Melphalan flufenamide (multiple myeloma (after at least 3 prior therapies, combination with dexamethasone))

Resolution of: 16 March 2023/ 23 May 2023 Valid until: unlimited
Entry into force on: 16 March 2023/ 25 May 2023
Federal Gazette, BAnz AT 16 03 2023 B2/ 23 06 203 B4

Therapeutic indication (according to the marketing authorisation of 17 August 2022):

Pepaxti is indicated, in combination with dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy. For patients with a prior autologous stem cell transplantation, the time to progression should be at least 3 years from transplantation.

Therapeutic indication of the resolution (resolution of 16 March 2023):

see therapeutic indication according to marketing authorisation

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

Adults with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy; the time to progression at least three years for subjects with prior autologous stem cell transplantation

Appropriate comparator therapy:

A patient-individual therapy under selection of:

- Bortezomib monotherapy
- Bortezomib + pegylated liposomal doxorubicin
- Bortezomib + dexamethasone
- Carfilzomib + lenalidomide and dexamethasone
- Carfilzomib + dexamethasone
- Daratumumab + lenalidomide + dexamethasone
- Daratumumab + bortezomib + dexamethasone
- Daratumumab monotherapy (only for subjects with disease progression on last therapy)
- Daratumumab + pomalidomide + dexamethasone
- Elotuzumab + lenalidomide + dexamethasone

- Elotuzumab + pomalidomide + dexamethasone (only for subjects with disease progression on last therapy)
- Isatuximab + pomalidomide + dexamethasone (only for subjects with disease progression on the last therapy)
- Ixazomib + lenalidomide + dexamethasone
- Lenalidomide + dexamethasone
- Panobinostat + bortezomib and dexamethasone
- Pomalidomide + bortezomib and dexamethasone
- Pomalidomide + dexamethasone (only for subjects with disease progression on the last therapy)
- Cyclophosphamide (in combination with other antineoplastic medicinal products)
- Melphalan
- Doxorubicin
- Carmustine (in combination with other cytostatic agents and a corticosteroid, especially prednisone)
- Vincristine
- Dexamethasone
- Prednisolone
- Prednisone
- Best supportive care

taking into account prior therapies as well as the severity and duration of the response.

Extent and probability of the additional benefit of melphalan flufenamide in combination with dexamethasone compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

Adults with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy; the time to progression at least three years for subjects with prior autologous stem cell transplantation

No adequate 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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

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

Adults with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy; the time to progression at least three years for subjects with prior autologous stem cell transplantation

approx. 1,200 – 1,300 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 Pepaxti (active ingredient: melphalan flufenamide) at the following publicly accessible link (last access: 12 December 2022):

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

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

4. Treatment costs

Annual treatment costs:

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

Adults with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy; the time to progression at least three years for subjects with prior autologous stem cell transplantation

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Melphalan flufenamide in combination with dexamethasone	
Melphalan flufenamide	€ 158,123.68
Dexamethasone	€ 193.44
Total	€ 158,317.12
Appropriate comparator therapy	
Bortezomib monotherapy	
Bortezomib	€ 5,602.24
Bortezomib in combination with pegylated liposomal doxorubicin	
Bortezomib	€ 5,602.24
Doxorubicin (pegylated, lysosomal)	€ 17,454.00
Total	€ 23,056.24
Bortezomib in combination with dexamethasone	
Bortezomib	€ 2,801.12 - € 5,602.24
Dexamethasone	€ 104.10 - € 168.90
Total	€ 2,905.22 - € 5,771.14
Carfilzomib in combination with lenalidomide and dexamethasone	
Carfilzomib	€ 76,695.24
Lenalidomide	€ 774.93
Dexamethasone	€ 193.44
Total	€ 77,663.61
Additionally required SHI services	€ 106.40
Carfilzomib in combination with dexamethasone	
Carfilzomib	€ 144,716.22

Designation of the therapy	Annual treatment costs/ patient
Dexamethasone	€ 243.05
Total	€ 144,959.27
Additionally required SHI services	€ 106.40
Daratumumab in combination with lenalidomide and dexamethasone	
Daratumumab	€ 128,183.14
Lenalidomide	€ 774.93
Dexamethasone	€ 107.88
Total	€ 129,065.95
Additionally required SHI services	€ 341.49 - € 344.80
Daratumumab in combination with bortezomib and dexamethasone	
Daratumumab	€ 117,036.78
Bortezomib	€ 5,602.24
Dexamethasone	€ 147.23
Total	€ 122,786.25
Additionally required SHI services	€ 292.01 - € 295.02
Daratumumab monotherapy (only for subjects with disease progression on last therapy)	
Daratumumab	€ 128,183.14
Additionally required SHI services	€ 399.30 - € 649.54
Elotuzumab in combination with lenalidomide and dexamethasone	
Elotuzumab	€ 84,540.00
Lenalidomide	€ 774.93
Dexamethasone	€ 185.70
Total	€ 85,500.63
Additionally required SHI services	€ 359.57 - € 363.88
Elotuzumab + pomalidomide + dexamethasone (only for subjects with disease progression on last therapy)	
Elotuzumab	€ 84,540.00
Pomalidomide	€ 106,253.29
Dexamethasone	€ 188.54
Total	€ 190,981.83
Additionally required SHI services	€ 266.74 - € 269.47
Isatuximab in combination with pomalidomide and dexamethasone (only for subjects with disease progression on last therapy)	
Isatuximab	€ 73,272.92
Pomalidomide	€ 106,253.29
Dexamethasone	€ 89.28

