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
Pertuzumab (reassessment after the deadline: breast cancer, early at high risk of recurrence, adjuvant treatment, combination with trastuzumab and chemotherapy)

of 16 March 2023

At its session on 16 March 2023, 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. Annex XII is amended as follows:**

1. **The information on pertuzumab in the version of the resolution of 20 December 2018 (BAnz AT 22.02.2021 B4), last modified on 21 January 2021, is repealed.**
2. **In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Pertuzumab in the version of the resolution of 18 February 2016:**

**Pertuzumab**

Resolution of: 16 March 2023
Entry into force on: 16 March 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

**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.

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

See therapeutic indication according to marketing authorisation.

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

Adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence.

**Appropriate comparator therapy:**

a therapeutic regimen containing trastuzumab, a taxane (paclitaxel or docetaxel) and, if appropriate, an anthracycline (doxorubicin or epirubicin)

**Extent and probability of the additional benefit of pertuzumab in combination with trastuzumab and chemotherapy compared to trastuzumab in combination with chemotherapy:**

Indication of a minor additional benefit

**Study results according to endpoints:**[1]

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-103) unless otherwise indicated.

**Summary of results for relevant clinical endpoints**

| Endpoint category | Direction of effect/ risk of bias | Summary |
|---|---|---|
| Mortality | ↔ | No relevant difference for the benefit assessment |
| Morbidity | ↑↑ | Advantages in the prevention of recurrences |
| Health-related quality of life | ↔ | No relevant difference for the benefit assessment |
| Side effects | ↓↓ | Disadvantages in the endpoints serious adverse events (SAE) and severe AEs (CTCAE grade ≥ 3) |

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

APHINITY study: Pertuzumab + trastuzumab + chemotherapy **vs** placebo + trastuzumab + chemotherapy

Relevant sub-population: Adults with HER2-positive early stage breast cancer at high risk of recurrence according to the marketing authorisation, defined as nodal-positive or hormone receptor-negative disease (approximately 75% of the study population)

**Mortality**

| Endpoint | Pertuzumab + trastuzumab + chemotherapy | | Placebo + trastuzumab + chemotherapy | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Median survival time in months [95% CI]<br>*Patients with event n (%)* | N | Median survival time in months [95% CI]<br>*Patients with event n (%)* | HR[a] [95% CI] p value |
| **Overall survival** (data cut-off: 10.01.2022) | | | | | |
| | 1,811 | n.r. [n.c.; n.c.]<br>*140 (7.7)* | 1,823 | n.r. [n.c.; n.c.]<br>*175 (9.6)* | 0.798 [0.638; 0.996] 0.046 |

**Morbidity**

| Endpoint | Pertuzumab + trastuzumab + chemotherapy | | Placebo + trastuzumab + chemotherapy | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI] p value Absolute difference[b] |
| **Recurrences** (data cut-off: 10.01.2022) | | | | | |
| Recurrence rate | 1,811 | 256 (14.1) | 1,823 | 347 (19.0) | 0.74 [0.64; 0.86] < 0.001[c] AD: 4.9% |
| Recurrent ipsilateral invasive local breast cancer | 1,811 | 16 (6.3) | 1,823 | 38 (11.0) | – |
| Recurrent ipsilateral invasive regional breast cancer | 1,811 | 11 (4.3) | 1,823 | 14 (4.0) | – |
| Distant recurrence | 1,811 | 132 (51.6) | 1,823 | 174 (50.1) | – |
| Contralateral invasive breast cancer | 1,811 | 22 (8.6) | 1,823 | 25 (7.2) | – |
| Secondary primary cancer (not breast cancer) | 1,811 | 43 (16.8) | 1,823 | 52 (15.0) | – |
| DCIS (ipsilateral or contralateral) | 1,811 | 7 (2.7) | 1,823 | 16 (4.6) | – |
| Death from any cause | 1,811 | 25 (9.8) | 1,823 | 28 (8.1) | – |
| Disease-free survival | 1,811 | 256 (14.1) Median time to event: n.r. [n.c.; n.c.] | 1,823 | 347 (19.0) Median time to event: n.r. [n.c.; n.c.] | HR[a]: 0.72 [0.62; 0.85] < 0.001 |

