Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Resolutions on the Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V – Pertuzumab (New Therapeutic Indication: Breast Cancer, Adjuvant Treatment)

of 20 December 2018

At its session on 20 December 2018 the Federal Joint Committee (G-BA) resolved 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 18 October 2018 (Federal Gazette, BAnz AT 4 January 2019 B3), as follows:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of pertuzumab in accordance with the resolution of 18 February 2016:

Pertuzumab

Resolution of: 20 December 2018
Entry into force on: 20 December 2018
Federal Gazette, BAnz AT 24 January 2019 B2

New therapeutic indication (according to the marketing authorisation of 31 May 2018):

Perjeta is indicated for use in combination with trastuzumab and chemotherapy in the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence.

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

Adult patients with HER2-positive early breast cancer at high risk of recurrence for adjuvant treatment

Appropriate comparator therapy:

A therapy scheme containing trastuzumab, a taxane (paclitaxel or docetaxel) and, if applicable, an anthracycline (doxorubicin or epirubicin).

Extent and probability of the additional benefit compared with trastuzumab + chemotherapy:

Hint for a minor additional benefit.

Study results according to endpoints:[1]

APHINITY study:

Pertuzumab + trastuzumab + chemotherapy **vs** trastuzumab + chemotherapy

Study design: randomised, double-blind, two-armed

Relevant sub-population: Patients at high risk of recurrence according to the marketing authorisation; defined as nodal-positive or hormone receptor-negative disease (approx. 75% of the study population)

Mortality

Endpoint	**Pertuzumab + trastuzumab + chemotherapy**		**Trastuzumab + chemotherapy**		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value Absolute difference (AD)[a]
Overall survival					
	1811	72 (4.0) Median time to event: n.a. [n.a.; n.a.]	1823	80 (4.4) Median time to event: n.a. [n.a.; n.a.]	HR[b]: 0.89 [0.65; 1.23] 0.486

Morbidity

Endpoint	**Pertuzumab + trastuzumab + chemotherapy**		**Trastuzumab + chemotherapy**		Intervention vs control
	N	Median time to event [95% CI] Patients with event n (%)	N	Median time to event [95% CI] Patients with event n (%)	Effect estimator [95% CI] p value Absolute difference (AD)[a]
Disease-free survival (DFS)[c]					
	1811	n.a. [n.a.; n.a.] 166 (9.2)	1823	n.a. [n.a.; n.a.] 211 (11.6)	HR: 0.78 [0.64; 0.96] 0.019[d]

(Continuation)

[1] Data from the dossier assessment of the IQWiG (A18-41) and the addendum (A18-76) unless otherwise indicated.

Endpoint	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value Absolute difference (AD)[a]
Recurrences (event rate)[e]					
	1811	166 (9.2)	1823	211 (11.6)	RR: 0.79 [0.65; 0.96] 0.018[f] AD: − 2.4%
Symptomatology[g]					
EORTC QLQ-C30 symptom scales – Patients with deterioration by ≥ 10 points					
Fatigue					
End of the anti-HER2 therapy	1538	703 (45.7)	1597	642 (40.2)	RR: 1.14 [1.05; 1.24] 0.001 AD: + 5.5%
36-month follow-up	1361	437 (32.1)	1327	474 (35.7)	RR: 0.90 [0.81; 1.00] 0.054
Nausea and vomiting					
End of the anti-HER2 therapy	1542	184 (11.9)	1598	176 (11.0)	RR: 1.08 [0.89; 1.32] 0.411
Sub-groups: Age					
< 65 years	1361	151 (11.1)	1423	161 (11.3)	RR: 0.98 [0.80; 1.21] 0.855
≥ 65 years	181	33 (18.2)	175	15 (8.6)	RR: 2.13 [1.20; 3.78] 0.010
36-month follow-up	1363	125 (9.2)	1328	132 (9.9)	RR: 0.92 [0.73; 1.15] 0.453
Pain					
End of the anti-HER2 therapy	1541	420 (27.3)	1597	461 (28.9)	RR: 0.94 [0.84; 1.05] 0.297
36-month follow-up	1362	316 (23.2)	1328	318 (23.9)	RR: 0.97 [0.84; 1.11] 0.643

