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) Elranatamab (multiple myeloma, at least 3 prior therapies)

of 4 July 2024

At its session on 4 July 2024, 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 Elranatamab as follows:

Elranatamab

Resolution of: 4 July 2024

Entry into force on: 4 July 2024

Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 7 December 2023):

Elrexfio is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Therapeutic indication of the resolution (resolution of 4 July 2024):

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 three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Appropriate comparator therapy:

A patient-individual therapy under selection of:

- carfilzomib in combination with lenalidomide and dexamethasone
- elotuzumab in combination with lenalidomide and dexamethasone
- elotuzumab in combination with pomalidomide and dexamethasone
- daratumumab in combination with bortezomib and dexamethasone
- daratumumab in combination with lenalidomide and dexamethasone
- daratumumab in combination with carfilzomib and dexamethasone
- daratumumab in combination with pomalidomide and dexamethasone (only for subjects who are refractory to lenalidomide)
- isatuximab in combination with carfilzomib and dexamethasone
- isatuximab in combination with pomalidomide and dexamethasone

- pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)
- ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)
- carfilzomib in combination with dexamethasone

taking into account the active ingredients and combinations of active ingredients used in the prior therapies as well as the type and duration of the response to the respective prior therapies

Extent and probability of the additional benefit of elranatamab compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Appropriate comparator therapy:

A patient-individual therapy under selection of:

- carfilzomib in combination with lenalidomide and dexamethasone
- elotuzumab in combination with lenalidomide and dexamethasone
- elotuzumab in combination with pomalidomide and dexamethasone
- daratumumab in combination with bortezomib and dexamethasone
- daratumumab in combination with lenalidomide and dexamethasone
- daratumumab in combination with carfilzomib and dexamethasone
- daratumumab in combination with pomalidomide and dexamethasone
- isatuximab in combination with carfilzomib and dexamethasone
- isatuximab in combination with pomalidomide and dexamethasone
- pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)
- ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)
- panobinostat in combination with bortezomib and dexamethasone
- carfilzomib in combination with dexamethasone

- pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)
- lenalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)
- bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)
- bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)
- daratumumab monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)
- cyclophosphamide as monotherapy or in combination with dexamethasone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)
- 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)

taking into account the general condition, the active ingredients and combinations of active ingredients used in the prior therapies and the type and duration of the response to the respective prior therapies

Extent and probability of the additional benefit of elranatamab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

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	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		

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

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	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

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Approx. 150 – 160 patients

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

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 Elrexfio (active ingredient: elranatamab) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 21 June 2024):

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

Treatment with elranatamab 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 a patient card.

The patient card is intended to explain the risks of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome and when patients should seek urgent medical treatment in the event of signs and symptoms. In addition, the patient card reminds patients that they should stay close to a medical facility and be monitored daily for signs and symptoms for 48 hours after being administered the step-up doses.

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The EMA will assess new information on this medicinal product at least annually and update the product information as necessary.

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 three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Elranatamab	€ 285,685.65- € 390,211.61
Additionally required SHI services	€ 64.25
Appropriate comparator therapy:	
A patient-individual therapy under selection of:	
carfilzomib in combination with lenalidomide and dexamethasone	
Carfilzomib	€ 80,017.58
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 80,674.46
Additionally required SHI services	€ 11.40
Carfilzomib in combination with dexamethasone	
Carfilzomib	€ 150,928.12
Dexamethasone	€ 243.11
Total	€ 151,171.23
Daratumumab in combination with lenalidomide and dexamethasone	
Daratumumab	€ 133,581.01
Lenalidomide	€ 463.41
Dexamethasone	€ 107.90
Total	€ 134,152.32
Additionally required SHI services	€ 251.75 - € 255.05