| Endpoint | Pertuzumab + trastuzumab + chemotherapy | | Placebo + trastuzumab + chemotherapy | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI] p value[d] Absolute difference[b] |
| **Symptomatology (EORTC QLQ-C30) - deterioration by ≥ 10 points** (data cut-off: 19.12.2016) | | | | | |
| Fatigue | | | | | |
| End of anti-HER2 therapy | 1,538 | 703 (45.7) | 1,597 | 642 (40.2) | 1.14 [1.05; 1.24] 0.001 AD: 5.5% |
| 36-month follow-up | 1,361 | 437 (32.1) | 1,327 | 474 (35.7) | 0.90 [0.81; 1.00] 0.054 |
| Nausea and vomiting | | | | | |
| End of anti-HER2 therapy | 1,542 | 184 (11.9) | 1,598 | 176 (11.0) | 1.08 [0.89; 1.32] 0.411 |
| 36-month follow-up | 1,363 | 125 (9.2) | 1,328 | 132 (9.9) | 0.92 [0.73; 1.15] 0.453 |
| Pain | | | | | |
| End of anti-HER2 therapy | 1,541 | 420 (27.3) | 1,597 | 461 (28.9) | 0.94 [0.84; 1.05] 0.297 |
| 36-month follow-up | 1,362 | 316 (23.2) | 1,328 | 318 (23.9) | 0.97 [0.84; 1.11] 0.643 |
| Dyspnoea | | | | | |
| End of anti-HER2 therapy | 1,539 | 392 (25.5) | 1,592 | 375 (23.6) | 1.08 [0.96; 1.22] 0.214 |
| 36-month follow-up | 1,361 | 278 (20.4) | 1,321 | 303 (22.9) | 0.90 [0.78; 1.03] 0.133 |
| Insomnia | | | | | |
| End of anti-HER2 therapy | 1,538 | 430 (28.0) | 1,591 | 405 (25.5) | 1.10 [0.98; 1.24] 0.104 |
| 36-month follow-up | 1,362 | 318 (23.3) | 1,322 | 333 (25.2) | 0.93 [0.81; 1.06] 0.279 |

| | | | | | |
|---|---|---|---|---|---|
| Loss of appetite | | | | | |
| End of anti-HER2 therapy | 1,538 | 235 (15.3) | 1,594 | 180 (11.3) | 1.35<br>[1.13; 1.62]<br>0.001<br>AD: 4% |
| 36-month follow-up | 1,361 | 121 (8.9) | 1,326 | 125 (9.4) | 0.95<br>[0.75; 1.20]<br>0.647 |
| Constipation | | | | | |
| End of anti-HER2 therapy | 1,538 | 202 (13.1) | 1,593 | 248 (15.6) | 0.84<br>[0.71; 1.00]<br>0.055 |
| 36-month follow-up | 1,363 | 219 (16.1) | 1,321 | 201 (15.2) | 1.06<br>[0.89; 1.26]<br>0.537 |
| Diarrhoea | | | | | |
| End of anti-HER2 therapy | 1,532 | 458 (29.9) | 1,590 | 213 (13.4) | 2.23<br>[1.92; 2.58]<br>< 0.001<br>AD: 16.5% |
| 36-month follow-up | 1,358 | 100 (7.4) | 1,322 | 128 (9.7) | 0.76<br>[0.59; 0.97]<br>0.031<br>AD: 2.3% |
| **Symptomatology (EORTC QLQ-BR23) - deterioration by ≥ 10 points** (data cut-off: 19.12.2016) | | | | | |
| Side effects of systemic therapy | | | | | |
| End of anti-HER2 therapy | 1,535 | 416 (27.1) | 1,591 | 426 (26.8) | 1.02<br>[0.91; 1.14]<br>0.742 |
| 36-month follow-up | 1,358 | 313 (23.0) | 1,321 | 318 (24.1) | 0.96<br>[0.83; 1.10]<br>0.522 |
| Chest symptoms | | | | | |
| End of anti-HER2 therapy | 1,532 | 292 (19.1) | 1,580 | 246 (15.6) | 1.23<br>[1.05; 1.43]<br>0.009<br>AD: 3.5% |
| 36-month follow-up | 1,355 | 154 (11.4) | 1,318 | 141 (10.7) | 1.06<br>[0.85; 1.31]<br>0.610 |
| Arm symptoms | | | | | |
| End of anti-HER2 therapy | 1,532 | 417 (27.2) | 1,581 | 454 (28.7) | 0.94<br>[0.84; 1.05]<br>0.296 |

