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, first-line, suitable for stem cell transplantation, combination with bortezomib, lenalidomide and dexamethasone)

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. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Daratumumab in accordance with the resolution of 16 May 2024:

Daratumumab

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 21 October 2024):

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

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

See new therapeutic indication according to marketing authorisation.

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

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

Appropriate comparator therapy:

- An induction therapy consisting of:
  - bortezomib + thalidomide + dexamethasone (VTd)

    or
  - bortezomib + cyclophosphamide + dexamethasone (VCd) [only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive]

    or
  - daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd)
- followed by a high-dose therapy with melphalan and subsequent autologous stem cell transplant
- followed by a consolidation therapy with D-VTd (only if an induction therapy with D-VTd is administered)

  followed by maintenance treatment with lenalidomide

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

An additional benefit is not proven.

Study results according to endpoints:[1]

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

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
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

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

Approx. 1,750 to 1,910 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: 21 February 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

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A24-114) unless otherwise indicated.

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.

Adults with newly diagnosed multiple myeloma who are eligible 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	
Induction	
Daratumumab	€ 71,418.00
Bortezomib	€ 2,805.44
Lenalidomide	€ 142.89
Dexamethasone	€ 104.31
Total induction	€ 74,470.64
High-dose chemotherapy and subsequent autologous stem cell transplant	
High-dose chemotherapy with autologous stem cell transplant	€ 26,244.72
Consolidation	
Daratumumab	€ 23,806.00
Bortezomib	€ 1,402.72
Lenalidomide	€ 71.45
Dexamethasone	€ 81.95
Total consolidation	€ 25,362.12
Maintenance	
Daratumumab	€ 36,899.30
Lenalidomide	€ 295.31
Total maintenance	€ 37,194.61
Total	
Induction + high-dose chemotherapy with autologous stem cell transplant + consolidation + maintenance	€ 163,272.09
Additionally required SHI services	€ 251.41 – € 254.59

Appropriate comparator therapy:	
Bortezomib + thalidomide + dexamethasone (VTd)	
Induction	
Bortezomib	€ 2,805.44 – € 4,208.16
Thalidomide	€ 2,166.24 – € 11,914.32
Dexamethasone	€ 159.64 – € 186.26
Total induction	€ 5,131.32 – € 16,308.74
High-dose therapy with melphalan and subsequent autologous stem cell transplant	
High-dose therapy with melphalan and subsequent autologous stem cell transplant	€ 26,244.72
Maintenance	
Lenalidomide	€ 295.31 (for 6 cycles of induction therapy) – € 390.57 (for 4 cycles of induction therapy)
Total	
Induction + high-dose therapy with melphalan and subsequent autologous stem cell transplant + maintenance	€ 31,766.61 - € -42,848.77
Additionally required SHI services	€ 10.49
Bortezomib + cyclophosphamide + dexamethasone (VCd) (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)	
Induction	
Bortezomib	€ 2,104.08 – € 2,805.44
Cyclophosphamide	€ 133.75 – € 194.27
Dexamethasone	€ 159.64
Total induction	€ 2,397.47 – € 3,159.35
High-dose therapy with melphalan and subsequent autologous stem cell transplant	
High-dose therapy with melphalan and subsequent autologous stem cell transplant	€ 26,244.72
Maintenance	
Lenalidomide	€ 438.21 (for 4 cycles of induction therapy) – € 476.31 (for 3 cycles of induction therapy)
Total	
Induction + high-dose therapy with melphalan and subsequent autologous stem cell transplant + maintenance	€ 29,118.50 – € 29,842.28
Additionally required SHI services	€ 10.49
Daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd)	
Induction	

Daratumumab	€ 71,418.00
Bortezomib	€ 2,805.44
Thalidomide	€ 4,332.48
Dexamethasone	€ 60.22
Total induction	€ 78,616.14
High-dose therapy with melphalan and subsequent autologous stem cell transplant	
High-dose therapy with melphalan and subsequent autologous stem cell transplant	€ 26,244.72
Consolidation	
Daratumumab	€ 23,806.00
Bortezomib	€ 1,402.72
Thalidomide	€ 2,166.24
Dexamethasone	€ 36.62
Total consolidation	€ 27,411.58
Maintenance	
Lenalidomide	€ 295.31
Total	
Induction + high-dose therapy with melphalan and subsequent autologous stem cell transplant + consolidation + maintenance	€ 132,567.75
Additionally required SHI services	€ 210.96 - € 213.83

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					
Daratumumab in combination with bortezomib, lenalidomide and dexamethasone (induction + consolidation)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	24.0	€ 2,400

Appropriate comparator therapy					
Bortezomib + thalidomide + dexamethasone (VTd) (induction)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	16 – 24	€ 1,600 – € 2,400
Bortezomib + cyclophosphamide + dexamethasone (VCd) (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive) (induction)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	12.0 – 16.0	€ 1,200 - € 1,600
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	3.0 – 4.0	€ 300 – € 400
Daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd) (induction + consolidation)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	24.0	€ 2,400

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 eligible for autologous stem cell transplant

- 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