Endpoint **Date**	**Pertuzumab + trastuzumab + chemotherapy**		**Trastuzumab + chemotherapy**		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
Dyspnoea					
End of the anti-HER2 therapy	1539	392 (25.5)	1592	375 (23.6)	RR: 1.08 [0.96; 1.22] 0.214
36-month follow-up	1361	278 (20.4)	1321	303 (22.9)	RR: 0.90 [0.78; 1.03] 0.133
Insomnia					
End of the anti-HER2 therapy	1538	430 (28.0)	1591	405 (25.5)	RR: 1.10 [0.98; 1.24] 0.104
36-month follow-up	1362	318 (23.3)	1322	333 (25.2)	RR: 0.93 [0.81; 1.06] 0.279
Loss of appetite					
End of the anti-HER2 therapy	1538	235 (15.3)	1594	180 (11.3)	RR: 1.35 [1.13; 1.62] 0.001 AD: + 4.0%
Sub-groups: Age					
< 65 years	1358	192 (14.1)	1419	165 (11.6)	RR: 1.22 [1.00; 1.48] 0.049
≥ 65 years	180	43 (23.9)	175	15 (8.6)	RR: 2.79 [1.61; 4.83] < 0.001
36-month follow-up	1361	121 (8.9)	1326	125 (9.4)	RR: 0.95 [0.75; 1.20] 0.647
Constipation					
End of the anti-HER2 therapy	1538	202 (13.1)	1593	248 (15.6)	RR: 0.84 [0.71; 1.00] 0.055
36-month follow-up	1363	219 (16.1)	1321	201 (15.2)	RR: 1.06 [0.89; 1.26] 0.537

Endpoint Date	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
Diarrhoea					
End of the anti-HER2 therapy	1532	458 (29.9)	1590	213 (13.4)	RR: 2.23 [1.92; 2.58] < 0.001 AD: + 16.5%
36-month follow-up	1358	100 (7.4)	1322	128 (9.7)	RR: 0.76 [0.59; 0.97] 0.031 AD: − 2.3%
EORTC QLQ-BR23 symptom scales – Patients with deterioration by ≥ 10 points					
Side effects of the systemic therapy					
End of the anti-HER2 therapy	1535	416 (27.1)	1591	426 (26.8)	RR: 1.02 [0.91; 1.14] 0.742
36-month follow-up	1358	313 (23.0)	1321	318 (24.1)	RR: 0.96 [0.83; 1.10] 0.522
Symptoms in the chest area					
End of the anti-HER2 therapy	1532	292 (19.1)	1580	246 (15.6)	RR: 1.23 [1.05; 1.43] 0.009 AD: + 3.5%
36-month follow-up	1355	154 (11.4)	1318	141 (10.7)	RR: 1.06 [0.85; 1.31] 0.610
Symptoms in the arm area					
End of the anti-HER2 therapy	1532	417 (27.2)	1581	454 (28.7)	RR: 0.94 [0.84; 1.05] 0.296
36-month follow-up	1355	320 (23.6)	1320	336 (25.5)	RR: 0.92 [0.81; 1.05] 0.227

(Continuation)

Endpoint Date	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
Burden of hair loss					
End of the anti-HER2 therapy	57	10 (17.5)	54	16 (29.6)	RR: 0.59 [0.29; 1.19] 0.137[i]
36-month follow-up	73	18 (24.7)	77	20 (26.0)	RR: 0.89 [0.50; 1.58] 0.696

Health-related quality of life

Endpoint Date	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
EORTC QLQ-C30 functional scales – Patients with deterioration by ≥ 10 points					
Global health status					
End of the anti-HER2 therapy	1532	428 (27.9)	1589	421 (26.5)	RR: 1.05 [0.94; 1.18] 0.416
36-month follow-up	1357	295 (21.7)	1320	320 (24.2)	RR: 0.89 [0.78; 1.02] 0.106

(Continuation)

Endpoint **Date**	**Pertuzumab + trastuzumab + chemotherapy**		**Trastuzumab + chemotherapy**		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
Physical functioning					
End of the anti-HER2 therapy	1543	358 (23.2)	1597	361 (22.6)	RR: 1.03 [0.90; 1.17] 0.664
Sub-groups: Age					
< 65 years	1362	290 (21.3)	1422	316 (22.2)	RR: 0.96 [0.83; 1.10] 0.552
≥ 65 years	181	68 (37.6)	175	45 (25.7)	RR: 1.46 [1.07; 2.00] 0.018
36-month follow-up	1363	236 (17.3)	1329	234 (17.6)	RR: 0.98 [0.83; 1.15] 0.800
Role functioning					
End of the anti-HER2 therapy	1540	383 (24.9)	1594	368 (23.1)	RR: 1.08 [0.95; 1.22] 0.221
36-month follow-up	1362	216 (15.9)	1327	243 (18.3)	RR: 0.87 [0.73; 1.03] 0.098
Sub-groups: Age					
< 65 years	1209	173 (14.3)	1185	212 (17.9)	RR: 0.80 [0.67; 0.96] 0.017
≥ 65 years	153	43 (28.1)	142	31 (21.8)	RR: 1.29 [0.86; 1.92] 0.217
Emotional functioning					
End of the anti-HER2 therapy	1535	388 (25.3)	1593	393 (24.7)	RR: 1.02 [0.91; 1.16] 0.715
36-month follow-up	1359	302 (22.2)	1324	337 (25.5)	RR: 0.87 [0.76; 1.00] 0.047 AD: − 3.3%

