Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Atezolizumab (New Therapeutic Indication: Advanced Small Cell Lung Cancer, First Line, Combination with Carboplatin and Etoposide)

of 2 April 2020

On 2 April 2020, the Federal Joint Committee (G-BA) resolved by written statement to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (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 on DD Month YYYY (Federal Gazette, BAnz AT DD MM YYYY BX), as follows:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of atezolizumab in accordance with the resolution of 20 June 2019:

Atezolizumab

Resolution of: 2 April 2020
Entry into force on: 2 April 2020
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 3 September 2019):

Tecentriq®, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Note: Tecentriq® with the active ingredient atezolizumab is approved in various strengths. In the aforementioned therapeutic indication "Tecentriq® 1,200 mg concentrate for solution for infusion" is approved.

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

Adult patients with extensive-stage small cell lung cancer (ES-SCLC); first-line treatment

Appropriate comparator therapy:

- Cisplatin and etoposide

or

- Carboplatin and etoposide

Extent and probability of the additional benefit of atezolizumab in combination with carboplatin and etoposide compared with carboplatin in combination with etoposide:

Hint for a minor additional benefit.

Study results according to endpoints:[1]

Adult patients with extensive-stage small cell lung cancer (ES-SCLC); first-line treatment

IMpower133 study – global cohort: Atezolizumab + carboplatin + etoposide **vs** carboplatin + etoposide

IMpower133 study – China Atezolizumab + carboplatin + etoposide **vs** carboplatin + etoposide (additional cohort to the IMpower133 study in China)

Mortality

Endpoint	**Atezolizumab + carboplatin + etoposide**		**Carboplatin + etoposide**		**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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
Overall survival					
Impower133 – global cohort (DC: 24 January 2019)	201	12.3 [10.8; 15.8] 142 (70.6)	202	10.3 [9.3; 11.3] 160 (79.2)	0.76 [0.60; 0.95] 0.015 AD = 2.0 months
IMpower133 – Chinese cohort (DC 31 July 2019)	57	11.4 [8.8; 15.4] 41 (71.9)	53	11.9 [10.0; 14.7] 41 (77.4)	0.93 [0.60; 1.43] 0.734
Total					0.79 [0.65; 0.97] 0.026

Morbidity

Endpoint	**Atezolizumab + carboplatin + etoposide**		**Carboplatin + etoposide**		**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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
Progression-free survival (PFS)[2]					
Impower133 – global cohort	201	5.2 [4.4; 5.6]	202	4.3 [4.2; 4.5]	0.77 [0.62; 0.96]

[1] Data from the dossier evaluation of the IQWiG (A19-86) and the addendum (A20-18) unless otherwise indicated.

[2] Data from the dossier on atezolizumab in combination with etoposide and carboplatin (Module 4A) submitted 2 October 2019

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
(DC: 24 April 2018)		171 (85.1)		189 (93.6)	0.0170 AD = 0.9 months
IMpower133 – cohort China (DC: 29 October 2018)	57	5.3 [4.2; 5.7] 48 (84.2)	53	4.4 [4.3; 5.4] 47 (88.7)	0.79 [0.52; 1.20] 0.2700
Total					No data available
Symptomatology (EORTC QLQ-C30 symptom scales)[b]					
Loss of appetite					
Impower133 – global cohort (DC: 24 April 2018)	201	6.0 [4.7; 8.9] 87 (43.3)	202	7.1 [5.3; 10.2] 85 (42.1)	1.02 [0.75; 1.38] 0.904
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	9.9 [2.4; n.c.] 22 (38.6)	53	9.4 [2.8; n.c.] 24 (45.3)	0.92 [0.51; 1.67] 0.794
Total					1.00 [0.76; 1.31] 0.990
Diarrhoea					
Impower133 – global cohort (DC: 24 April 2018)	201	14.1 [8.8; n.c.] 60 (29.9)	202	10.2 [6.8; n.c.] 67 (33.2)	0.85 [0.60; 1.21] 0.362
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. 10 (17.5)	53	n.a. 8 (15.1)	1.55 [0.61; 3.95] 0.353
Total					0.92 [0.66; 1.27] 0.598
Dyspnoea					
Impower133 – global cohort (DC: 24 April 2018)	201	12.2 [10.1; n.c.] 63 (31.3)	202	8.6 [6.3; n.c.] 72 (35.6)	0.75 [0.53; 1.06] 0.102
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. [4.0; n.c.] 18 (31.6)	53	n.a. [7.3; n.c.] 16 (30.2)	1.29 [0.65; 2.57] 0.463

