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
Ciltacabtagene autoleucel (new therapeutic indication/ reassessment of an orphan drug after exceeding the 30 million euro limit: multiple myeloma, after at least 1 prior therapy, refractory to lenalidomide)

of 15 May 2025

At their session on 15 May 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 is amended as follows:

1. **The information on ciltacabtagene autoleucel in the version of the resolution of 17 August 2023 (Federal Gazette, BAnz AT 11.09.2023 B1) is repealed.**
2. **Annex XII shall be amended in alphabetical order to include the active ingredient Ciltacabtagene autoleucel as follows:**

Ciltacabtagene autoleucel

Resolution of: 15 May 2025
Entry into force on: 15 May 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 19 April 2024):

Carvykti is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least one prior therapy, including an immunomodulatory agent and a proteasome inhibitor, have demonstrated disease progression on the last therapy, and are refractory to lenalidomide.

Therapeutic indication of the resolution (resolution of 15 May 2025):

See therapeutic indication according to marketing authorisation.

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

a) Adults with relapsed and refractory multiple myeloma, who have received at least one prior therapy, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

Appropriate comparator therapy:

An individualised therapy with selection of

- daratumumab in combination with bortezomib and dexamethasone,
- daratumumab in combination with carfilzomib and dexamethasone,
- daratumumab in combination with pomalidomide and dexamethasone (DPd),
- isatuximab in combination with carfilzomib and dexamethasone,
- isatuximab in combination with pomalidomide and dexamethasone (only for subjects with at least two prior therapies),
- elotuzumab in combination with pomalidomide and dexamethasone (only for subjects with at least two prior therapies),
- pomalidomide in combination with bortezomib and dexamethasone (PVd, only for subjects who are refractory to an anti-CD38 antibody),
- pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies),
- carfilzomib in combination with dexamethasone,

- panobinostat in combination with bortezomib and dexamethasone (only for subjects who have received at least four prior therapies),
- bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies),
- bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies),
- daratumumab monotherapy (only for at least triple-refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies),
- cyclophosphamide as monotherapy or in combination with dexamethasone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies),
- melphalan as monotherapy or in combination with prednisolone or prednisone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies),
- high-dose therapy with autologous stem cell transplant (only for subjects who have undergone prior therapy and are eligible for an autologous stem cell transplant; after achieving remission)

  and

- high-dose therapy with allogeneic stem cell transplant[1] (only for subjects who have undergone prior therapy and are eligible for an allogeneic stem cell transplant; after achieving remission)

[1] The regulations of the G-BA apply in accordance with Section 136b, paragraph 1, sentence 1, number 2 SGB V for hospitals approved in accordance with Section 108 SGB V (minimum quantity regulations, MQR).

Extent and probability of the additional benefit of ciltacabtagene autoleucel compared to DPd or PVd:

a1) Adults with relapsed and refractory multiple myeloma, who have received one to three prior therapies, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

Hint for a considerable additional benefit

a2) Adults with relapsed and refractory multiple myeloma, who have received at least four prior therapies, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

An additional benefit is not proven.

Study results according to endpoints:[2]

a1) Adults with relapsed and refractory multiple myeloma, who have received one to three prior therapies, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑	Advantage in overall survival
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↔	Overall, no relevant differences for the benefit assessment; in detail, mainly disadvantages for specific AEs

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

[2] Data from the dossier assessment of the IQWiG (A24-116) and from the addendum (A25-48), unless otherwise indicated.