(Continuation)

Endpoint	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
Cognitive functioning					
End of the anti-HER2 therapy	1536	607 (39.5)	1592	632 (39.7)	RR: 1.00 [0.91; 1.09] 0.923
36-month follow-up	1360	490 (36.0)	1324	494 (37.3)	RR: 0.96 [0.97; 1.06] 0.436
Social functioning					
End of the anti-HER2 therapy	1535	349 (22.7)	1590	376 (23.6)	RR: 0.96 [0.85; 1.09] 0.540
36-month follow-up	1360	209 (15.4)	1323	237 (17.9)	RR: 0.86 [0.73; 1.02] 0.085
EORTC QLQ-BR23 functional scales – Patients with deterioration by ≥ 10 points					
Body image					
End of the anti-HER2 therapy	1521	578 (38.0)	1573	642 (40.8)	RR: 0.93 [0.86; 1.02] 0.126
36-month follow-up	1342	388 (28.9)	1304	411 (31.5)	RR: 0.92 [0.82; 1.03] 0.145
Sexual activity					
End of the anti-HER2 therapy	1456	336 (23.1)	1509	358 (23.7)	RR: 0.97 [0.85; 1.11] 0.680
36-month follow-up	1279	258 (20.2)	1251	269 (21.5)	RR: 0.93 [0.80; 1.09] 0.377
Sexual enjoyment					
End of the anti-HER2 therapy	437	147 (33.6)	481	159 (33.1)	RR: 1.02 [0.85; 1.23] 0.829
36-month follow-up	383	113 (29.5)	402	118 (29.4)	RR: 1.03 [0.83; 1.27] 0.822

Endpoint	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[g] Absolute difference (AD)[a]
Future perspective					
End of the anti-HER2 therapy	1518	272 (17.9)	1576	292 (18.5)	RR: 0.97 [0.84; 1.13] 0.697
36-month follow-up	1340	191 (14.3)	1304	188 (14.4)	RR: 0.99 [0.82; 1.19] 0.918

Side effects

Endpoint	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value Absolute difference (AD)[a]
Total adverse events					
	1783	1782 (> 99.9)	1822	1811 (99.4)	-
Serious adverse events (SAE)					
	1783	508 (28.5)	1822	444 (24.4)	RR: 1.17 [1.05; 1.30] 0.005 AD: + 4.1%
Severe adverse events (CTCAE grade ≥ 3)					
	1783	1128 (63.3)	1822	1043 (57.2)	RR: 1.11 [1.05; 1.17] < 0.001 AD: + 6.1%
Therapy discontinuations because of adverse events					
	1783	219 (12.3)	1822	219 (12.0)	RR: 1.02 [0.86; 1.22] 0.809
Specific adverse events[i]					
Diarrhoea	1783	1252 (70.2)	1822	812 (44.6)	RR: 1.58 [1.48; 1.67] < 0.001[h] AD: + 25.6%

Endpoint	Pertuzumab + trastuzumab + chemotherapy		Trastuzumab + chemotherapy		Intervention vs control
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value Absolute difference (AD)[a]
Diarrhoea (serious)	1783	41 (2.3)	1822	14 (0.8)	RR: 2.99 [1.64; 5.47] < 0.001[h] AD: + 1.5%
Cardiac insufficiency (serious)	1783	25 (1.4)	1822	12 (0.7)	RR: 2.13 [1.07; 4.22] 0.027[h] AD: + 0.7%
Metabolism and nutrition disorders (serious)	1783	30 (1.7)	1822	13 (0.7)	RR: 2.36 [1.23; 4.51] 0.007[h] AD: + 1.0%