| | | | | | |
|---|---|---|---|---|---|
| 36-month follow-up | 1,355 | 320 (23.6) | 1,320 | 336 (25.5) | 0.92 [0.81; 1.05] 0.227 |
| Burden due to hair loss | | | | | |
| End of anti-HER2 therapy | 57 | 10 (17.5) | 54 | 16 (29.6) | 0.59 [0.29; 1.19] 0.137 |
| 36-month follow-up | 73 | 18 (24.7) | 77 | 20 (26.0) | 0.89 [0.50; 1.58] 0.696 |

**Health-related quality of life**

| **Endpoint** | **Pertuzumab + trastuzumab + chemotherapy** | | **Placebo + trastuzumab + chemotherapy** | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI] p value[d] |
| **EORTC QLQ-C30 - deterioration by ≥ 10 points** (data cut-off: 19.12.2016) | | | | | |
| Global health status | | | | | |
| End of anti-HER2 therapy | 1,532 | 428 (27.9) | 1,589 | 421 (26.5) | 1.05 [0.94; 1.18] 0.416 |
| 36-month follow-up | 1,357 | 295 (21.7) | 1,320 | 320 (24.2) | 0.89 [0.78; 1.02] 0.106 |
| Physical functioning | | | | | |
| End of anti-HER2 therapy | 1,543 | 358 (23.2) | 1,597 | 361 (22.6) | 1.03 [0.90; 1.17] 0.664 |
| 36-month follow-up | 1,363 | 236 (17.3) | 1,329 | 234 (17.6) | 0.98 [0.83; 1.15] 0.800 |
| Role functioning | | | | | |
| End of anti-HER2 therapy | 1,540 | 383 (24.9) | 1,594 | 368 (23.1) | 1.08 [0.95; 1.22] 0.221 |
| 36-month follow-up | 1,362 | 216 (15.9) | 1,327 | 243 (18.3) | 0.87 [0.73; 1.03] 0.098 |
| Emotional functioning | | | | | |
| End of anti-HER2 therapy | 1,535 | 388 (25.3) | 1,593 | 393 (24.7) | 1.02 [0.91; 1.16] 0.715 |

| | | | | | |
|---|---|---|---|---|---|
| 36-month follow-up | 1,359 | 302 (22.2) | 1,324 | 337 (25.5) | 0.87<br>[0.76; 1.00]<br>0.047<br>AD: 3.3% |
| Cognitive functioning | | | | | |
| End of anti-HER2 therapy | 1,536 | 607 (39.5) | 1,592 | 632 (39.7) | 1.00<br>[0.91; 1.09]<br>0.923 |
| 36-month follow-up | 1,360 | 490 (36.0) | 1,324 | 494 (37.3) | 0.96<br>[0.87; 1.06]<br>0.436 |
| Social functioning | | | | | |
| End of anti-HER2 therapy | 1,535 | 349 (22.7) | 1,590 | 376 (23.6) | 0.96<br>[0.85; 1.09]<br>0.540 |
| 36-month follow-up | 1,360 | 209 (15.4) | 1,323 | 237 (17.9) | 0.86<br>[0.73; 1.02]<br>0.085 |
| **EORTC QLQ-BR23 - deterioration by ≥ 10 points** (data cut-off: 19.12.2016) | | | | | |
| Body image | | | | | |
| End of anti-HER2 therapy | 1,521 | 407 (26.8) | 1,573 | 472 (30.0) | 0.90<br>[0.80; 1.00]<br>0.056 |
| 36-month follow-up | 1,342 | 272 (20.3) | 1,304 | 300 (23.0) | 0.88<br>[0.76; 1.02]<br>0.086 |
| Sexual activity | | | | | |
| End of anti-HER2 therapy | 1456 | 336 (23.1) | 1,509 | 358 (23.7) | 0.97<br>[0.85; 1.11]<br>0.680 |
| 36-month follow-up | 1279 | 258 (20.2) | 1251 | 269 (21.5) | 0.93<br>[0.80; 1.09]<br>0.377 |
| Sex pleasure | | | | | |
| End of anti-HER2 therapy | 437 | 147 (33.6) | 481 | 159 (33.1) | 1.02<br>[0.85; 1.23]<br>0.829 |
| 36-month follow-up | 383 | 113 (29.5) | 402 | 118 (29.4) | 1.03<br>[0.83; 1.27]<br>0.822 |
| Future prospects | | | | | |
| End of anti-HER2 therapy | 1,518 | 272 (17.9) | 1,576 | 292 (18.5) | 0.97<br>[0.84; 1.13]<br>0.697 |