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
Total					0.84 [0.61; 1.14] 0.260
Fatigue					
Impower133 – global cohort (DC: 24 April 2018)	201	2.8 [1.9; 3.7] 107 (53.2)	202	2.3 [1.8; 3.6] 119 (58.9)	0.88 [0.67; 1.15] 0.332
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	1.9 [0.9; 3.5] 34 (59.6)	53	2.8 [2.1; 6.1] 33 (62.3)	1.24 [0.75; 2.03] 0.402
Total					0.95 [0.75; 1.21] 0.681
Insomnia					
Impower133 – global cohort (DC: 24 April 2018)	201	10.4 [6.4; n.c.] 71 (35.3)	202	9.0 [5.6; n.c.] 74 (36.6)	0.95 [0.69; 1.32] 0.772
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	11.1 [7.6; n.c.] 18 (31.6)	53	12.7 [9.4; n.c.] 19 (35.8)	0.79 [0.41; 1.52] 0.473
Total					0.92 [0.69; 1.23] 0.555
Pain					
Impower133 – global cohort (DC: 24 April 2018)	201	6.0 [4.1; 7.4] 89 (44.3)	202	4.9 [3.5; 7.1] 93 (46.0)	0.90 [0.67; 1.21] 0.490
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	3.8 [2.3; 11.1] 29 (50.9)	53	4.1 [2.3; 12.7] 31 (58.5)	0.96 [0.57; 1.60] 0.868
Total					0.91 [0.71; 1.18] 0.494
Nausea and vomiting					
Impower133 – global cohort	201	3.9 [2.6; 6.6]	202	3.5 [2.3; 5.0]	0.97 [0.73; 1.28]

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
(DC: 24 April 2018)		98 (48.8)		99 (49.0)	0.814
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	10.9 [2.9; n.c.] 22 (38.6)	53	11.2 [n.c.] 17 (32.1)	1.25 [0.66; 2.39] 0.492
Total					1.01 [0.78; 1.31] 0.939
Constipation					
Impower133 – global cohort (DC: 24 April 2018)	201	5.3 [3.0; 10.5] 87 (43.3)	202	6.3 [3.0; 9.0] 89 (44.1)	1.00 [0.74; 1.35] 0.989
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	9.9 [4.4; n.c.] 19 (33.3)	53	n.a. [9.7; n.c.] 19 (35.8)	0.97 [0.51; 1.85] 0.936
Total					0.99 [0.76; 1.31] 0.969
Symptomatology (EORTC QLQ-LC13 symptom scales)[b]					
Alopecia					
Impower133 – global cohort (DC: 24 April 2018)	201	0.8 [0.8; 0.8] 154 (76.6)	202	0.8 [0.8; 0.9] 157 (77.7)	1.08 [0.84; 1.37] 0.563
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	0.8 [0.7; 0.9] 42 (73.7)	53	0.7 [0.7; 0.8] 38 (71.7)	1.04 [0.64; 1.69] 0.873
Total					1.07 [0.86; 1.33] 0.534
Haemoptysis					
Impower133 – global cohort (DC: 24 April 2018)	201	n.a. 22 (10.9)	202	n.a. 25 (12.4)	0.81 [0.46; 1.44] 0.473
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. 3 (5.3)	53	n.a. 8 (15.1)	0.42 [0.11; 1.60] 0.192

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
Total					0.73 [0.43; 1.24] 0.244
Dysphagia					
Impower133 – global cohort (DC: 24 April 2018)	201	n.a. [10.6; n.c.] 49 (24.4)	202	16.6 [8.4; n.c.] 61 (30.2)	0.73 [0.50; 1.07] 0.105
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	12.3 [12.3; n.c.] 11 (19.3)	53	9.7 [8.8; n.c.] 13 (24.5)	0.84 [0.37; 1.90] 0.677
Total					0.75 [0.53; 1.06] 0.100
Dyspnoea					
Impower133 – global cohort (DC: 24 April 2018)	201	4.4 [2.8; 7.6] 90 (44.8)	202	2.8 [2.2; 5.6] 103 (51.0)	0.85 [0.64; 1.14] 0.270
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	2.3 [1.5; 3.5] 33 (57.9)	53	2.9 [1.8; n.c.] 30 (56.6)	1.34 [0.81; 2.22] 0.259
Total					0.95 [0.74; 1.22] 0.695
Coughing					
Impower133 – global cohort (DC: 24 April 2018)	201	n.a. [11.6; n.c.] 53 (26.4)	202	11.6 [6.7; 16.6] 65 (32.2)	0.76 [0.53; 1.10] 0.142
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. [4.0; n.c.] 19 (33.3)	53	7.3 [4.3; n.c.] 24 (45.3)	0.88 [0.48; 1.62] 0.682
Total					0.79 [0.58; 1.08] 0.140
Mouth pain					
Impower133 – global cohort	201	14.1 [10.0; n.c.]	202	10.6 [5.1; n.c.]	0.80 [0.57; 1.13]

