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
Daratumumab (new therapeutic indication: multiple myeloma, ineligible for stem cell transplant, combination with bortezomib, lenalidomide and dexamethasone)

of 19 February 2026

At their session on 19 February 2026, 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. In Annex XII, the following information shall be added after No. 5 to the information on the benefit assessment of Daratumumab in accordance with the resolution of 21 August 2025:

Daratumumab

Resolution of: 19 February 2026
Entry into force on: 19 February 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 4 April 2025):

DARZALEX is indicated in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma.

Therapeutic indication of the resolution (resolution of 19 February 2026):

DARZALEX is indicated in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.

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

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

Appropriate comparator therapy:

– Daratumumab in combination with lenalidomide and dexamethasone

or

– daratumumab in combination with bortezomib, melphalan and prednisone

or

– bortezomib in combination with melphalan and prednisone

or

– bortezomib in combination with lenalidomide and dexamethasone

or

– thalidomide in combination with melphalan and prednisone

or

– bortezomib in combination with cyclophosphamide and dexamethasone (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)

Extent and probability of the additional benefit of daratumumab in combination with bortezomib, lenalidomide and dexamethasone compared to bortezomib, lenalidomide and dexamethasone:

Hint for a minor additional benefit

Study results according to endpoints:[1]

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

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	↑	Advantage in health status
Health-related quality of life	↔	No relevant difference for the benefit assessment.
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		

CEPHEUS study:

- Open-label, randomised phase III study
- Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd) **versus** bortezomib + lenalidomide + dexamethasone (VRd)
- Data cut-off: final data cut-off from 8 October 2025

[1] Data from the dossier assessment of the IQWiG (A25-108) and from the addendum (A26-02), unless otherwise indicated.

Mortality

Endpoint	Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd)[a]		Bortezomib + lenalidomide + dexamethasone (VRd)[b]		D-VRd[a] vs VRd[b]
	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 [c] Absolute difference (AD)[d]
Overall survival					
	144	n.r. 48 (33.3)	145	n.r. [78.1; n.r.] 53 (36.6)	0.84 [0.57; 1.24] 0.378

Morbidity

Endpoint	Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd)[a]		Bortezomib + lenalidomide + dexamethasone (VRd)[b]		D-VRd[a] vs VRd[b]
	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 [c] Absolute difference (AD)[d]
Progression-free survival (PFS)[e]					
	144	n.r. 48 (33.3)	145	49.6 [41.9; 61.9] 73 (50.3)	0.52 [0.36; 0.75] 0.0004
Sustained MRD negativity rate (3 years), threshold value 10^{-5} cells[e] (presented additionally)					
	144	- 47 (32.6%)	145	- 26 (17.9%)	Odds ratio[f]: 2.22 [1.28; 3.84] 0.0042
Symptomatology (EORTC QLQ-C30) - Time to first deterioration[g,h]					
Fatigue	138	1.4 [1.0; 1.7] 100 (72.5[i])	137	1.5 [1.5; 2.2] 103 (75.2[i])	1.08 [0.81; 1.44] 0.599
Nausea and vomiting	138	6.0 [4.2; 16.9] 85 (61.6[i])	137	11.4 [4.5; 45.5] 70 (51.1[i])	1.23 [0.89; 1.70] 0.207
Pain	138	3.7 [2.3; 8.3] 79 (57.2[i])	137	3.5 [2.8; 4.0] 88 (64.2[i])	0.91 [0.67; 1.24] 0.560

Dyspnoea	138	3.1 [2.2; 3.7] 101 (73.2[i])	137	5.3 [2.9; 11.1] 88 (64.2[i])	1.23 [0.92; 1.65] 0.160
Insomnia	138	2.8 [1.8; 3.9] 102 (73.9[i])	137	2.8 [2.2; 4.2] 93 (67.9[i])	1.04 [0.78; 1.39] 0.783
Appetite loss	138	4.4 [3.5; 5.1] 100 (72.5[i])	137	3.6 [2.6; 4.6] 97 (70.1[i])	0.93 [0.70; 1.24] 0.634
Constipation	138	3.1 [1.6; 5.6] 94 (68.1[i])	137	1.6 [1.4; 2.4] 106 (77.4[i])	0.69 [0.51; 0.92] 0.011 AD: + 1.5 months
Diarrhoea	138	4.7 [3.5; 6.0] 117 (84,8[i])	137	3.7 [2.8; 4.4] 108 (78.8[i])	0.91 [0.70; 1.20] 0.502
Symptomatology (EORTC QLQ-MY20) - Time to first deterioration[g,h]					
Symptoms of disease	136	11.6 [4.6; 26.9] 73 (53.7[i])	135	13.9 [7.5; 28.2] 78 (57.8 [i])	1.07 [0.77; 1.48] 0.699
Side effects	136	2.4 [2.1; 3.5] 99 (72.8[i])	135	2.9 [2.1; 4.2] 94 (69.6[i])	1.17 [0.88; 1.57] 0.279
Health status (EQ-5D VAS) – Time to confirmed permanent deterioration[h,j,k]					
	121	n.r. 15 (12.4[i])	125	n.r. 27 (21.6[i])	0.43 [0.23; 0.81] 0.009