Open-label, randomised phase III CARTITUDE-4 study

- Ciltacabtagene autoleucel versus individualised therapy with selection of DPd or PVd
- Adults with one to three prior therapies
- Fourth data cut-off: 1 May 2024, final pre-specified analysis of progression-free survival, pre-specified second interim analysis of overall survival

Mortality

Endpoint	**Ciltacabtagene autoleucel**		**Individualised therapy with selection of DPd or PVd**		Intervention vs control
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a]
Overall survival					
	208	n.r. 50 (24.0)	211	n.r. [37.75; n.c.] 83 (39.3)	0.55 [0.39; 0.79]; < 0.001[b]
		Survival rate in per cent [95% CI][c]		Survival rate in per cent [95% CI][c]	
At study month 6	208	91.3 [86.6; 94.5]	211	94.2 [90.1; 96.7]	-
At study month 12	208	84.1 [78.4; 88.4]	211	83.6 [77.9; 88.0]	-
At study month 18	208	82.2 [76.3; 86.8]	211	74.4 [67.9; 79.8]	-
At study month 24	208	78.8 [72.6; 83.8]	211	66.2 [59.3; 72.2]	-
At study month 30	208	76.2 [69.6; 81.6]	211	63.3 [56.1; 69.6]	-
At study month 36	208	76.2 [69.6; 81.6]	211	53.1 [39.6; 65.0]	-

Morbidity

Endpoint	Ciltacabtagene autoleucel		Individualised therapy with selection of DPd or PVd		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a]
Progression-free survival (PFS)[c]					
	208	n.r. [34.50; n.r.] 89 (42.8%)	211	11.79 [9.66; 14.00] 153 (72.5%)	0.39 [0.30; 0.51] < 0.0001
Symptomatology					
EORTC QLQ-C30	No suitable data[d]				
PGIS	No suitable data[d]				
Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q)	No suitable data[d]				
Health status					
EQ-5D VAS	No suitable data[d]				

Health-related quality of life

Endpoint	Ciltacabtagene autoleucel		Individualised therapy with selection of DPd or PVd		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a]
EORTC QLQ-C30					
	No suitable data[d]				

Side effects

Endpoint	Ciltacabtagene autoleucel		Individualised therapy with selection of DPd or PVd		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a]
Total adverse events (AEs, presented additionally)[e]					
	208	0.20 [0.13; 0.26] 208 (100)	208	0.13 [0.07; 0.20] 208 (100)	-
Serious adverse events (SAE)[e]					
	208	9.86 [5.62; 15.57] 139 (66.8)	208	19.48 [12.42; 25.23] 99 (47.6)	1.25 [0.96; 1.63]; 0.103
Severe adverse events (CTCAE grade 3 or 4)[e]					
	208	0.72 [0.56; 0.76] 203 (97.6)	208	0.69 [0.49; 0.72] 202 (97.1)	0.93 [0.75; 1.14]; 0.455
Therapy discontinuation due to adverse events[f]					
	208	n.r. 6 (2.9)	208	n.r. [37.19; n.c.] 44 (21.2)	0.47 [0.18; 1.21]; 0.116
PRO-CTCAE					
	No suitable data[d]				
Specific adverse events[e]					
Cytokine release syndrome	No suitable data[g]				
Severe neurological toxicity (SAE, SOC nervous system disorders)[e]	208	n.r. 26 (12.5)	208	n.r. 6 (2.9)	3.38 [1.38; 8.29]; 0.008
Infusion-related reactions	No suitable data[g]				
Severe infections (SAE, SOC infections and infestations)[e]	208	n.r. [31.57; n.c.] 84 (40.4)	208	n.r. [24.81; n.c.] 63 (30.3)	0.95 [0.68; 1.34]; 0.779

