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 and Daratumumab (new therapeutic indication: smouldering multiple myeloma (SMM))

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 the active ingredient in the version of the resolution of 19 February 2026 on the therapeutic indication "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":**

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 18 July 2025):

DARZALEX as monotherapy is indicated for the treatment of adult patients with smouldering multiple myeloma at high risk of developing multiple myeloma.

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

See new therapeutic indication according to marketing authorisation.

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

Adults with smouldering multiple myeloma at high risk of developing multiple myeloma

Appropriate comparator therapy:

- Monitoring wait-and-see approach

Extent and probability of the additional benefit of daratumumab compared to monitoring wait-and-see approach:

Hint for a minor additional benefit.

Study results according to endpoints:[1]

Adults with smouldering multiple myeloma at high risk of developing multiple myeloma

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑	Advantage in overall survival.
Morbidity	↑	Advantages in the endpoints of pain and dyspnoea.
Health-related quality of life	↑	Advantages in the endpoints of global health status and emotional functioning.
Side effects	↔	No relevant differences 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		

AQUILA study:

- Study design: open-label, randomised phase III study, data cut-off from 01.05.2024
- Comparison: Daratumumab **vs** monitoring wait-and-see approach

Mortality

Endpoint	Daratumumab		Monitoring wait-and-see approach		Daratumumab vs Monitoring wait-and-see approach
	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] Absolute Difference (AD)[b]
Overall survival					
	194	n.r. 15 (7.7)	196	n.r. 26 (13.3)	0.52 [0.27; 0.98] 0.0419

[1] Data from the dossier assessment of the IQWiG (A25-109) and from the addendum (A26-03), unless otherwise indicated.

Morbidity

Endpoint	Daratumumab		Monitoring wait-and-see approach		Daratumumab vs Monitoring wait-and-see approach
	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] Absolute Difference (AD)[b]
Progression-free survival[c]					
	194	n.r. [66.69; n.c.] 67 (34.5)	196	41.46 [26.41; 53.32] 99 (50.5)	0.49 [0.36; 0.67] < 0.0001
Symptomatology					
EORTC QLQ-C30 (time to first deterioration)[d]					
Fatigue	194	10.22 [5.72; 14.32] 128 (66.0)	196	13.73 [6.64; 14.06] 126 (64.3)	0.88 [0.69; 1.13] 0.321
Nausea and vomiting	194	68.24 [61.57; n.c.] 65 (33.5)	196	67.68 [51.28; n.c.] 65 (33.2)	0.78 [0.55; 1.11] 0.169
Pain	194	25.23 [14.13; 35.98] 116 (59.8)	196	14.72 [11.17; 27.63] 118 (60.2)	0.73 [0.57; 0.95] 0.020 AD: + 10.51 months
Dyspnoea	194	60.72 [41.40; n.c.] 83 (42.8)	196	31.11 [24.64; 63.08] 88 (44.9)	0.71 [0.53; 0.97] 0.031 AD: + 29.61 months
Insomnia	194	35.48 [19.75; 52.47] 104 (53.6)	196	26.51 [18.04; 47.47] 93 (47.4)	0.91 [0.69; 1.21] 0.509
Appetite loss	194	67.71 [60.62; n.c.] 71 (36.6)	196	57.95 [33.25; 67.68] 74 (37.8)	0.78 [0.56; 1.08] 0.142
Constipation	194	63.77 [49.41; 67.71] 82 (42.3)	196	49.51 [41.43; 58.02] 77 (39.3)	0.85 [0.62; 1.16] 0.309
Diarrhoea	194	n.r. [48.13; n.c.] 75 (38.7)	196	50.63 [36.01; n.c.] 71 (36.2)	0.94 [0.68; 1.31] 0.723
Health status					
EQ-5D VAS (time to first deterioration)[e]					
	194	60.85 [49.84; n.c.] 80 (41.2)	196	55.20 [33.58; n.c.] 79 (40.3)	0.83 [0.61; 1.14] 0.256

Health-related quality of life

Endpoint	Daratumumab		Monitoring wait-and-see approach		Daratumumab vs Monitoring wait-and-see approach
	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] Absolute Difference (AD)[b]
EORTC QLQ-C30 (time to first deterioration) [d]					
Global health status	194	29.37 [14.32; 48.13] 108 (55.7)	196	18.96 [10.94; 26.18] 111 (56.6)	0.76 [0.58; 0.99] 0.045 AD: + 10.41 months
Physical functioning	194	41.76 [29.18; 60.62] 103 (53.1)	196	30.69 [18.07; 46.39] 97 (49.5)	0.83 [0.63; 1.10] 0.190
Role functioning	194	19.25 [13.96; 25.86] 115 (59.3)	196	20.47 [13.80; 31.44] 110 (56.1)	0.89 [0.68; 1.15] 0.365
Emotional functioning	194	53.95 [36.27; 61.70] 91 (46.9)	196	29.77 [23.85; 49.71] 95 (48.5)	0.69 [0.51; 0.92] 0.012 AD: + 24.18 months
Cognitive functioning	194	50.76 [28.16; 64.23] 92 (47.4)	196	28.09 [17.15; 47.47] 97 (49.5)	0.77 [0.57; 1.02] 0.070
Social functioning	194	49.81 [25.04; 62.00] 94 (48.5)	196	38.80 [30.82; 50.63] 92 (46.9)	0.87 [0.65; 1.16] 0.338