| | | | | | |
|---|---|---|---|---|---|
| 36-month follow-up | 1,340 | 191 (14.3) | 1,304 | 188 (14.4) | 0.99<br>[0.82; 1.19]<br>0.918 |

**Side effects**

| **Endpoint** | **Pertuzumab + trastuzumab + chemotherapy** | | **Placebo + trastuzumab + chemotherapy** | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR<br>[95% CI]<br>p value |
| **Total adverse events (presented additionally)** (data cut-off: 19.12.2016) | | | | | |
| | 1,783 | 1,782 (> 99.9) | 1,822 | 1,813 (99.5) | - |
| **Serious adverse events (SAEs)** | | | | | |
| | 1,783 | 509 (28.5) | 1,822 | 446 (24.5) | 1.17<br>[1.05; 1.30]<br>0.006<br>AD: 4% |
| **Severe adverse events (CTCAE grade 3 or 4)** | | | | | |
| | 1,783 | 1142 (64.0) | 1,822 | 1056 (58.0) | 1.11<br>[1.05; 1.16]<br>< 0.001<br>AD: 10% |
| **Therapy discontinuation due to adverse events** | | | | | |
| | 1,783 | 220 (12.3) | 1,822 | 219 (12.0) | 1.03<br>[0.86; 1.22]<br>0.770 |
| **Specific adverse events** | | | | | |
| Diarrhoea (PT, AE) | 1,783 | 1255 (70.4) | 1,822 | 824 (45.2) | 1.56<br>[1.47; 1.65]<br>< 0.001[c]<br>AD: 25.2% |
| Pruritus (PT, AE) | 1,783 | 261 (14.6) | 1,822 | 163 (8.9) | 1.64<br>[1.36; 1.97]<br>< 0.001[c]<br>AD: 5.7% |
| Heart failure (PT, SAE) | 1,783 | 25 (1.4) | 1,822 | 13 (0.7) | 1.97<br>[1.01; 3.83]<br>0.043[c]<br>AD: 0.7% |
| Anaemia (PT, severe AE) | 1,783 | 120 (6.7) | 1,822 | 86 (4.7) | 1.43<br>[1.09; 1.87]<br>0.010[c]<br>AD: 2% |