Endpoint	Ciltacabtagene autoleucel		Individualised therapy with selection of DPd or PVd		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a]
Secondary malignancies	No suitable data[g]				
Headache (PT, AEs)[e]	208	n.r. 58 (27.9)	208	n.r. 27 (13.0)	3.09 [1.87; 5.10]; < 0.001
Insomnia (PT, AEs)[e]	208	n.r. 23 (11.1)	208	n.r. 55 (26.4)	0.43 [0.26; 0.70]; < 0.001
Thrombocytopenia (PT, severe AEs, CTCAE grade 3 or 4)[e]	208	n.r. [5.95; n.c.] 89 (42.8)	208	n.r. 41 (19.7)	2.49 [1.70; 3.64]; < 0.001
Anaemia (PT, severe AEs, CTCAE grade 3 or 4)[e]	208	n.r. 80 (38.5)	208	n.r. 33 (15.9)	2.88 [1.90; 4.37]; < 0.001
Lymphopenia (PT, severe AEs, CTCAE grade 3 or 4)[e]	208	n.r. 46 (22.1)	208	n.r. 25 (12.0)	2.02 [1.22; 3.33]; 0.006
Leukopenia (PT, severe AEs, CTCAE grade 3 or 4)[e]	208	n.r. 27 (13.0)	208	n.r. 10 (4.8)	2.75 [1.33; 5.69]; 0.006
Metabolism and nutrition disorders (SOC, severe AEs, CTCAE grade 3 or 4)[e]	208	n.r. 33 (15.9)	208	n.r. 15 (7.2)	2.47 [1.30; 4.69]; 0.006
Hypogammaglobulinaemia (PT, severe AEs, CTCAE grade 3 or 4)[e]	208	n.r. [8.02; n.c.] 12 (5.8)	208	n.r. 2 (1.0)	52.86 [5.41; 516.19]; < 0.001

[a] HR, CI and p value: Cox proportional hazards model, stratified by comparator therapy of principal investigator's choice (DPd vs PVd), ISS stage (I vs II vs III) and number of prior lines of therapy (one vs two or three)
[b] p value: Log-rank test, stratified by comparator therapy of the principal investigator's choice (DPd vs PVd), ISS stage (I vs II vs III) and number of prior lines of therapy (one vs two or three)
[c] Information from the European Public Assessment Report (EPAR) on Carvykti from 22 February 2024

Endpoint	Ciltacabtagene autoleucel		Individualised therapy with selection of DPd or PVd		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a]

[d] Patient-reported endpoints are not suitable for the benefit assessment, as there was no data collection in relevant sections of the CAR-T cell therapy in the intervention arm, thus rendering a fair comparison with the control group impossible

[e] Data from sensitivity analysis 1 from IQWiG's addendum (A25-48), AEs, SAEs and severe AEs are included up to the end of the maximum duration of observation, in which a complete assessment of all events for the individual patients was made

[f] Discontinuation of at least one therapy component; in the intervention arm, only events up to the infusion of ciltacabtagene autoleucel that led to the discontinuation of at least one therapy component of the bridge therapy are collected.

[g] No suitable data, as it is unclear to what extent the AEs of special interest were systematically collected using a pre-specified list. In addition, the current duration of observation of secondary malignancies is too short.

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; DPd = daratumumab in combination with pomalidomide and dexamethasone; EORTC = European Organisation for Research and Treatment; HR = hazard ratio; ISS = International Staging System; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PGIS = Patient's global Impression of Severity; PRO-CTCAE = patient-reported outcomes version of the CTCAE; PT = preferred term; PVd = pomalidomide in combination with bortezomib and dexamethasone; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

a2) Adults with relapsed and refractory multiple myeloma, who have received at least four prior therapies, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

No data are available to allow an assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.

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

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

a1) Adults with relapsed and refractory multiple myeloma, who have received one to three prior therapies, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

Approx. 1,180 – 2,460 patients

a2) Adults with relapsed and refractory multiple myeloma, who have received at least four prior therapies, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

Approx. 1,100 – 1,180 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 Carvykti (active ingredient: ciltacabtagene autoleucel) at the following publicly accessible link (last access: 8 April 2025):

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

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material and a patient emergency card. Training material for all healthcare professionals who will prescribe, dispense, and administer ciltacabtagene autoleucel includes instructions for identifying, preventing, treating, and monitoring cytokine release syndrome and neurological side effects as well as on the risk of secondary malignancy with T cell origin. It also includes instructions on storage and transport as well as the cell thawing process, availability of one dose of tocilizumab at the point of treatment, provision of relevant information to patients, and full and appropriate reporting of side effects.

The patient training programme should explain the risks of cytokine release syndrome and serious neurologic side effects as well as the need to report symptoms immediately to the treating physician, and to carry the patient emergency card at all times.