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
(DC: 24 April 2018)		63 (31.3)		71 (35.1)	0.214
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. 10 (17.5)	53	n.a. 13 (24.5)	0.85 [0.37; 1.95] 0.707
Total					0.81 [0.59; 1.11] 0.184
Peripheral neuropathy					
Impower133 – global cohort (DC: 24 April 2018)	201	5.1 [3.6; 7.9] 87 (43.3)	202	7.0 [5.1; 9.0] 79 (39.1)	1.10 [0.81; 1.50] 0.540
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. [5.8; n.c.] 17 (29.8)	53	8.7 [5.1; 12.7] 22 (41.5)	0.86 [0.45; 1.65] 0.654
Total					1.05 [0.80; 1.39] 0.724
Pain (arm/shoulder)					
Impower133 – global cohort (DC: 24 April 2018)	201	6.9 [5.1; 10.4] 78 (38.8)	202	6.2 [4.2; 10.6] 80 (39.6)	0.93 [0.68; 1.28] 0.671
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	n.a. [4.6; n.c.] 19 (33.3)	53	9.7 [7.1; n.c.] 20 (37.7)	0.96 [0.50; 1.83] 0.898
Total					0.94 [0.70; 1.24] 0.647
Pain (chest)					
Impower133 – global cohort (DC: 24 April 2018)	201	10.9 [6.0; n.c.] 66 (32.8)	202	11.6 [6.1; n.c.] 65 (32.2)	0.99 [0.70; 1.40] 0.958
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	11.1 [3.8; n.c.] 18 (31.6)	53	7.1 [2.3; n.c.] 25 (47.2)	0.64 [0.35; 1.19] 0.157
Total					0.89 [0.66; 1.20]

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
					0.451
Pain (other)					
Impower133 – global cohort (DC: 24 April 2018)	201	6.5 [3.9; 8.1] 84 (41.8)	202	6.2 [4.4; 10.4] 79 (39.1)	1.04 [0.77; 1.42] 0.789
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	3.8 [2.3; n.c.] 27 (47.4)	53	7.2 [4.1; 12.7] 26 (49.1)	1.38 [0.79; 2.39] 0.254
Total					1.11 [0.85; 1.45] 0.440
Health status (EQ-5D VAS)[c]					
Impower133 – global cohort (DC: 24 April 2018)	201	4.7 [3.1; 7.3] 94 (46.8)	202	5.6 [3.6; 9.0] 83 (41.1)	1.11 [0.82; 1.50] 0.491
IMpower133 – China (DC: 29 October 2018)	57	4.2 [2.3; n.c.] 29 (50.9)	53	4.1 [1.5; n.c.] 28 (52.8)	1.01 [0.60; 1.72] 0.960
Total					1.08 [0.83; 1.41] 0.544

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		Intervention vs Control
	N	Values at start of study MV (SD) Values at week 12 MV (SD)	N	Values at start of study MV (SD) Values at week 12 MV (SD)	Mean difference [95% CI] p value
Health status (EQ-5D VAS) (presented as a supplement)[d]					
IMpower133 (DC: 24 April 2018)	132	63.43 (19.46) 69.80 (18.87)	146	65.10 (20.55) 72.10 (18.28)	− 2.30 [−6.68; 2.08] no data available

IMpower133 – China (DC: 29 October 2018)	38	77.86 (13.45) 78.24 (11.72)	42	77.49 (16.76) 78.10 (14.24)	0.14 [−5.55; 5.83] no data available
Total					−1.39 [−4.86; 2.08] 0.431