Daratumumab in combination with pomalidomide and dexamethasone (only for subjects who are refractory to lenalidomide)	
Daratumumab	€ 133,581.01
Pomalidomide	€ 111,053.02
Dexamethasone	€ 107.90
Total	€ 244,741.93
Additionally required SHI services	€ 251.75 - € 255.05
Daratumumab in combination with bortezomib and dexamethasone	
Daratumumab	€ 121,965.27
Bortezomib	€ 5,603.52
Dexamethasone	€ 147.30
Total	€ 127,716.09
Additionally required SHI services	€ 201.81 - € 204.82
Daratumumab in combination with carfilzomib and dexamethasone	
Daratumumab	€ 133,581.01
Carfilzomib	€ 150,928.12
Dexamethasone	€ 174.17
Total	€ 284,683.30
Additionally required SHI services	€ 222.71 - € 226.01
Elotuzumab in combination with lenalidomide and dexamethasone	
Elotuzumab	€ 88,213.80
Lenalidomide	€ 463.41
Dexamethasone	€ 185.74
Total	€ 88,862.95
Additionally required SHI services	€ 271.51 - € 275.81
Elotuzumab + pomalidomide + dexamethasone	
Elotuzumab	€ 88,213.80
Pomalidomide	€ 111,053.02
Dexamethasone	€ 188.58
Total	€ 199,455.40
Additionally required SHI services	€ 176.13 - € 178.86
Isatuximab in combination with pomalidomide and dexamethasone	
Isatuximab	€ 69,231.68
Pomalidomide	€ 111,053.02
Dexamethasone	€ 193.47
Total	€ 180,478.17
Additionally required SHI services	€ 11.40

Isatuximab in combination with carfilzomib and dexamethasone	
Isatuximab	€ 69,231.68
Carfilzomib	€ 150,928.12
Dexamethasone	€ 630.40
Total	€ 220,790.20
Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)	
Ixazomib	€ 78,848.90
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 79,505.78
Additionally required SHI services	€ 11.40
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)	
Pomalidomide	€ 99,093.46
Bortezomib	€ 8,895.59
Dexamethasone	€ 237.50
Total	€ 108,226.55
Additionally required SHI services	€ 11.40

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2024)

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Elranatamab	€ 285,685.65- € 390,211.61
Additionally required SHI services	€ 64.25
Appropriate comparator therapy:	
A patient-individual therapy under selection of:	
Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)	
Bortezomib	€ 5,603.52
Doxorubicin (pegylated, liposomal)	€ 17,454.64
Total	€ 23,058.16

Designation of the therapy	Annual treatment costs/ patient
Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)	
Bortezomib	€ 2,801.76 - € 5,603.52
Dexamethasone	€ 104.18 - € 168.97
Total	€ 2,905.94 - € 5,772.49
Carfilzomib in combination with lenalidomide and dexamethasone	
Carfilzomib	€ 80,017.58
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 80,674.46
Additionally required SHI services	€ 11.40
Carfilzomib in combination with dexamethasone	
Carfilzomib	€ 150,928.12
Dexamethasone	€ 243.11
Total	€ 151,171.23
Cyclophosphamide monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)	
Cyclophosphamide	€ 515.75 - € 4,452.39
Cyclophosphamide in combination with dexamethasone	
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)	
Daratumumab	€ 133,581.01
Additionally required SHI services	€ 314.15 - € 574.20
Daratumumab in combination with lenalidomide and dexamethasone	
Daratumumab	€ 133,581.01
Lenalidomide	€ 463.41
Dexamethasone	€ 107.90
Total	€ 134,152.32
Additionally required SHI services	€ 251.75 - € 255.05
Daratumumab in combination with pomalidomide and dexamethasone	
Daratumumab	€ 133,581.01
Pomalidomide	€ 111,053.02
Dexamethasone	€ 107.90

Designation of the therapy	Annual treatment costs/ patient
Total	€ 244,741.93
Additionally required SHI services	€ 251.75 - € 255.05
Daratumumab in combination with bortezomib and dexamethasone	
Daratumumab	€ 121,965.27
Bortezomib	€ 5,603.52
Dexamethasone	€ 147.30
Total	€ 127,716.09
Additionally required SHI services	€ 201.81 - € 204.82
Daratumumab in combination with carfilzomib and dexamethasone	
Daratumumab	€ 133,581.01
Carfilzomib	€ 150,928.12
Dexamethasone	€ 174.17
Total	€ 284,683.30
Additionally required SHI services	€ 222.71 - € 226.01
Elotuzumab in combination with lenalidomide and dexamethasone	
Elotuzumab	€ 88,213.80
Lenalidomide	€ 463.41
Dexamethasone	€ 185.74
Total	€ 88,862.95
Additionally required SHI services	€ 271.51 - € 275.81
Elotuzumab + pomalidomide + dexamethasone	
Elotuzumab	€ 88,213.80
Pomalidomide	€ 111,053.02
Dexamethasone	€ 188.58
Total	€ 199,455.40
Additionally required SHI services	€ 176.13 - € 178.86
Isatuximab in combination with pomalidomide and dexamethasone	
Isatuximab	€ 69,231.68
Pomalidomide	€ 111,053.02
Dexamethasone	€ 193.47
Total	€ 180,478.17
Additionally required SHI services	€ 11.40
Isatuximab in combination with carfilzomib and dexamethasone	
Isatuximab	€ 69,231.68
Carfilzomib	€ 150,928.12

Designation of the therapy	Annual treatment costs/ patient
Dexamethasone	€ 630.40
Total	€ 220,790.20
Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)	
Ixazomib	€ 78,848.90
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 79,505.78
Additionally required SHI services	€ 11.40
Lenalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)	
Lenalidomide	€ 463.41
Dexamethasone	€ 312.53
Total	€ 775.94
Additionally required SHI services	€ 11.40
Melphalan monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)	
Melphalan	€ 602.16
Melphalan in combination with prednisone or prednisolone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)	
Melphalan	€ 402.98 - € 602.16
Prednisone	€ 133.54 - € 199.54
Total	€ 536.52 - € 801.70
Prednisolone	€ 62.71 - € 93.70
Total	€ 465.69 - € 695.86
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)	
Pomalidomide	€ 99,093.46
Bortezomib	€ 8,895.59
Dexamethasone	€ 237.50
Total	€ 108,226.55
Additionally required SHI services	€ 11.40
Pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)	
Pomalidomide	€ 111,053.02
Dexamethasone	€ 193.47
Total	€ 111,246.49

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI services	€ 11.40
Panobinostat in combination with bortezomib and dexamethasone	
Panobinostat	€ 35,134.16 - € 70,268.32
Bortezomib	€ 5,603.52 - € 8,405.28
Dexamethasone	€ 168.97 - € 233.76
Total	€ 40,906.65 - € 78,907.36

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2024)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient year	Costs/ patient year
Appropriate comparator therapy					
Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200
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)					
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 lenalidomide and dexamethasone					
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1st - 12th cycle: 6 From 13th cycle: 4	76.0	€ 7,600
Carfilzomib in combination with dexamethasone					
Carfilzomib	Surcharge for production of a parenteral	€ 100	6	78.0	€ 7,800

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient year	Costs/ patient year
	preparation containing cytostatic agents				
Cyclophosphamide monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
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 parenteral preparation containing cytostatic agents	€ 100	6	78.0	€ 7,800
Elotuzumab in combination with lenalidomide and dexamethasone					
Elotuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1st - 2nd cycle: 4 From 3rd cycle: 2	30.0	€ 3,000

Elotuzumab + pomalidomide + dexamethasone					
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					
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
Panobinostat in combination with bortezomib and dexamethasone					
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 and lenalidomide)					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1st - 8th cycle: 4 From 9th cycle: 2	50.8	€ 5,080
Melphalan monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					

Melphalan	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0	€ 1,300
Melphalan in combination with prednisolone or prednisone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
Melphalan	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	8.7 – 13.0	€ 870 - € 1,300

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 three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

- 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 authorised in monotherapy.

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

- 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 authorised 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 4 July 2024.

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

Berlin, 4 July 2024

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

Prof. Hecken