Ciltacabtagene autoleucel must be used in a qualified treatment facility. The quality assurance measures according to the ATMP Quality Assurance Guideline apply to the use of the medicinal product for novel therapies (Advanced Therapy Medicinal Product, ATMP) ciltacabtagene autoleucel in the therapeutic indication of multiple myeloma. Annex 1 "Use of CAR-T cells in B-cell neoplasms" of the ATMP Quality Assurance Guideline provides further details.

A Direct Healthcare Professional Communication ("Rote-Hand-Brief") which reports on the occurrence of secondary malignancies of T-cell origin, including chimeric antigen receptor (CAR)-positive malignancies, is available for the currently approved CD19- or BCMA-targeted CAR T-cell therapies. Patients who have been treated with CAR-T cell products should therefore be monitored throughout their lives for the occurrence of secondary malignancies.

4. Treatment costs

Annual treatment costs:

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

a) Adults with relapsed and refractory multiple myeloma, who have received at least one prior therapy, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ciltacabtagene autoleucel[3,4,5]	€ 285,000
Additionally required SHI services	€ 778.41 – € 778.74
Appropriate comparator therapy:	
An individualised therapy with selection of	
Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies)	
Bortezomib	€ 5,610.88
Doxorubicin (pegylated, liposomal)	€ 17,458.32
Total	€ 23,069.20
Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies)	
Bortezomib	€ 2,805.44 – € 5,610.88
Dexamethasone	€ 104.64 – € 169.43
Total	€ 2,910.08 – € 5,780.31
Carfilzomib in combination with dexamethasone	
Carfilzomib	€ 150,998.96
Dexamethasone	€ 243.59
Total	€ 151,242.55
Cyclophosphamide as monotherapy (only for at least triple-refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)	
Cyclophosphamide	€ 579.58 – € 5,247.18

[3] Ciltacabtagene autoleucel is used once only.

[4] It concerns only the cost of the medicinal product Carvykti.

[5] Since leukapheresis is part of the manufacture of the medicinal product pursuant to Section 4, paragraph 14 Medicinal Products Act (AMG), no further costs are incurred in this respect for the medicinal product to be assessed.

Designation of the therapy	Annual treatment costs/ patient
Cyclophosphamide in combination with dexamethasone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)	
Cyclophosphamide	Not calculable
Dexamethasone	Not calculable
Total	Not calculable
Daratumumab monotherapy (only for at least triple-refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)	
Daratumumab	€ 136,884.50
Additionally required SHI services	€ 323.88 – € 594.36
Daratumumab in combination with pomalidomide and dexamethasone	
Daratumumab	€ 136,884.50
Pomalidomide	€ 34,049.47
Dexamethasone	€ 108.03
Total	€ 171,042.00
Additionally required SHI services	€ 260.33 – € 263.63
Daratumumab in combination with bortezomib and dexamethasone	
Daratumumab	€ 124,981.50
Bortezomib	€ 5,610.88
Dexamethasone	€ 147.76
Total	€ 130,740.14
Additionally required SHI services	€ 209.57 – € 212.58
Daratumumab in combination with carfilzomib and dexamethasone	
Daratumumab	€ 136,884.50
Carfilzomib	€ 150,998.96
Dexamethasone	€ 174.49
Total	€ 288,057.95
Additionally required SHI services	€ 231.29 – € 234.59
Elotuzumab in combination with pomalidomide and dexamethasone (only for subjects with at least two prior therapies)	
Elotuzumab	€ 88,227.60
Pomalidomide	€ 34,049.47
Dexamethasone	€ 188.86
Total	€ 122,465.93
Additionally required SHI services	€ 183.45 – € 186.18
Isatuximab in combination with pomalidomide and dexamethasone (only for subjects with at least two prior therapies)	

