

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

Resolution of: 4 July 2024

Valid until: unlimited

Entry into force on: 4 July 2024

Federal Gazette, BAnz AT 15 08 2024 B2

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

Elrexio 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.

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## 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 Elrexio (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/elrexio-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/elrexio-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:	
<i>carfilzomib in combination with lenalidomide and dexamethasone</i>	
Carfilzomib	€ 80,017.58
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 80,674.46
Additionally required SHI services	€ 11.40
<i>Carfilzomib in combination with dexamethasone</i>	
Carfilzomib	€ 150,928.12
Dexamethasone	€ 243.11
Total	€ 151,171.23
<i>Daratumumab in combination with lenalidomide and dexamethasone</i>	
Daratumumab	€ 133,581.01
Lenalidomide	€ 463.41
Dexamethasone	€ 107.90
Total	€ 134,152.32
Additionally required SHI services	€ 251.75 - € 255.05

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

<i>Isatuximab in combination with carfilzomib and dexamethasone</i>	
Isatuximab	€ 69,231.68
Carfilzomib	€ 150,928.12
Dexamethasone	€ 630.40
Total	€ 220,790.20
<i>Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)</i>	
Ixazomib	€ 78,848.90
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 79,505.78
Additionally required SHI services	€ 11.40
<i>Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)</i>	
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:	
<i>Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)</i>	
Bortezomib	€ 5,603.52
Doxorubicin (pegylated, liposomal)	€ 17,454.64
Total	€ 23,058.16



Designation of the therapy	Annual treatment costs/ patient
<i>Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)</i>	
Bortezomib	€ 2,801.76 - € 5,603.52
Dexamethasone	€ 104.18 - € 168.97
Total	€ 2,905.94 - € 5,772.49
<i>Carfilzomib in combination with lenalidomide and dexamethasone</i>	
Carfilzomib	€ 80,017.58
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 80,674.46
Additionally required SHI services	€ 11.40
<i>Carfilzomib in combination with dexamethasone</i>	
Carfilzomib	€ 150,928.12
Dexamethasone	€ 243.11
Total	€ 151,171.23
<i>Cyclophosphamide monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)</i>	
Cyclophosphamide	€ 515.75 - € 4,452.39
<i>Cyclophosphamide in combination with dexamethasone</i>	
Cyclophosphamide	Not calculable
Dexamethasone	Not calculable
Total	Not calculable
<i>Daratumumab monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)</i>	
Daratumumab	€ 133,581.01
Additionally required SHI services	€ 314.15 - € 574.20
<i>Daratumumab in combination with lenalidomide and dexamethasone</i>	
Daratumumab	€ 133,581.01
Lenalidomide	€ 463.41
Dexamethasone	€ 107.90
Total	€ 134,152.32
Additionally required SHI services	€ 251.75 - € 255.05
<i>Daratumumab in combination with pomalidomide and dexamethasone</i>	
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
<i>Daratumumab in combination with bortezomib and dexamethasone</i>	
Daratumumab	€ 121,965.27
Bortezomib	€ 5,603.52
Dexamethasone	€ 147.30
Total	€ 127,716.09
Additionally required SHI services	€ 201.81 - € 204.82
<i>Daratumumab in combination with carfilzomib and dexamethasone</i>	
Daratumumab	€ 133,581.01
Carfilzomib	€ 150,928.12
Dexamethasone	€ 174.17
Total	€ 284,683.30
Additionally required SHI services	€ 222.71 - € 226.01
<i>Elotuzumab in combination with lenalidomide and dexamethasone</i>	
Elotuzumab	€ 88,213.80
Lenalidomide	€ 463.41
Dexamethasone	€ 185.74
Total	€ 88,862.95
Additionally required SHI services	€ 271.51 - € 275.81
<i>Elotuzumab + pomalidomide + dexamethasone</i>	
Elotuzumab	€ 88,213.80
Pomalidomide	€ 111,053.02
Dexamethasone	€ 188.58
Total	€ 199,455.40
Additionally required SHI services	€ 176.13 - € 178.86
<i>Isatuximab in combination with pomalidomide and dexamethasone</i>	
Isatuximab	€ 69,231.68
Pomalidomide	€ 111,053.02
Dexamethasone	€ 193.47
Total	€ 180,478.17
Additionally required SHI services	€ 11.40
<i>Isatuximab in combination with carfilzomib and dexamethasone</i>	
Isatuximab	€ 69,231.68
Carfilzomib	€ 150,928.12

Designation of the therapy	Annual treatment costs/ patient
Dexamethasone	€ 630.40
Total	€ 220,790.20
<i>Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)</i>	
Ixazomib	€ 78,848.90
Lenalidomide	€ 463.41
Dexamethasone	€ 193.47
Total	€ 79,505.78
Additionally required SHI services	€ 11.40
<i>Lenalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)</i>	
Lenalidomide	€ 463.41
Dexamethasone	€ 312.53
Total	€ 775.94
Additionally required SHI services	€ 11.40
<i>Melphalan monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)</i>	
Melphalan	€ 602.16
<i>Melphalan in combination with prednisone or prednisolone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)</i>	
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
<i>Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)</i>	
Pomalidomide	€ 99,093.46
Bortezomib	€ 8,895.59
Dexamethasone	€ 237.50
Total	€ 108,226.55
Additionally required SHI services	€ 11.40
<i>Pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)</i>	
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
<i>Panobinostat in combination with bortezomib and dexamethasone</i>	
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					
<i>Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)</i>					
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
<i>Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)</i>					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	16.0 – 32.0	€ 1,600 - € 3,200
<i>Carfilzomib in combination with lenalidomide and dexamethasone</i>					
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1st - 12th cycle: 6 From 13th cycle: 4	76.0	€ 7,600
<i>Carfilzomib in combination with dexamethasone</i>					
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				
<i>Cyclophosphamide monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)</i>					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0 – 365.0	€ 1,300 - € 36,500
<i>Daratumumab in combination with bortezomib and dexamethasone</i>					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200
<i>Daratumumab in combination with carfilzomib and dexamethasone</i>					
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	6	78.0	€ 7,800
<i>Elotuzumab in combination with lenalidomide and dexamethasone</i>					
Elotuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	<u>1st - 2nd cycle:</u> 4 <u>From 3rd cycle:</u> 2	30.0	€ 3,000

<i>Elotuzumab + pomalidomide + dexamethasone</i>					
Elotuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	<u>1st - 2nd cycle:</u> 4  <u>From 3rd cycle:</u> 1	19.0	€ 1,900
<i>Isatuximab in combination with pomalidomide and dexamethasone</i>					
Isatuximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	<u>1st cycle:</u> 4  <u>From 2nd cycle:</u> 2	28.0	€ 2,800
<i>Isatuximab in combination with carfilzomib and dexamethasone</i>					
Isatuximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	<u>1st cycle:</u> 4  <u>From 2nd cycle:</u> 2	28.0	€ 2,800
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	6	78.0	€ 7,800
<i>Panobinostat in combination with bortezomib and dexamethasone</i>					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	<u>1st – 8th cycle:</u> 4  <u>9th - 16th cycle:</u> 2	32 – 48	€ 3,200 – € 4,800
<i>Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)</i>					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	<u>1st - 8th cycle:</u> 4 <u>From 9th cycle:</u> 2	50.8	€ 5,080
<i>Melphalan monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)</i>					

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