Side effects

Endpoint	Daratumumab		Monitoring wait-and-see approach		Daratumumab vs Monitoring wait-and-see approach
	N	Median in months [95% CI] *Patients with event n (%)*	N	Median in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a] Absolute Difference (AD)[b]
Total adverse events (presented additionally)					
	193	0.13 [0.07; 0.26] 187 (96.9)	196	3.68 [2.89; 5.06] 162 (82.7)	–
Serious adverse events (SAEs)					
	193	n.r. [36.93; n.c.] 56 (29.0)	196	n.r. 38 (19.4)	1.47 [0.97; 2.22]; 0.071
Severe adverse events (CTCAE grade 3 or 4)					
	193	36.93 [35.74; n.c.] 78 (40.4)	196	n.r. 60 (30.6)	1.33 [0.94; 1.86]; 0.102
Therapy discontinuation due to adverse events					
No suitable data[f]					
Specific adverse events					
General disorders and administration site conditions (SOC, AEs)	193	4.96 [2.37; 10.68] 126 (65.3)	196	n.r. 57 (29.1)	3.40 [2.48; 4.67]; < 0.001
Gastrointestinal disorders (SOC, AEs)	193	10.88 [7.10; 14.82] 119 (61.7)	196	n.r. 52 (26.5)	3.10 [2.23; 4.29]; < 0.001
Nervous system disorders (SOC, AEs)	193	32.89 [13.31; n.c.] 94 (48.7)	196	n.r. 43 (21.9)	2.73 [1.90; 3.92]; < 0.001
Respiratory, thoracic and mediastinal disorders (SOC, AEs)	193	n.r. [20.47; n.c.] 85 (44.0)	196	n.r. 41 (20.9)	2.52 [1.73; 3.66]; < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)	193	n.r. [36.47; n.c.] 77 (39.9)	196	n.r. 20 (10.2)	4.48 [2.73; 7.33]; < 0.001
Insomnia (PT, AEs)	193	n.r. 43 (22.3)	196	n.r. 5 (2.6)	9.48 [3.75; 23.97]; < 0.001
Vascular disorders (SOC, AEs)	193	n.r. 51 (26.4)	196	n.r. 23 (11.7)	2.35 [1.43; 3.85]; < 0.001

Ear and labyrinth disorders (SOC, AEs)	193	n.r. 21 (10.9)	196	n.r. 6 (3.1)	3.61 [1.46; 8.95]; 0.006
Infections and infestations (SOC, severe AEs)	193	n.r. [36.93; n.c.] 32 (16.6)	196	n.r. 9 (4.6)	3.71 [1.74; 7.93]; < 0.001

[a] Cox proportional hazards model with treatment as the only explanatory variable and with the stratification factor - number of risk factors associated with progression to multiple myeloma (< 3 risk factors vs ≥ 3 risk factors).
[b] Data on absolute difference (AD) only in the case of statistically significant difference; own calculation
[c] Results from the pharmaceutical company's dossier.
[d] An increase in score by ≥ 10 points compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100).
[e] A decrease in score by ≥ 15 points compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100).
[f] AEs leading to therapy discontinuation are only assessed in the intervention arm. In the intervention arm, 11 (5.7%) patients discontinued therapy due to AEs.

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR = hazard ratio; 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; PT = preferred term; QLQ-C30 = Quality of Life Questionnaire – Core 30; SOC = system organ class; AE = adverse event; SAE = serious adverse event; VAS = visual analogue scale; vs = versus

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

Adults with smouldering multiple myeloma at high risk of developing multiple myeloma

Approx. 160 to 325 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: 12 January 2026):

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:

Adults with smouldering multiple myeloma at high risk of developing multiple myeloma

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Daratumumab	€ 133,586.30
Additionally required SHI services	*€ 10.49*
Appropriate comparator therapy:	
Monitoring wait-and-see approach	Not calculable

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

Other SHI services:

not applicable

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 smouldering multiple myeloma at high risk of developing multiple myeloma

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient approved in monotherapy.

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