Designation of the therapy	Annual treatment costs/ patient
Total	€ 179,615.49
Additionally required SHI services	€ 106.40
Ixazomib in combination with lenalidomide and dexamethasone	
Ixazomib	€ 75,468.38
Lenalidomide	€ 774.93
Dexamethasone	€ 193.44
Total	€ 76,436.75
Additionally required SHI services	€ 106.40
Lenalidomide in combination with dexamethasone	
Lenalidomide	€ 774.93
Dexamethasone	€ 312.48
Total	€ 1,087.41
Additionally required SHI services	€ 106.40
Panobinostat in combination with bortezomib and dexamethasone	
Panobinostat	€ 33,633.12 - € 67,266.24
Bortezomib	€ 5,602.24 - € 8,403.36
Dexamethasone	€ 168.90 - € 233.70
Total	€ 39,404.26 - € 75,903.30
Pomalidomide in combination with bortezomib and dexamethasone	
Pomalidomide	€ 94,810.63
Bortezomib	€ 8,893.56
Dexamethasone	€ 237.44
Total	€ 103,941.62
Additionally required SHI services	€ 106.40
Pomalidomide in combination with dexamethasone (only for subjects with disease progression on last therapy)	
Pomalidomide	€ 106,253.29
Dexamethasone	€ 193.44
Total	€ 106,446.73
Additionally required SHI services	€ 106.40
Cyclophosphamide (in combination with other antineoplastic medicinal products)	
Cyclophosphamide	€ 198.28
Melphalan	€ 332.40
Carmustine	€ 38,015.12
Vincristine	€ 357.55

Designation of the therapy	Annual treatment costs/ patient
Prednisone	€ 132.64
Total	€ 39,035.99
Melphalan	
Melphalan	€ 603.20
Doxorubicin	
Doxorubicin	€ 2,497.92 - € 3,746.88
Carmustine (in combination with other cytostatic agents and a corticosteroid, especially prednisone)	
Carmustine	€ 38,015.12
Cyclophosphamide	€ 198.28
Melphalan	€ 332.40
Vincristine	€ 357.55
Prednisone	€ 132.64
Total	€ 39,035.99
Vincristine	
Vincristine	€ 1,791.20
Dexamethasone	
Dexamethasone	€ 877.50
Daratumumab in combination with pomalidomide and dexamethasone	
Daratumumab	€ 128,183.14
Pomalidomide	€ 106,253.29
Dexamethasone	€ 107.88
Total	€ 234,544.31
Additionally required SHI services	€ 341.49 - € 344.80
Prednisolone	
Prednisolone	Incalculable
Prednisone	
Prednisone	Incalculable
Best supportive care	
Best supportive care[1]	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 March 2023)

1 When comparing melphalan flufenamide with best supportive care, the costs of best supportive care are to be considered additionally also for the medicinal product to be assessed

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:					
Melphalan flufenamide in combination with dexamethasone					
Melphalan flufenamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0	€ 1,300
Appropriate comparator therapy					
Bortezomib monotherapy					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200
Bortezomib in combination with pegylated liposomal doxorubicin					
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					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	16.0 - 32.0	€ 1,600 - € 3,200

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
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 preparation containing cytostatic agents	€ 100	6	78.0	€ 7,800
Daratumumab in combination with bortezomib and dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	4	32.0	€ 3,200
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 (only for subjects with disease progression on last therapy)					
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

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Isatuximab in combination with pomalidomide and dexamethasone (only for subjects with disease progression on last therapy)					
Isatuximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1st cycle 4 From 2nd cycle 2	28.0	€ 2,800
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	32.0 - 48.0	€ 3,200 - € 4,800
Pomalidomide in combination with bortezomib and dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1st - 8th cycle 4 From 9th cycle 2	50.8	€ 5,800
Cyclophosphamide (in combination with other antineoplastic medicinal products)					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	10.4	€ 1,040
Carmustine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	10.4	€ 1,040
Vincristine	Surcharge for production of a	€ 100	1	10.4	€ 1,040

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	parenteral preparation containing cytostatic agents				
Melphalan monotherapy					
Melphalan	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0	€ 1,300
Carmustine					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	10.4	€ 1,040
Carmustine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	10.4	€ 1,040
Vincristine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	10.4	€ 1,040
Doxorubicin monotherapy					
Doxorubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6.0 - 9.0	€ 6,000 - € 9,000
Vincristine monotherapy					

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Vincristine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	52.1	€ 5,210

5. 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 Melphalan Flufenamide

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients, which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with melphalan flufenamide for the treatment of adult patients with multiple myeloma who have previously received at least three lines of therapy, whose disease is refractory to at least one proteasome inhibitor, an immunomodulatory agent and a CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last line of therapy (for patients with prior autologous stem cell transplantation, the time to progression after transplantation should be at least 3 years):

Adults with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy; the time to progression at least three years for subjects with prior autologous stem cell transplantation

- No active ingredient that can be used in a combination therapy that 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.