[a] Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
[b] Cox model stratified by nodal status, type of adjuvant chemotherapy, hormone receptor status, and protocol version; p value: stratified log-rank test
[c] Operationalised as the time from the day of randomisation to the first occurrence of any of the following events: ipsilateral invasive local breast cancer recurrence, ipsilateral invasive regional breast cancer recurrence, remote recurrence, contralateral invasive breast cancer, secondary primary carcinoma (no breast cancer), DCIS (ipsilateral or contralateral), or death (by any cause)
[d] Cox model stratified by nodal status, type of adjuvant chemotherapy, hormone receptor status, and protocol version; p value: stratified log-rank test
[e] Recurrence rate in accordance with operationalisation for DFS
[f] Calculation of the IQWiG: RR, 95% CI, asymptotic, unconditional exact test (CSZ method)
[g] RR and p value from log-binomial regression adjusted for nodal status, type of adjuvant chemotherapy, hormone receptor status, and protocol version
[h] Calculation of the IQWiG: RR, 95% CI, asymptotic, unconditional exact test (CSZ method)
[i] Selection according to the methodology of the IQWiG; selection using events that occurred in the study based on frequency and differences between treatment arms and taking into account patient relevance. In addition, AE that are of particular importance for the clinical presentation or for the active ingredients used in the study.

Abbreviations used:
AD: Absolute difference; CTCAE: Common Terminology Criteria for Adverse Events; DCIS: ductal carcinoma in situ; DFS: disease-free survival; EORTC QLQ-C30: EORTC Quality of life Questionnaire core 30; EORTC QLQ-BR23: EORTC Quality of life Questionnaire and breast cancer specific module 23; HR: hazard ratio; CI: confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; n.a.: not achieved; RR: relative risk; SAE: serious adverse event; AE: adverse event; vs: versus

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

approx. 3,020 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 Perjeta® (active ingredient: pertuzumab) at the following publicly accessible link (last access: 13 September 2018):

http://www.ema.europa.eu/docs/de_DE/document_library/EPAR_-_Product_Information/human/002547/WC500140980.pdf

Treatment with pertuzumab may be initiated and monitored only by specialists in internal medicine, haematology, and oncology, specialists in gynaecology and obstetrics, and specialists participating in the Oncology Agreement who are experienced in the therapy of patients with breast cancer.

Pertuzumab should be administered by a healthcare professional prepared to manage anaphylaxis and in an environment where full resuscitation facilities are immediately available.

In older patients, disadvantageous therapy effects are seen in individual aspects of symptomatology and health-related quality of life (see study results presented above); these should be weighed up before the therapy decision is made.

4. Treatment costs

Annual treatment costs:

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Pertuzumab	€ 52,849.64
+ trastuzumab	€ 37,945.64
In combination with one of the following chemotherapy regimes:	
+ 5-fluorouracil + epirubicin + cyclophosphamide (FEC), docetaxel	
5-fluorouracil	€ 33.28 – 66.56
Epirubicin	€ 1,376.10 – 2,503.16
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 95,519.49 – 98,941.69
+ 5-fluorouracil + epirubicin + cyclophosphamide (FEC), paclitaxel (q1w)	
5-fluorouracil	€ 33.28 – 66.56
Epirubicin	€ 1,376.10 – 2,503.16
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 98,352.51 – 99,512.85
+ 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), docetaxel	
5-fluorouracil	€ 33.28 – 66.56
Doxorubicin	€ 851.07 – 1,134.76
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 94,994.46 – 97,573.29
+ 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), paclitaxel (q1w)	
5-fluorouracil	€ 33.28 – 66.56
Doxorubicin	€ 851.07 – 1,134.76
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 97,827.48 – 98,144.45

(Continuation)

Designation of the therapy	Annual treatment costs/patient
+ doxorubicin + cyclophosphamide (AC), docetaxel	
Doxorubicin	€ 1,278.40
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 95,388.51 – 97,650.37
+ doxorubicin + cyclophosphamide (AC), paclitaxel (q1w)	
Doxorubicin	€ 1,278.40
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 98,221.53
+ doxorubicin + cyclophosphamide (AC), paclitaxel (q3w)	
Doxorubicin	€ 1,278.40
Cyclophosphamide	€ 44.65
Paclitaxel (q3w)	€ 4,469.08 – 5,402.76
Total	€ 96,587.41 – 97,521.09
+ epirubicin + cyclophosphamide (EC), docetaxel	
Epirubicin	€ 1,834.80 – 2,503.16
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 95,944.91 – 98,875.13
+ epirubicin + cyclophosphamide (EC), paclitaxel (q1w)	
Epirubicin	€ 1,834.80 – 2,503.16
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 98,777.93 – 99,446.29
+ docetaxel + carboplatin	
Docetaxel	€ 6,540.36
Carboplatin	€ 1,898.70
Total	€ 99,234.34

(Continuation)

Designation of the therapy	Annual treatment costs/patient
Appropriate comparator therapy:	
Trastuzumab	€ 37,945.64
In combination with one of the following chemotherapy regimes:	
+ 5-fluorouracil + epirubicin + cyclophosphamide (FEC), docetaxel	
5-fluorouracil	€ 33.28 – 66.56
Epirubicin	€ 1,376.10 – 2,503.16
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 42,669.85 – 46,092.05
+ 5-fluorouracil + epirubicin + cyclophosphamide (FEC), paclitaxel (q1w)	
5-fluorouracil	€ 33.28 – 66.56
Epirubicin	€ 1,376.10 – 2,503.16
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 45,502.87 – 46,663.21
+ 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), docetaxel	
5-fluorouracil	€ 33.28 – 66.56
Doxorubicin	€ 851.07 – 1,134.76
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 42,144.82 – 44,723.65
+ 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), paclitaxel (q1w)	
5-fluorouracil	€ 33.28 – 66.56
Doxorubicin	€ 851.07 – 1,134.76
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 44,977.84 – 45,294.81
+ doxorubicin + cyclophosphamide (AC), docetaxel	
Doxorubicin	€ 1,278.40
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 42,538.87 – 44,800.73

(Continuation)

Designation of the therapy	Annual treatment costs/patient
+ doxorubicin + cyclophosphamide (AC), paclitaxel (q1w)	
Doxorubicin	€ 1,278.40
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 45,371.89
+ doxorubicin + cyclophosphamide (AC), paclitaxel (q3w)	
Doxorubicin	€ 1,278.40
Cyclophosphamide	€ 44.65
Paclitaxel (q3w)	€ 4,469.08 – 5,402.76
Total	€ 43,737.77 – 44,671.45
+ epirubicin + cyclophosphamide (EC), docetaxel	
Epirubicin	€ 1,834.80 – 2,503.16
Cyclophosphamide	€ 44.65
Docetaxel	€ 3,270.18 – 5,532.04
Total	€ 43,095.27 – 46,025.49
+ epirubicin + cyclophosphamide (EC), paclitaxel (q1w)	
Epirubicin	€ 1,834.80 – 2,503.16
Cyclophosphamide	€ 44.65
Paclitaxel (q1w)	€ 6,103.20
Total	€ 45,928.29 – 46,596.65
+ docetaxel + carboplatin	
Docetaxel	€ 6,540.36
Carboplatin	€ 2,087.40
Total	€ 46,573.40

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2018

Costs for additionally required SHI services: not applicable

Other services covered by SHI funds:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed:					
Pertuzumab	a	€ 71	1	18	€ 1,278
Trastuzumab	a	€ 71	1	18	€ 1,278
In combination with one of the following chemotherapy regimes:					
5-fluorouracil + epirubicin + cyclophosphamide (FEC)	b	€ 81	3	9 to 12	€ 729 – 972
+ docetaxel	b	€ 81	1	3 to 4	€ 243 – 324
+ paclitaxel (q1w)	b	€ 81	3	9 to 12	€ 729 – 972
5-fluorouracil + doxorubicin + cyclophosphamide (FAC)	b	€ 81	3	9 to 12	€ 729 – 972
+ docetaxel	b	€ 81	1	3 to 4	€ 243 – 324
+ paclitaxel (q1w)	b	€ 81	1	12	€ 972
Doxorubicin + cyclophosphamide (AC)	b	€ 81	2	8	€ 648
+ docetaxel	b	€ 81	1	3 to 4	€ 243 – 324
+ paclitaxel (q1w)	b	€ 81	1	12	€ 972
+ paclitaxel (q3w)	b	€ 81	1	4	€ 324
Epirubicin + cyclophosphamide (EC)	b	€ 81	2	8	€ 648
+ docetaxel	b	€ 81	1	3 to 4	€ 243 – 324
+ paclitaxel (q1w)	b	€ 81	1	12	€ 972
docetaxel + carboplatin	b	€ 81	2	12	€ 972
Appropriate comparator therapy:					
For the appropriate comparator therapy, the costs for the other SHI services correspond to those of the medicinal product to be assessed minus pertuzumab.					
a: Surcharge for the preparation of a parenteral solution containing monoclonal antibodies b: Surcharge for production of a parenteral preparation containing cytostatic agents					

II. Entry into force

1. **The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 20 December 2018.**

2. **The period of validity of the resolution is limited to 2 January 2022.**

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

Berlin, 20 December 2018

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

Prof. Hecken