-related quality of life

Endpoint	Serplulimab + CE or atezolizumab + CE		CE		Group difference
	N[a]	Median survival time in months [95% CI] Patients with event n (%)	*N*[a]	Median survival time in months [95% CI] Patients with event n (%)	*Hazard ratio [95% CI] p value*
EORTC QLQ-C30					
Second data cut-off[b]					

Endpoint	Serplulimab + CE or atezolizumab + CE	CE	Group difference
Indirect comparison via bridge comparator: Serplulimab + CE vs atezolizumab + CE	No usable data available[i]		

Side effects

Endpoint	Serplulimab + CE or atezolizumab + CE		CE		Group difference
	N[a]	Patients with event n (%)	N[a]	Patients with event n (%)	Effect estimator [95% CI] p value
Second data cut-off[k]					
Severe adverse events (CTCAE grade 3 or 4)					
Serplulimab + CE vs placebo + CE ASTRUM-005	389	289 (74.3)	196	138 (70.4)	RR: 1.06[l] [0.95; 1.18] 0.33
Atezolizumab + CE vs placebo + CE IMpower133	255	182 (71.4)	248	179 (72.2)	RR: 0.99[l] [0.89; 1.10] 0.84
Indirect comparison via bridge comparator: Serplulimab + CE vs atezolizumab + CE. RR [95% CI] p value	No usable data available[l]				
Serious adverse events (SAE)					
Serplulimab + CE vs placebo + CE ASTRUM-005	389	146 (37.5)	196	71 (36.2)	HR: 0.89[m,n] [0.66; 1.18] n.d.
Atezolizumab + CE vs placebo + CE IMpower133	255	95 (37.3)	248	82 (33.1)	HR: 1.16[m,n] [0.86; 1.56] n.d.
Indirect comparison via bridge comparator: Serplulimab + CE vs atezolizumab + CE[g] HR [95% CI] p value	0.76 [0.5; 1.15] 0.20				
Therapy discontinuation due to adverse events[o,p]					
Serplulimab + CE vs placebo + CE ASTRUM-005	389	38 (9.8)	196	18 (9.2)	HR: 0.81[m,n] [0.46; 1.43] n.d.

Atezolizumab + CE vs placebo + CE IMpower133	255	29 (11.4)	248	6 (2.4)	-[q]
Indirect comparison via bridge comparator: Serplulimab + CE vs atezolizumab + CE. HR [95% CI] p value	0.24 (0.08; 0.69) 0.01				

Abbreviations used:

CE = carboplatin + etoposide; CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; n.d.= no data available; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; (S)AE = (serious) adverse event; vs = versus

a The number corresponds to those subjects who were used to calculate the respective statistics.

b ASTRUM-005 study: Kaplan-Meier method, calculation of the 95% CI using the Brookmeyer-Crowley method. IMpower133 study: Stratified Cox regression model, stratified by sex and ECOG-PS at the start of treatment (global cohort) or sex (China cohort).

c Data cut-offs with comparable observation periods. ASTRUM-005 study: 2nd data cut-off from 13.06.2022; IMpower133 study global cohort: 2nd data cut-off from 24.01.2019; IMpower133 study China cohort: 3rd data cut-off from 31.07.2019.

d Cox proportional hazards model. ASTRUM-005 study: Stratified by PD-L1 expression level (negative, positive, not evaluable/ not present), brain metastases (yes, no) and age (≥ 65, < 65 years). IMpower133 study: stratified by sex and ECOG-PS at the start of treatment (global cohort) or by sex (China cohort).

e Stratified log-rank test.

f Fixed-effect meta-analysis. Source: Addendum to the benefit assessment of atezolizumab (2019-10-15-D-491) of 2 April 2020.

g Indirect comparison according to Bucher. Own calculation.

h The requirement for reliability of data of an adjusted indirect comparison is not met

i Due to different data collection and evaluation strategies of the EORTC QLQ-C30, no usable data are available for the adjusted indirect comparison.

k ASTRUM-005 study: 2nd data cut-off from 13.06.2022; IMpower133 study global cohort: 1st data cut-off from 24.04.2018; IMpower133 study China cohort: 3rd data cut-off from 31.07.2019. For the global cohort of the IMpower133 study, only the hazard ratios of the direct comparisons (atezolizumab vs placebo) for the first data cut-off are available for the safety endpoints. It is assumed that the duration of observation for these endpoints did not differ significantly between the first and second data cut-offs of the global cohort of the IMpower133 study.

l The use of RR is inadequate in the available data basis, as a different duration of observation can be assumed for this endpoint due to the different treatment duration in the serplulimab arm compared to the placebo arm in the ASTRUM-005 study.

m Time-to-event analyses (time to first occurrence of an AE) were made using an unstratified Cox regression model.

n The reference is placebo + chemotherapy.

o Study participants received study medication until disease progression, unacceptable toxicity, initiation of other antineoplastic therapy, withdrawal of informed consent, or death, whichever occurred first. At the principal investigator's discretion, the study treatment could continue to be administered even after disease progression if a clinical benefit was to be expected. These possible therapy discontinuation reasons that may occur prior to potential discontinuation due to

	AEs thus represent a competing event, which is why the reliability of data and interpretability of the results is limited.
p	Percentage of discontinuations of at least one component of the study medication (serplulimab or atezolizumab and/or carboplatin or etoposide).
q	The pooled HR cannot be estimated since no events occurred in the placebo arm of the China cohort. Evaluations for the entire cohort of the IMpower133 study at the level of patient-individual data are not available.
r	Indirect comparison according to Bucher. Only the global cohort of the IMpower133 study is considered here as a pooled HR could not be estimated for the IMpower244 study. Information provided by the pharmaceutical company in the dossier on serplulimab.

2. Number of patients or demarcation of patient groups eligible for treatment

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

3,210 – 7,719 patients

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.

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Serplulimab	€ 92,126.74
Carboplatin	€ 5,620.68
Etoposide	€ 2,991.22 - € 5,365.12

Designation of the therapy	Annual treatment costs/ patient
Total	*€ 100,738.64 - € 103,112.54*

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 August 2025)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Serplulimab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0	€ 1,300
Etoposide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	13.0 or 17.4	€ 3,900 or € 5,220

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

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

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

- 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.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. 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.

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% 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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 16 October 2025.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 16 October 2025

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

Prof. Hecken