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 (reassessment after the deadline (multiple myeloma, after at least 1 prior therapy, combination with lenalidomide and dexamethasone or with bortezomib and dexamethasone))

of 15 September 2022

At its session on 15 September 2022, 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 information on the benefit assessment of daratumumab in the version of the resolution of 15 February 2018 (Federal Gazette, BAnz AT 15.03.2018 B3), last amended by the announcement of the resolution of 17 June 2021 (Federal Gazette, BAnz AT 02.07.2021 B3) on patient group a) shall be amended as follows:**

1. Before number 1 "Additional benefit of the medicinal product in relation to the appropriate comparator therapy", the following section is added to the section "Therapeutic indication (according to the marketing authorisation of 20 May 2016)":

"**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."

2. Number 1 "Additional benefit of the medicinal product in relation to the appropriate comparator therapy" shall be amended as follows:

a) in the section preceding the heading "Study results according to endpoints:", the section following point a) shall be replaced by the following section a):

"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) The section under the heading "Study results according to endpoints" shall be amended as follows:

aa) The information in the footnote 1 "[1]Data from IQWiG's dossier assessment (A17-40) and the addendum (A18-03), unless otherwise indicated" shall be replaced by the following information: "[1] Data from IQWiG's dossier assessment (A22-40), unless otherwise indicated.".

bb) The section following point a) shall be replaced by the following section a):

"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

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]	283	17.51 [13.93; 20.83]	0.47 [0.38; 0.57]

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]
		181 (63.3%)		223 (78.8%)	< 0.0001 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

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]
					[0.81; 1.12] 0.566
Dyspnoea					
CASTOR	251	3.6 [2.8; 4.9] 145 (57.8)	247	2.9 [2.3; 4.3] 128 (51.8)	0.92 [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					

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]
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 [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

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]
Emotional functioning					
CASTOR	251	6.0 [4.5; 10.5] 131 (52.2)	247	4.9 [3.5; 7.1] 110 (44.5)	0.83 [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					

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]
CASTOR					
Stage I	98	1.4 [1.1; 3.0] 79 (80.6)	92	5.4 [2.1; n.c.] 45 (48.9)	1.77 [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]

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]
					0.099[h]
Specific adverse events					
Reaction in connection with an infusion					
CASTOR	Evaluation unsuitable[f]				
POLLUX					
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]

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]
					0.013
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	243	n.a. 10 (4.1)	237	n.a. 3 (1.3)	3.00 [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).

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]

[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

"

3. Number 2 "Number of patients or demarcation of patient groups eligible for treatment" is amended as follows:

   a) In the heading, the words "patients and" shall be inserted after the words "number of".

   b) The section after point a) is replaced by the following section a):

   "

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

   approx. 4,700 to 7,000 patients".

4. The information in number 3 "Requirements for a quality-assured application" is replaced by the following:

"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."

5. Number 4 "Treatment costs" is amended as follows:

a) Under the heading 'Annual treatment costs:', the following sentence is inserted:

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

b) The section after point a) is replaced by the following section a):

"

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	

Designation of the therapy	Annual treatment costs/ patient
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
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

"

II. Entry into force

1. **The resolution will enter into force on the day of its publication on the website of the G-BA on 15 September 2022.**

2. **The limitation on the period of validity of the resolution of 15 February 2018 (Federal Gazette, Banz AT 15.03.2018 B3) last amended by the announcement of the resolution of 17 June 2021 (Federal Gazette, Banz AT 02.07.2021 B3) is repealed.**

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

Berlin, 15 September 2022

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

Prof. Hecken