Health-related quality of life

Endpoint	**Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd)[a]**		**Bortezomib + lenalidomide + dexamethasone (VRd)[b]**		**D-VRd[a] vs VRd[b]**
	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 [c] Absolute difference (AD)[d]
EORTC QLQ-C30 - Time to first deterioration[h,l]					
Global health status	138	2.1 [1.6; 3.2] 86 (62.3[i])	137	2.8 [2.2; 4.4] 82 (59.9[i])	1.19 [0.87; 1.63] 0.274
Physical functioning	138	3.0 [1.7; 4.3] 90 (65.2[i])	137	3.5 [2.8; 4.5] 92 (67.2[i])	1.11 [0.83; 1.50] 0.484
Role functioning	138	2.1 [1.5; 3.1] 89 (64.5[i])	137	2.8 [2.1; 3.6] 92 (67.2[i])	1.04 [0.77; 1.40] 0.819

Emotional functioning	138	9.3 [3.3; 23.3] 75 (54.3[i])	137	5.3 [3.5; 12.5] 83 (60.6[i])	0.88 [0.63; 1.21] 0.420
Cognitive functioning	138	2.6 [1.8; 3.5] 105 (76.1[i])	137	3.5 [2.3; 4.9] 104 (75.9[i])	1.18 [0.89; 1.57] 0.244
Social functioning	138	2.8 [1.5; 3.3] 92 (66.7[i])	137	2.5 [1.8; 3.2] 95 (69.3[i])	0.97 [0.72; 1.31] 0.858
EORTC QLQ-MY20 - Time to first deterioration[h,l]					
Future prospects	136	8.4 [2.8; 48.5] 69 (50.7[i])	135	13.7 [4.2; 36.1] 73 (54.1[i])	1.03 [0.74; 1.44] 0.867
Body image	136	8.7 [3.5; 16.6] 80 (58.8[i])	135	11.6 [4.2; 50.5] 66 (48.9[i])	1.31 [0.94; 1.83] 0.105

Side effects

Endpoint	**Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd)[a]**		**Bortezomib + lenalidomide + dexamethasone (VRd)[b]**		**D-VRd[a] vs VRd[b]**
	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 [c] Absolute difference (AD)[d]
Total adverse events (presented additionally)					
	144	0.1 [0.1; 0.3] 144 (100)	142	0.2 [0.1; 0.3] 142 (100)	–
Serious adverse events (SAEs)					
	144	12.3 [5.5; 22.1] 109 (75.7)	142	8.3 [4.0; 16.6] 99 (69.7)	0.94 [0.72; 1.25] 0.686
Severe adverse events (CTCAE grade 3 or 4)					
	144	0.9 [0.7; 1.6] 135 (93.8)	142	1.5 [1.0; 2.1] 126 (88.7)	1.05 [0.82; 1.36] 0.686
Therapy discontinuation due to adverse events (≥ 1 active ingredient component)					
	144	58.4 [44.3; n.r.] 67 (46.5)	142	44.2 [26.5; 67.5] 75 (52.8)	0.72 [0.52; 1.003] 0.052
Specific adverse events					
Peripheral neuropathy (HLT, severe AEs)	144	n.r. 18 (12.5)	142	n.r. 16 (11.3)	1.12 [0.57; 2.21] 0.735

a. Followed by therapy with daratumumab + lenalidomide + dexamethasone from cycle 9
b. Followed by therapy with lenalidomide + dexamethasone from cycle 9
c. Effect, CI and p value according to specifications of the pharmaceutical company: Cox proportional hazards model; stratified in each case by ISS stage (I vs II vs III) and age/ ASCT eligibility (≥ 70 years vs < 70 years ineligible for ASCT vs < 70 years rejection of ASCT). For the endpoint of overall survival, the p value from the accordingly stratified log-rank test is presented.
d. Indication of absolute difference (AD) only in case of statistically significant difference; own calculation.
e. Information from the pharmaceutical company's statement.
f. Odds ratio (including 95% CI and p value) calculated using the Cochran-Mantel-Haenszel method with the stratification factors of ISS stage (stage I vs stage II vs stage III) and age/ ASCT eligibility (< 70 years ineligible, < 70 years rejection of transplant, ≥ 70 years). An OR (odds ratio) > 1 indicates an advantage of D-VRd.
g. An increase in EORTC QLQ-C30 and EORTC QLQ-MY20 scores by ≥ 10 points compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100).
h. In accordance with Module 4 A, only patients with a baseline value and at least one further value during the course of the study are included in the evaluations.
i. IQWiG calculation
j. Operationalisation reflects a combination of confirmed and permanent deterioration.
k. A decrease in EQ-5D VAS score by ≥ 15 points compared to the start of study is considered as clinically relevant deterioration (scale range: 0 to 100).
l. A decrease in EORTC QLQ-C30 and EORTC QLQ-MY20 scores by ≥ 10 points compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100).