Health-related quality of life

Endpoint	**Atezolizumab + carboplatin + etoposide**		**Carboplatin + etoposide**		**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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
EORTC QLQ-C30 functional scales[c]					
Global health status					
Impower133 – global cohort (DC: 24 April 2018)	201	6.5 [4.5; 10.4] 88 (43.8)	202	7.6 [4.2; 9.6] 81 (40.1)	1.01 [0.74; 1.37] 0.971
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	3.8 [2.1; 7.7] 32 (56.1)	53	9.4 [5.7; n.c.] 22 (41.5)	1.87 [1.07; 3.25] 0.025
Total					1.17 [0.89; 1.53] 0.260
Emotional function					
Impower133 – global cohort (DC: 24 April 2018)	201	n.a. [7.1; n.c.] 66 (32.8)	202	8.8 [7.6; n.c.] 74 (36.6)	0.85 [0.61; 1.19] 0.344
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	9.9 [3.0; n.c.] 23 (40.4)	53	4.2 [2.7; 12.7] 27 (50.9)	0.87 [0.49; 1.55] 0.632
Total					0.85 [0.64; 1.14] 0.288
Cognitive function					
Impower133 – global cohort (DC: 24 April 2018)	201	4.2 [2.8; 6.0] 99 (49.3)	202	4.4 [3.0; 7.0] 96 (47.5)	1.00 [0.75; 1.34] 0.979
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	3.8 [2.8; 9.9] 28 (49.1)	53	3.6 [1.4; 7.3] 31 (58.5)	0.81 [0.48; 1.38]

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
					0.442
Total					0.95 [0.74; 1.23] 0.706
Physical function					
Impower133 – global cohort (DC: 24 April 2018)	201	5.4 [3.5; 7.2] 98 (48.8)	202	6.2 [3.5; 8.7] 89 (44.1)	1.10 [0.82; 1.47] 0.540
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	3.8 [2.9; 9.9] 30 (52.6)	53	8.3 [3.1; n.c.] 24 (45.3)	1.38 [0.80; 2.38] 0.239
Total					1.16 [0.89; 1.50] 0.267
Role function					
Impower133 – global cohort (DC: 24 April 2018)	201	3.7 [3.0; 5.3] 103 (51.2)	202	3.7 [2.6; 5.6] 98 (48.5)	1.04 [0.79; 1.38] 0.774
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	3.8 [2.3; 9.9] 30 (52.6)	53	7.0 [3.1; n.c.] 25 (47.2)	1.30 [0.76; 2.23] 0.335
Total					1.09 [0.85; 1.40] 0.494
Social function					
Impower133 – global cohort (DC: 24 April 2018)	201	7.0 [3.9 15.6] 83 (41.3)	202	2.8 [2.1; 5.6] 99 (49.0)	0.73 [0.54; 0.98] 0.038 AD = 4.2 months
IMpower133 – Chinese cohort (DC: 29 October 2018)	57	4.0 [1.5; n.c.] 29 (50.9)	53	2.3 [2.1; n.c.] 29 (54.7)	0.97 [0.57; 1.68] 0.925

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
Total					0.78 [0.60; 1.01] 0.062

Side effects

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
Total adverse events (presented additionally)					
Impower133 – global cohort (DC: 24 April 2018)	198	no data available 198 (100)	196	no data available 189 (96.4)	-
IMpower133 – Chinese cohort (DC: 31 July 2019)	57	no data available 57 (100)	52	no data available 52 (100)	-
Serious adverse events (SAE)					
Impower133 – global cohort (DS: 24 April 2018)	198	no data available 74 (37.4)	196	no data available 68 (34.7)	1.12 [0.81; 1.56] 0.494
IMpower133 – Chinese cohort (DC: 31 July 2019)	57	no data available 21 (36.8)	52	no data available 14 (26.9)	1.36 [0.69; 2.69] 0.370
Total					1.16 [0.86; 1.56] no data available
Severe adverse events (CTCAE grade 3 or 4)					
Impower133 – global cohort	198	no data available	196	no data available	1.07 [0.84; 1.37]

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		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 (%)*	Hazard Ratio [95% CI] p value Absolute difference (AD)[a]
(DC: 24 April 2018)		136 (68.7)[e]		136 (69.4)[e]	0.570
IMpower133 – Chinese cohort (DC: 31 July 2019)	57	no data available 46 (80.7)	52	no data available 43 (82.7)	1.06 [0.69; 1.62] 0.784
Total					1.07 [0.86; 1.32] no data available
Therapy discontinuation because of adverse events[f]					
Impower133 – global cohort (DC: 24 April 2018)	198	no data available 22 (11.1)	196	no data available 6 (3.1)	3.42 [1.38; 8.48] 0.005 AD = n.c.
IMpower133 – Chinese cohort (DC: 31 July 2019)	57	no data available 7 (12.3)	52	no data available 0 (0)	n.c. 0.010
Total					n.c.