| | | | | | |
|---|---|---|---|---|---|
| Diarrhoea (PT, severe AE) | 1,783 | 168 (9.4) | 1,822 | 71 (3.9) | 2.42<br>[1.85; 3.17]<br>< 0.001[c]<br>AD: 5.5% |
| Stomatitis (PT, severe AE) | 1,783 | 38 (2.1) | 1,822 | 18 (1.0) | 2.16<br>[1.24; 3.77]<br>0.006[c]<br>AD: 1.1% |
| Fatigue (PT, severe AE) | 1,783 | 69 (3.9) | 1,822 | 49 (2.7) | 1.44<br>[1.00; 2.06]<br>0.047[c]<br>AD: 1.2% |
| Leukopenia (PT, severe AE) | 1,783 | 92 (5.2) | 1,822 | 65 (3.6) | 1.45<br>[1.06; 1.97]<br>0.019[c]<br>AD: 1.6% |
| Metabolism and nutrition disorders (SOC, severe AE) | 1,783 | 89 (5.0) | 1,822 | 47 (2.6) | 1.94<br>[1.37; 2.74]<br>< 0.001[c]<br>AD: 2.4% |
| Musculoskeletal and connective tissue disorders (SOC, severe AE) | 1,783 | 33 (1.9) | 1,822 | 55 (3.0) | 0.61<br>[0.40; 0.94]<br>0.023[c]<br>AD: 1.1% |
| Skin and subcutaneous tissue disorders (SOC, severe AE) | 1,783 | 63 (3.5) | 1,822 | 36 (2.0) | 1.79<br>[1.19; 2.68]<br>0.004[c]<br>AD: 1.5% |

[a] Cox model stratified by nodal status, type of adjuvant chemotherapy, hormone receptor status and protocol version; p value from stratified log-rank test
[b] Data on absolute difference (AD) only in the case of statistically significant difference; own calculation
[c] 95% CI asymptotic, unconditional exact test (CSZ method)
[d] RR and p value from log-binomial regression adjusted by nodal status, type of adjuvant chemotherapy, hormone receptor status and protocol version

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR: hazard ratio; n.d.: no data available; CI: confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.r. = not reached; PT: preferred term; QLQ-BR23 = Quality of Life Questionnaire - Breast Cancer 23; QLQ-C30 = Quality of Life Questionnaire - Core 30; RR: relative risk; SOC: system organ class; SAE: serious adverse event; AE: adverse event; vs: versus

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

approx. 1,910 - 3,060 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: 2 February 2023):

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

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

Pertuzumab should be used by medical professionals trained in the treatment of anaphylaxis and in an environment where full resuscitation equipment is immediately available.

## 4. Treatment costs

**Annual treatment costs:**

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Pertuzumab | € 47,708.05 |
| + trastuzumab | € 36,772.80 |
| In combination with one of the following chemotherapy regimens: | |
| + 5-fluorouracil + epirubicin + cyclophosphamide (FEC), docetaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Epirubicin | € 1,403.31 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 88,025.67 - € 90,727.08 |
| + 5-fluorouracil + epirubicin + cyclophosphamide (FEC), paclitaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Epirubicin | € 1,403.31 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 90,860.01 - € 92,032.68 |
| *Additionally required SHI services* | *€ 213.84* |
| + 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), docetaxel | |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| 5-fluorouracil | € 42.66 - € 86.24 |
| Doxorubicin | € 851.25 - € 1,135.00 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 87,473.61 - € 89,329.68 |
| + 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), paclitaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Doxorubicin | € 851.25 - € 1,135.00 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 90,307.95 - € 90,635.28 |
| *Additionally required SHI services* | *€ 213.84* |
| + doxorubicin + cyclophosphamide (AC), docetaxel | |
| Doxorubicin | € 1,278.96 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 87,858.66 - € 89,387.40 |
| + doxorubicin + cyclophosphamide (AC), paclitaxel | |
| Doxorubicin | € 1,278.96 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 90,693.00 |
| *Additionally required SHI services* | *€ 213.84* |
| + epirubicin + cyclophosphamide (EC), docetaxel | |
| Epirubicin | € 1,871.08 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 88,450.78 - € 90,640.84 |
| + epirubicin + cyclophosphamide (EC), paclitaxel | |
| Epirubicin | € 1,871.08 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 91,285.12 - € 91,946.44 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| *Additionally required SHI services* | *€ 213.84* |
| + docetaxel + carboplatin | |
| Docetaxel | € 4,102.20 |
| Carboplatin | € 1,899.54 |
| Total | € 90,482.59 |
| Appropriate comparator therapy: | |
| Trastuzumab | € 36,772.80 |
| In combination with one of the following chemotherapy regimens: | |
| + 5-fluorouracil + epirubicin + cyclophosphamide (FEC), docetaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Epirubicin | € 1,403.31 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 40,317.62 - € 43,019.03 |
| + 5-fluorouracil + epirubicin + cyclophosphamide (FEC), paclitaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Epirubicin | € 1,403.31 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 43,151.96 - € 44,324.63 |
| *Additionally required SHI services* | *€ 213.84* |
| + 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), docetaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Doxorubicin | € 851.25 - € 1,135.00 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 39,765.56 - € 41,621.63 |
| + 5-fluorouracil + doxorubicin + cyclophosphamide (FAC), paclitaxel | |
| 5-fluorouracil | € 42.66 - € 86.24 |
| Doxorubicin | € 851.25 - € 1,135.00 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 42,599.90 - € 42,927.23 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| *Additionally required SHI services* | *€ 213.84* |
| + doxorubicin + cyclophosphamide (AC), docetaxel | |
| Doxorubicin | € 1,278.96 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 40,150.61 - € 41,679.35 |
| + doxorubicin + cyclophosphamide (AC), paclitaxel | |
| Doxorubicin | € 1,278.96 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 42,984.95 |
| *Additionally required SHI services* | *€ 213.84* |
| + epirubicin + cyclophosphamide (EC), docetaxel | |
| Epirubicin | € 1,871.08 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Docetaxel | € 2,051.10 - € 3,579.84 |
| Total | € 40,742.73 - € 42,932.79 |
| + epirubicin + cyclophosphamide (EC), paclitaxel | |
| Epirubicin | € 1,871.08 - € 2,532.40 |
| Cyclophosphamide | € 47.75 |
| Paclitaxel | € 4,885.44 |
| Total | € 43,577.07 - € 44,238.39 |
| *Additionally required SHI services* | *€ 213.84* |
| + docetaxel + carboplatin | |
| Docetaxel | € 4,102.20 |
| Carboplatin | € 2,088.66 |
| Total | € 42,963.66 |