Abbreviations used:
AD = absolute difference; ASCT = autologous stem cell transplant; CTCAE = Common Terminology Criteria for Adverse Events; D-VRd = daratumumab + bortezomib + lenalidomide + dexamethasone; EORTC = European Organisation for Research and Treatment of Cancer; HLT = High Level Term; HR = hazard ratio; ISS = International Staging System; CI = confidence interval; MRD = minimal residual disease; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PFS = progression-free survival; pU = pharmaceutical company; QLQ-C30 = Quality of Life Questionnaire − Core 30; QLQ-MY20 = Quality of Life Questionnaire – Multiple Myeloma 20; SAE = serious adverse event; AE = adverse event; VRd = bortezomib + lenalidomide + dexamethasone; VAS = visual analogue scale; vs = versus.

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

<u>Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant</u>

Approx. 3,450 to 3,680 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 Darzalex (active ingredient: daratumumab) at the following publicly accessible link (last access: 2 December 2025):

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

Treatment with daratumumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with multiple myeloma.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material and a patient identification card. The training material for medical professionals and blood banks contains instructions on how to manage the risk of daratumumab interfering with blood typing (indirect antihuman globulin test or Coombs test). Interference with blood typing induced by daratumumab may persist for up to six months after the last infusion of the medicinal product; therefore, medical professionals should advise patients to carry their patient identification card with them for up to six months after the end of the treatment.

4. Treatment costs

Annual treatment costs:

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

Annual treatment costs:

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Daratumumab in combination with bortezomib, lenalidomide and dexamethasone	
Daratumumab	€ 110,353.90
Bortezomib	€ 5,610.88
Lenalidomide	€ 440.59
Dexamethasone	€ 225.99
Total:	€ 116,631.36
Additionally required SHI costs	€ 225.26 – € 227.99
Appropriate comparator therapy:	

Designation of the therapy	Annual treatment costs/ patient
Daratumumab in combination with lenalidomide and dexamethasone	
Daratumumab	€ 133,586.30
Lenalidomide	€ 464.40
Dexamethasone	€ 108.03
Total:	€ 134,158.73
Additionally required SHI costs	€ 261.25 – € 264.55
daratumumab in combination with bortezomib, melphalan and prednisone	
Daratumumab	€ 124,293.34
Bortezomib	€ 6,803.19
Melphalan	€ 313.64
Prednisone	€ 73.19
Total:	€ 131,483.36
Additionally required SHI costs	€ 214.21 – € 217.28
bortezomib in combination with melphalan and prednisone	
Bortezomib	€ 8,907.27
Melphalan	€ 313.64
Prednisone	€ 97.59
Total:	€ 9,318.50
bortezomib in combination with lenalidomide and dexamethasone	
Induction	
Bortezomib	€ 5,610.88
Lenalidomide	€ 190.52
Dexamethasone	€ 169.43
Follow-up treatment	
Lenalidomide	€ 250.06
Dexamethasone	€ 104.31
Total:	€ 6,325.20
Additionally required SHI costs	€ 10.49

thalidomide in combination with melphalan and prednisone

Designation of the therapy	Annual treatment costs/ patient
Thalidomide	€ 15,011.72
Melphalan	€ 348.49
Prednisone	€ 134.10
Total:	€ 15,494.31
Additionally required SHI costs	€ 10.49
Bortezomib in combination with cyclophosphamide and dexamethasone (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)	
Bortezomib	€ 12,203.66
Cyclophosphamide	€ 790.83
Dexamethasone	€ 518.55
Total:	€ 13,513.04
Total:	€ 13,513.04

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 December 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					
Daratumumab in combination with bortezomib, lenalidomide and dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	8	32.0	€ 3,200
Appropriate comparator therapy					
daratumumab in combination with bortezomib, melphalan and prednisone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4 – 8	38.8	€ 3,880

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Bortezomib in combination with melphalan and prednisone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4 – 8	50.8	€ 5,080
Bortezomib in combination with lenalidomide and dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200
Bortezomib in combination with cyclophosphamide and dexamethasone (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	69.6	€ 6,960
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740

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:

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

- 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.

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 19 February 2026.

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

Berlin, 19 February 2026

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

Prof. Hecken