Designation of the therapy	Annual treatment costs/ patient
Isatuximab	€ 69,257.44
Pomalidomide	€ 34,049.47
Dexamethasone	€ 193.71
Total	€ 103,500.62
Additionally required SHI services	€ 10.49
Isatuximab in combination with carfilzomib and dexamethasone	
Isatuximab	€ 69,257.44
Carfilzomib	€ 150,998.96
Dexamethasone	€ 639.61
Total	€ 220,896.01
Melphalan monotherapy (only for at least triple-refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)	
Melphalan	€ 605.15
Melphalan in combination with prednisone or prednisolone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)	
Melphalan	€ 404.99 – € 605.15
Prednisone	€ 134.10 – € 200.38
Total	€ 539.09 – € 805.53
Prednisolone	€ 63.27 – € 94.54
Total	€ 468.26 – € 699.69
Panobinostat in combination with bortezomib and dexamethasone (only for subjects who have received at least four prior therapies)	
Panobinostat	€ 35,136.00 – € 70,272.00
Bortezomib	€ 5,610.88 – € 8,416.32
Dexamethasone	€ 169.43 – € 234.22
Total	€ 40,916.31 – € 78,922.54
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody)	
Pomalidomide	€ 30,382.60
Bortezomib	€ 8,907.27
Dexamethasone	€ 237.97
Total	€ 39,527.84
Additionally required SHI services	€ 10.49
Pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies)	
Pomalidomide	€ 34,049.47

Designation of the therapy	Annual treatment costs/ patient
Dexamethasone	€ 193.71
Total	€ 34,243.18
Additionally required SHI services	€ 10.49
high-dose therapy with autologous stem cell transplant (only for subjects who have undergone prior therapy and are eligible for an autologous stem cell transplant; after achieving remission)	
High-dose therapy with autologous stem cell transplant	€ 26,244.72
High-dose therapy with allogeneic stem cell transplant (only for subjects who have undergone prior therapy and are eligible for an allogeneic stem cell transplant; after achieving remission)	
High-dose therapy with allogeneic stem cell transplant	Not calculable

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

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed					
Ciltacabtagene autoleucel: lymphocyte depletion					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	3	€ 300
Fludarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	3	€ 300
Appropriate comparator therapy					
Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Doxorubicin (pegylated, liposomal)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	Day 4 21-day cycle	8.0	€ 800
Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy and have received at least four prior therapies)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	16.0 – 32.0	€ 1,600 - € 3,200
Carfilzomib in combination with dexamethasone					
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	6	78.0	€ 7,800
Cyclophosphamide monotherapy (only for at least triple-refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0 – 365.0	€ 1,300 – € 36,500
Daratumumab in combination with bortezomib and dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200
Daratumumab in combination with carfilzomib and dexamethasone					
Carfilzomib	Surcharge for production of a	€ 100	6	78.0	€ 7,800

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	parenteral preparation containing cytostatic agents				
Elotuzumab in combination with pomalidomide and dexamethasone (only for subjects with at least two prior therapies)					
Elotuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1st - 2nd cycle: 4 From 3rd cycle: 1	19.0	€ 1,900
Isatuximab in combination with pomalidomide and dexamethasone (only for subjects with at least two prior therapies)					
Isatuximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1st cycle: 4 From 2nd cycle: 2	28.0	€ 2,800
Isatuximab in combination with carfilzomib and dexamethasone					
Isatuximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1st cycle: 4 From 2nd cycle: 2	28.0	€ 2,800
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	6	78.0	€ 7,800
Melphalan monotherapy (only for at least triple-refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)					
Melphalan	Surcharge for production of a parenteral	€ 100	1	13.0	€ 1,300

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	preparation containing cytostatic agents				
Melphalan in combination with prednisolone or prednisone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy and have received at least four prior therapies)					
Melphalan	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	8.7 – 13.0	€ 870 - € 1,300
Panobinostat in combination with bortezomib and dexamethasone (only for subjects who have received at least four prior therapies)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1st – 8th cycle: 4 9th - 16th cycle: 2	32 – 48	€ 3,200 – € 4,800
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1st - 8th cycle: 4 From 9th cycle: 2	50.8	€ 5,080

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:

a) Adults with relapsed and refractory multiple myeloma, who have received at least one prior therapy, have demonstrated disease progression on the last therapy and are refractory to lenalidomide; pretreatment includes an immunomodulator and a proteasome inhibitor

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

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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 15 May 2025.

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

Berlin, 15 May 2025

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

Prof. Hecken