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

Other SHI services:

| Designation of the therapy | Type of service | Costs/ unit | Number/ cycle | Number/ patient/ year | Cost/ patient/ year |
|---|---|---|---|---|---|
| Medicinal product to be assessed: | | | | | |
| Pertuzumab | a | € 100 | 1 | 18 | € 1,800 |
| Trastuzumab | a | € 100 | 1 | 18 | € 1,800 |
| In combination with one of the following chemotherapy regimens: | | | | | |
| 5-fluorouracil + epirubicin + cyclophosphamide (FEC) | b | € 100 | 2 | 6 - 8 | € 600 - € 800 |
| + docetaxel | b | € 100 | 1 | 3 - 4 | € 300 - € 400 |
| + paclitaxel | b | € 100 | 1 | 12 | € 1,200 |
| 5-fluorouracil + doxorubicin + cyclophosphamide (FAC) | b | € 100 | 2 | 6 - 8 | € 600 - € 800 |
| + docetaxel | b | € 100 | 1 | 3 - 4 | € 300 - € 400 |
| + paclitaxel | b | € 100 | 1 | 12 | € 1,200 |
| Doxorubicin + cyclophosphamide (AC) | b | € 100 | 1 | 4 | € 400 |
| + docetaxel | b | € 100 | 1 | 3 - 4 | € 300 - € 400 |
| + paclitaxel | b | € 100 | 1 | 12 | € 1,200 |
| Epirubicin + cyclophosphamide (EC) | b | € 100 | 1 | 4 | € 400 |
| + docetaxel | b | € 100 | 1 | 3 - 4 | € 300 - € 400 |
| + paclitaxel | b | € 100 | 1 | 12 | € 1,200 |
| Docetaxel + carboplatin | b | € 100 | 2 | 12 | € 1,200 |
| 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<br>b: Surcharge for production of a parenteral preparation containing cytostatic agents | | | | | |

## 5. Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with Trastuzumab Deruxtecan

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients, which, on the basis of the marketing authorisation granted under Medicinal Products Act, can be used

in a combination therapy with pertuzumab for the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence:

Adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence.

- No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

**II. The resolution will enter into force on the day of its publication on the website of the G-BA on 16 March 2023.**

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

Berlin, 16 March 2023

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

Prof. Hecken