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		Intervention vs Control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
Specific adverse events[g]					
immune mediated AE					
Impower133 – global cohort	198	79 (39.9)	196	48 (24.5)	no data available

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		Intervention vs Control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
(DC: 24 April 2018)					
IMpower133 – Chinese cohort (DC: 24 January 2019)	57	31 (54.4)	52	20 (38.5)	no data available
Total					1.57 [1.23; 2.01] < 0.001
immune mediated SAE					
Impower133 – global cohort (DC: 24 April 2018)	198	13 (6.6)	196	7 (3.6)	no data available
IMpower133 – Chinese cohort (DC: 24 January 2019)	57	4 (7.0)	52	0 (0)	no data available
Total					2.36 [0.997; 5.60] 0.044b
Immune mediated AE with CTCAE grade 3 and 4					
Impower133 – global cohort (DC: 24 April 2018)	198	16 (8.1)	196	5 (2.6)	no data available
IMpower133 – Chinese cohort (DC: 24 January 2019)	57	4 (7.0)	52	4 (7.7)	no data available
Total					2.16 [1.004; 4.65] 0.043

[a] Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
[b] Time to first deterioration; defined as an increase of the score by ≥ 10 points compared with baseline
[c] Time to first deterioration, defined as a decrease of the score by ≥ 10 points compared with baseline
[d] Higher values signify a better health-related quality of life; positive effects mean an advantage for intervention
[e] Discrepancy between information in Modules 4 and 5 of the dossier. The data shown are from Module 4. These were used by IQWiG because no HRs were reported in the study report. In the study report, 133 (67.2%) patients were reported in the atezolizumab arm and 125 (63.8%) in the placebo arm.
[f] Discontinuation of at least one treatment component
[g] Selection in accordance with IQWiG methodology; selection based on those identified in the study

Endpoint	Atezolizumab + carboplatin + etoposide		Carboplatin + etoposide		Intervention vs Control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
Events based on frequency and differences between treatment arms and taking into account patient relevance.					

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; DC = data cut; HR = hazard ratio; CI = confidence interval; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.a. = not achieved; SD = standard deviation; vs = versus

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↑	Advantage in overall survival
Morbidity	↔	No differences relevant for the benefit assessment.
Health-related quality of life	↔	No differences relevant for the benefit assessment.
Side effects	↓	Disadvantages in the endpoint therapy discontinuations because of AE as well as in individual specific AE.

Explanations:
↑↑ positive statistically significant and relevant effect with high reliability of data
↑ positive statistically significant and relevant effect with low/unclear reliability of data
↔ no statistically significant or relevant difference
↓ negative statistically significant and relevant effect with low/unclear reliability of data
↓↓ negative statistically significant and relevant effect with high reliability of data
⍉ 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

Adult patients with extensive-stage small cell lung cancer (ES-SCLC); first-line treatment

approx. 7,280 to 8,550 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 Tecentriq® (active ingredient: atezolizumab) at the following publicly accessible link (last access: 10 December 2019):

https://www.ema.europa.eu/documents/product-information/tecentriq-epar-product-information_de.pdf

Treatment with atezolizumab may only be initiated and monitored by specialists in internal medicine, haematology, and oncology, specialists in internal medicine and pneumology, specialists in pulmonary medicine, and specialists participating in the Oncology Agreement who are experienced in the treatment of patients with small cell lung cancer.

According to the requirements for risk minimisation activities in the EPAR (European Public Assessment Report), the pharmaceutical company must provide the following information material on atezolizumab:

- Training material for health professionals
- Patient pass

The training material includes, in particular, instructions on how to deal with the immune mediated side effects potentially occurring under atezolizumab treatment as well as infusion-related reactions.

Patients with symptomatic brain metastases were disqualified from the IMpower133 study. Thus, no data are available for patients with symptomatic brain metastases.

4. Treatment costs

Annual treatment costs:

Adult patients with extensive-stage small cell lung cancer (ES-SCLC); first-line treatment

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Induction therapy	
Atezolizumab	€ 17,702.36
Carboplatin	€ 1,761.20
Etoposide	€ 918.00
Total	€ 20,381.56
Maintenance treatment	
Atezolizumab	€ 59,302.91
Appropriate comparator therapy:	
Cisplatin + etoposide	
Cisplatin	€ 2,007.44
Etoposide	€ 3,993.30

Designation of the therapy	Annual treatment costs/patient
Total	€ 6,000.74
Additionally required SHI services	€ 328.58 – 421.62
Carboplatin + etoposide	
Carboplatin	€ 7,661.22
Etoposide	€ 3,993.30
Total	€ 11,654.52

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 March 2020

Other services covered by SHI funds:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Atezolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Etoposide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	4	€ 324
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 2 April 2020.

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

Berlin, 2 April 2020

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken