Gemeinsamer Bundesausschuss

Daratumumab (new therapeutic indication; reassessment of an orphan drug after exceeding the 50 million euro limit)

Resolution of: 15 February 2018 / 15 September 2022 Valid until: unlimited
Entry into force on: 15 February 2018 / 15 September 2022
Federal Gazette, BAnz AT 15 03 2018 B3/ 13 10 2022 B1

New therapeutic indication (according to the marketing authorisation of 28 April 2017):

Darzalex is indicated in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Therapeutic indication (according to the marketing authorisation of 20 May 2016):

Darzalex is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

Therapeutic indication of the resolution (resolution of 15 September 2022):

Darzalex is indicated in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

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

a) Adults with multiple myeloma who have received at least one prior therapy

Appropriate comparator therapy:

− bortezomib in combination with pegylated liposomal doxorubicin

or

− bortezomib in combination with dexamethasone

or

− lenalidomide in combination with dexamethasone

or

− elotuzumab in combination with lenalidomide and dexamethasone

or

− carfilzomib in combination with lenalidomide and dexamethasone

or

− carfilzomib in combination with dexamethasone

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

Proof of a considerable additional benefit.

b) Daratumumab as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

Appropriate comparator therapy:

A patient-individual therapy according to the doctor's instructions, in particular depending on the prior therapies as well as the severity and duration of the response and in compliance with the marketing authorisation of the respective medicinal products.

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

An additional benefit is not proven.

Study results according to endpoints[1]:

a) Adults with multiple myeloma who have received at least one prior therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival
Morbidity	↔	No relevant differences for the benefit assessment
Health-related quality of life	↔	No relevant differences for the benefit assessment
Side effects	↓↓	Disadvantage in the endpoint of severe adverse events (CTCAE grade ≥ 3) and, in detail, of specific adverse events

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

[1] Data from IQWiG's dossier assessment (A22-40), unless otherwise indicated.

CASTOR study *(data cut-off: 28.06.2021)*:

Daratumumab + bortezomib + dexamethasone vs bortezomib + dexamethasone

Study design: randomised, open-label, actively controlled

POLLUX study *(data cut-off: 30.09.2021)*:

Daratumumab + lenalidomide + dexamethasone vs lenalidomide + dexamethasone

Study design: randomised, open-label, actively controlled

Mortality

Endpoint	**Daratumumab arm**		**Comparator arm**		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
CASTOR	251	49.6 [42.2; 62.3] 148 (59.0)	247	38.5 [31.2; 46.2] 171 (69.2)	0.74 [0.59; 0.92] 0.008 11.1 months
POLLUX	286	67.6 [53.1; 80.5] 153 (53.5)	283	51.8 [44.0; 60.0] 175 (61.8)	0.73 [0.58; 0.91] 0.005 15.8 months
Meta-analysis					0.74 [0.63; 0.86] < 0.001

Morbidity

Endpoint	**Daratumumab arm**		**Comparator arm**		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Progression-free survival (PFS) [b]					
CASTOR	251	16.72 [13.14; 19.38] 195 (77.7%)	247	7.06 [6.21; 7.66] 209 (84.6%)	0.31 [0.24; 0.39] < 0.0001 9.66 months
POLLUX	286	45.80 [34.14; 54.60] 181 (63.3%)	283	17.51 [13.93; 20.83] 223 (78.8%)	0.47 [0.38; 0.57] < 0.0001

Endpoint	Daratumumab arm		Comparator arm		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
					28.29 months
Disease symptomatology - time to deterioration [c]					
Symptom scales of the EORTC QLQ-C30					
Fatigue					
CASTOR	251	1.5 [1.5; 2.1] 180 (71.7)	247	2.1 [1.5; 2.9] 151 (61.1)	1.10 [0.88; 1.38] 0.379
POLLUX	286	1.9 [1.3; 2.0] 203 (71.0)	283	2.0 [1.9; 2.8] 193 (68.2)	1.08 [0.89; 1.33] 0.431
Meta-analysis					1.09 [0.94; 1.26] 0.266
Nausea and vomiting					
CASTOR	251	6.8 [5.0; 9.7] 133 (53.0)	247	n.a. [7.9; n.c.] 79 (32.0)	1.31 [0.98; 1.74] 0.069
POLLUX	286	13.0 [9.3; 16.9] 156 (54.5)	283	10.2 [5.8; 15.6] 145 (51.2)	0.89 [0.70; 1.12] 0.309
Meta-analysis					1.04 [0.87; 1.25] 0.677
Pain					
CASTOR	251	3.5 [2.8; 4.0] 156 (62.2)	247	3.6 [2.8; 4.9] 125 (50.6)	1.04 [0.82; 1.33] 0.738
POLLUX	286	5.6 [3.8; 10.3] 176 (61.5)	283	5.6 [3.7; 7.5] 174 (61.5)	0.89 [0.72; 1.11] 0.298
Meta-analysis					0.95 [0.81; 1.12] 0.566
Dyspnoea					
CASTOR	25	3.6	24	2.9	0.92

Endpoint	**Daratumumab arm**		**Comparator arm**		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
	1	[2.8; 4.9] 145 (57.8)	7	[2.3; 4.3] 128 (51.8)	[0.72; 1.18] 0.512
POLLUX	286	4.7 [2.9; 6.6] 176 (61.5)	283	5.7 [3.8; 8.4] 168 (59.4)	1.02 [0.82; 1.26] 0.876
Meta-analysis					0.98 [0.83; 1.15] 0.766
Insomnia					
CASTOR	251	2.4 [2.1; 3.5] 152 (60.6)	247	2.9 [2.1; 5.7] 118 (47.8)	1.08 [0.84; 1.39] 0.538
POLLUX	286	6.6 [4.7; 9.2] 163 (57.0)	283	3.8 [2.9; 5.8] 171 (60.4)	0.83 [0.67; 1.03] 0.092
Meta-analysis					0.93 [0.79; 1.09] 0.367
Appetite loss					
CASTOR	251	5.0 [4.2; 6.9] 138 (55.0)	247	6.0 [4.6; 7.0] 109 (44.1)	1.06 [0.82; 1.38] 0.632
POLLUX	286	7.2 [4.9; 10.3] 170 (59.4)	283	9.6 [5.3; 14.1] 148 (52.3)	1.12 [0.90; 1.40] 0.317
Meta-analysis					1.09 [0.92; 1.30] 0.293
Constipation					
CASTOR	251	8.8 [4.2; 16.6] 120 (47.8)	247	6.2 [4.5; n.c.] 100 (40.5)	1.01 [0.77; 1.33] 0.948
POLLUX	286	4.7 [2.9; 7.0] 162 (56.6)	283	3.3 [2.0; 5.7] 165 (58.3)	0.87 [0.70; 1.08] 0.214
Meta-analysis					0.92

Endpoint	Daratumumab arm		Comparator arm		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
					[0.78; 1.09] 0.346
Diarrhoea					
CASTOR	251	5.7 [4.2; 9.1] 141 (56.2)	247	6.6 [4.9; 10.1] 98 (39.7)	1.16 [0.89; 1.52] 0.284
POLLUX	286	5.7 [4.7; 7.6] 195 (68.2)	283	5.7 [4.6; 7.7] 190 (67.1)	0.90 [0.73; 1.11] 0.332
Meta-analysis					0.99 [0.84; 1.17] 0.916f
Health status					
EQ-5D VAS (time to deterioration) [d]					
CASTOR	251	10.1 [5.6; 28.2] 115 (45.8)	247	6.4 [4.4; n.c.] 98 (39.7)	0.88 [0.66; 1.16] 0.366
POLLUX	286	11.2 [7.9; 21.1] 145 (50.7)	283	11.6 [8.9; 18.6] 129 (45.6)	1.02 [0.80; 1.30] 0.896
Meta-analysis					0.96 [0.80; 1.15] 0.647

Health-related quality of life

Endpoint	**Daratumumab arm**		**Comparator arm**		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Health-related quality of life - time to deterioration [e]					
Global health status and functional scales of the EORTC QLQ-C30					
Global health status					
CASTOR	251	3.5 [2.8; 6.1] 139 (55.4)	247	4.0 [2.9; 5.1] 118 (47.8)	0.97 [0.76; 1.25] 0.831
POLLUX	286	4.7 [2.9; 7.4] 169 (59.1)	283	4.7 [2.9; 7.5] 169 (59.7)	0.92 [0.74; 1.15] 0.463
Meta-analysis					0.94 [0.80; 1.11] 0.475
Physical functioning					
CASTOR	251	4.4 [3.6; 5.7] 154 (61.4)	247	4.3 [3.5; 5.9] 119 (48.2)	0.98 [0.76; 1.26] 0.889
POLLUX	286	6.0 [4.0; 8.6] 169 (59.1)	283	7.5 [5.6; 10.2] 162 (57.2)	1.01 [0.81; 1.26] 0.909
Meta-analysis					1.00 [0.84; 1.18] 0.971
Role functioning					
CASTOR	251	2.3 [1.6; 2.9] 165 (65.7)	247	2.8 [2.1; 3.8] 131 (53.0)	1.18 [0.93; 1.49] 0.174
POLLUX	286	3.7 [2.8; 4.7] 195 (68.2)	283	3.1 [2.8; 4.7] 186 (65.7)	0.97 [0.79; 1.19] 0.770
Meta-analysis					1.06 [0.90; 1.23] 0.495
Emotional functioning					
CASTOR	25	6.0	24	4.9	0.83

Endpoint	**Daratumumab arm**		**Comparator arm**		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
	1	[4.5; 10.5] 131 (52.2)	7	[3.5; 7.1] 110 (44.5)	[0.64; 1.08] 0.169
POLLUX	286	6.6 [4.7; 11.4] 150 (52.4)	283	8.4 [4.9; 13.0] 143 (50.5)	1.04 [0.82; 1.31] 0.768
Meta-analysis					0.94 [0.79; 1.12] 0.492
Cognitive functioning					
CASTOR	251	3.5 [2.8; 4.2] 152 (60.6)	247	3.5 [2.3; 4.9] 124 (50.2)	0.95 [0.74; 1.21] 0.671
POLLUX	286	4.9 [3.8; 7.4] 192 (67.1)	283	4.7 [3.1; 6.6] 174 (61.5)	0.96 [0.78; 1.19] 0.703
Meta-analysis					0.96 [0.81; 1.12] 0.580
Social functioning					
CASTOR	251	2.9 [2.2; 3.6] 171 (68.1)	247	3.0 [2.2; 4.2] 130 (52.6)	1.12 [0.88; 1.42] 0.352
POLLUX	286	3.8 [3.0; 6.5] 181 (63.3)	283	2.9 [2.0; 4.6] 190 (67.1)	0.80 [0.65; 0.99] 0.038 0.9 months
Meta-analysis					0.93 [0.79; 1.08] 0.343

Side effects

Endpoint	Daratumumab arm		Comparator arm		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Adverse events (AEs) (presented additionally)					
CASTOR	243	0.03 [0.03; 0.10] 241 (99.2)	237	0.3 [0.3; 0.5] 226 (95.4)	-
POLLUX	283	0.03 [n.c.] 282 (99.6)	281	0.2 [0.1; 0.3] 274 (97.5)	-
Meta-analysis					
Serious adverse events (SAE)					
CASTOR	243	14.4 [6.7; 29.0] 134 (55.1)	237	n.a. 81 (34.2)	1.31 [0.98; 1.76] 0.071
POLLUX	283	14.3 [9.7; 17.5] 205 (72.4)	281	15.6 [11.8; 23.2] 148 (52.7)	1.08 [0.87; 1.35] 0.468
Meta-analysis					1.16 [0.97; 1.38] 0.102
Severe adverse events (CTCAE grade ≥ 3)					
CASTOR	243	1.2 [0.9; 1.2] 201 (82.7)	237	1.8 [1.2; 3.5] 151 (63.7)	1.40 [1.13; 1.75] 0.002 0.6 months
POLLUX	283	1.0 [0.7; 1.4] 262 (92.6)	281	3.4 [2.3; 4.7] 231 (82.2)	1.37 [1.14; 1.65] < 0.001 2.4 months
Meta-analysis					1.38 [1.20; 1.59] < 0.001
Effect modification by the "ISS stage" characteristic					
ISS stage					
CASTOR					
Stage I	98	1.4 [1.1; 3.0]	92	5.4 [2.1; n.c.]	1.77

Endpoint	Daratumumab arm		Comparator arm		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
		79 (80.6)		45 (48.9)	[1.22; 2.58] 0.003 4.0 months
Stage II	92	1.2 [0.7; 1.9] 76 (82.6)	97	1.3 [1.1; 2.9] 70 (72.2)	1.13 [0.81; 1.58] 0.462
Stage III	53	0.5 [0.3; 0.7] 46 (86.8)	48	0.7 [0.5; 1.7] 36 (75.0)	1.39 [0.89; 2.15] 0.148
POLLUX					
Stage I	136	0.8 [0.7; 1.8] 123 (90.4)	139	7.1 [3.7; 9.9] 107 (77.0)	1.66 [1.28; 2.16] < 0.001 6.3 months
Stage II	93	1.4 [0.7; 2.7] 89 (95.7)	86	2.4 [1.5; 3.8] 74 (86.0)	1.05 [0.77; 1.44] 0.759
Stage III	54	0.7 [0.7; 1.1] 50 (92.6)	56	1.2 [0.5; 2.3] 50 (89.3)	1.20 [0.81; 1.78] 0.369
					Interaction: 0.019[h]
Meta-analysis					
Stage I					1.70 [1.37; 2.10][h] < 0.001[h]
Stage II					1.09 [0.86; 1.37][h] 0.476[h]
Stage III					1.28 [0.95; 1.72][h] 0.099[h]
Specific adverse events					
Reaction in connection with an infusion					
CASTOR	Evaluation unsuitable[f]				
POLLUX					

Endpoint	**Daratumumab arm**		**Comparator arm**		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Peripheral neuropathy NRE (HLT, severe AE)[g]					
CASTOR	243	n.a. 14 (5.8)	237	n.a. 17 (7.2)	0.67 [0.32; 1.38] 0.276
Vomiting (PT, AE)					
CASTOR	243	n.a. 30 (12.3)	237	n.a. 9 (3.8)	2.89 [1.35; 6.18] 0.006
POLLUX	283	n.a. 66 (23.3)	281	n.a. 20 (7.1)	2.94 [1.77; 4.88] < 0.001
Meta-analysis					2.92 [1.92; 4.46] < 0.001[h]
Blood and lymphatic system disorders (SOC, severe AEs)					
CASTOR	243	1.9 [1.2; 14.8] 137 (56.4)	237	n.a. 95 (40.1)	1.62 [1.24; 2.12] < 0.001
POLLUX	283	3.5 [1.6; 8.9] 184 (65.0)	281	9.9 [6.7; 14.9] 163 (58.0)	1.21 [0.98; 1.51] 0.080
Meta-analysis					1.36 [1.15; 1.61] < 0.001[h]
Respiratory, thoracic and mediastinal disorders (SOC, severe AEs)					
CASTOR	243	n.a. 36 (14.8)	237	n.a. 12 (5.1)	2.36 [1.20; 4.64] 0.013
POLLUX	283	n.a. 43 (15.2)	281	n.a. 24 (8.5)	1.28 [0.76; 2.15] 0.354
Meta-analysis					1.61 [1.06; 2.43] 0.024[h]
Diarrhoea (PT, severe AEs)					
CASTOR	24	n.a.	23	n.a.	3.00

Endpoint	Daratumumab arm		Comparator arm		Intervention vs control
	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 (%)*	HR [95% CI] p value Absolute difference (AD)[a]
	3	10 (4.1)	7	3 (1.3)	[0.81; 11.14] 0.101
POLLUX	283	n.a. 29 (10.2)	281	n.a. 11 (3.9)	1.83 [0.90; 3.72] 0.096
Meta-analysis					2.05 [1.10; 3.82] 0.024[h]
Hypertension (PT, severe AEs)					
CASTOR	243	n.a. 18 (7.4)	237	n.a. 2 (0.8)	7.01 [1.60; 30.71] 0.010
POLLUX	283	n.a. 13 (4.6)	281	n.a. 5 (1.8)	1.82 [0.64; 5.20] 0.266
Meta-analysis					2.86 [1.22; 6.72] 0.016[h]

[a] Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
[b] Data from: Dossier on daratumumab Module 4A dated 31.03.2022
[c] Time to first deterioration. An increase in score by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).
[d] Time to first deterioration. A decrease in score by ≥ 15 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).
[e] Time to first deterioration. A decrease in score by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).
[f] The evaluation submitted by the pharmaceutical company is not suitable for the benefit assessment, but the results underlying the endpoint are additionally recorded via the specific AEs.
[g] This AE is specific for the active ingredient bortezomib and therefore, not relevant for the POLLUX study.
[h] IQWiG calculation

Abbreviations used:
AD = absolute difference; NRE = not recorded elsewhere; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HLT = high level term; HR = hazard ratio; ISS = International Staging System; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.a. = not achieved; QLQ-C30 = Quality of Life Questionnaire - Core 30; VAS = visual analogue scale; vs = versus

b) Daratumumab as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

No data are available to allow an assessment of the additional benefit.

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

a) Adults with multiple myeloma who have received at least one prior therapy

approx. 4,700 to 7,000 patients

b) Daratumumab as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

approx. 2,300 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 Darzalex (active ingredient: daratumumab) at the following publicly accessible link (last access: 1 June 2022):

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 European Medicines Agency (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 indirect Coombs test). Interference with blood typing induced by daratumumab may persist for up to 6 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 6 months after the end of the treatment.

4. Treatment costs

Annual treatment costs[2]:

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

a) Adults with multiple myeloma who have received at least one prior therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Daratumumab in combination with lenalidomide and dexamethasone	
Daratumumab	€ 133,535.38
Lenalidomide	€ 1,282.19
Dexamethasone	€ 108.01
Total	€ 134,975.58
Additionally required SHI services	€ 343.77 - € 344.44
Daratumumab in combination with bortezomib and dexamethasone	
Daratumumab	€ 121,969.26
Bortezomib	€ 27,823.68
Dexamethasone	€ 147.69
Total	€ 149,940.63
Additionally required SHI services	€ 294.09 - € 294.70
Appropriate comparator therapy:	
Bortezomib in combination with pegylated liposomal doxorubicin	
Bortezomib	€ 27,823.68
Doxorubicin (pegylated, liposomal)	€ 20,920.24
Total	€ 48,743.92
Bortezomib in combination with dexamethasone	
Bortezomib	€ 13,911.84 - € 27,823.68
Dexamethasone	€ 104.56 - € 169.36
Total	€ 14,016.40 - € 27,993.04
Lenalidomide in combination with dexamethasone	
Lenalidomide	€ 1,282.19
Dexamethasone	€ 312.87
Total	€ 1,595.06
Additionally required SHI services	€ 106.40
Elotuzumab in combination with lenalidomide and dexamethasone	
Elotuzumab	€ 88,225.80

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

Designation of the therapy	Annual treatment costs/ patient
Lenalidomide	€ 1,282.19
Dexamethasone	€ 186.01
Total	€ 89,694.00
Additionally required SHI services	€ 363.16 - € 364.03
Carfilzomib in combination with lenalidomide and dexamethasone	
Carfilzomib	€ 81,879.52
Lenalidomide	€ 1,282.19
Dexamethasone	€ 193.68
Total	€ 83,355.39
Additionally required SHI services	€ 106.40
Carfilzomib in combination with dexamethasone	
Carfilzomib	€ 154,432.44
Dexamethasone	€ 243.53
Total	€ 154,675.97
Additionally required SHI services	€ 106.40

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 August 2022)

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 and dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	4	32	€ 2,592
Appropriate comparator therapy:					
Bortezomib in combination with pegylated liposomal doxorubicin					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	4	32	€ 2,592

Doxorubicin (pegylated, liposomal)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	Day 4 21-day cycle	8	€ 648
Bortezomib in combination with dexamethasone					
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	4	16 - 32	€ 1,296 - € 2,592
Elotuzumab in combination with lenalidomide and dexamethasone					
Elotuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1st - 2nd cycle: 4 From 3rd cycle: 2	30	€ 2,130
Carfilzomib in combination with lenalidomide and dexamethasone					
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1st - 12th cycle: 6 From 13th cycle: 4	76	€ 6,156
Carfilzomib in combination with dexamethasone					
Carfilzomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	6	78	€ 6,318

b) Daratumumab as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be assessed:	
Daratumumab	€ 149,897.21
Additionally required SHI services	€ 615.18 - € 616.33
Appropriate comparator therapy[3]:	
Cyclophosphamide in combination with prednisone	
Cyclophosphamide	€ 655.24
Prednisone	€ 250.76
Total	€ 906.00
Melphalan in combination with prednisone	
Melphalan	€ 897.62
Prednisone	€ 191.76
Total	€ 1,089.38
Bortezomib in Kombination mit Dexamethason	
Bortezomib	€ 24,261.44 - € 48,522.88
Dexamethasone	€ 97.20 - € 156.87
Total	€ 24,358.64 - € 48,679.75
Lenalidomid in Kombination mit Dexamethason	
Lenalidomide	€ 96,968.95
Dexamethasone	€ 288.88
Total	€ 97,257.83
Elotuzumab in Kombination mit Lenalidomid und Dexamethason	
Elotuzumab	€ 88,207.80
Lenalidomide	€ 96,968.95
Dexamethasone	€ 174.35
Total	€ 185,351.10
Additionally required SHI services	€ 237.81 - € 239.30
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15.01.2018)

[3] Due to the numerous active ingredients approved in the therapeutic indication and possible concomitant active ingredients, some possible therapy regimens are presented here as examples.

Other SHI services:

Designation of the therapy	Type of service	Unit cost	Number per cycle	Number per patient per year	Costs per patient per year
Medicinal product to be assessed					
Daratumumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	23	€ 1,633
Appropriate comparator therapy					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17	€ 1,377
Bortezomib	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2 - 4	16 - 48	€ 1,296 - € 3,888
Elotuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1st – 2nd cycle 4 From 3rd cycle 2	30	€ 2,130