Gemeinsamer Bundesausschuss

Resolution

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-L):

Annex XII - Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V:

Pertuzumab/trastuzumab (breast cancer, HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence, neoadjuvant)

of 15 July 2021

At its session on 15 July 2021, 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 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 pertuzumab/trastuzumab in accordance with the resolution of 15 July 2021:

Pertuzumab/trastuzumab

Resolution of: 15 July 2021
Entry into force on: 15 July 2021
BAnz AT TT. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 21 December 2020):

Phesgo is indicated for use in combination with chemotherapy in the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.

Therapeutic indication of the resolution (resolution of 15 July 2021):

see therapeutic indication according to marketing authorisation.

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

Neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence

Appropriate comparator therapy for pertuzumab/trastuzumab in combination with chemotherapy:

a therapy 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/trastuzumab in combination with chemotherapy compared to trastuzumab in combination with docetaxel:

An additional benefit is not proven.

Study results according to endpoints:[1]

Neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence

[1] Data from the dossier assessment of the IQWiG (A15-34 and A21-10) 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	↔	No relevant difference for the benefit assessment.
Health-related quality of life	∅	There are no data.
Side effects	↔	No relevant difference for the benefit assessment.

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

NeoSphere study: Pertuzumab + trastuzumab + docetaxel **vs** trastuzumab + docetaxel

Mortality

Endpoint	Pertuzumab + trastuzumab + docetaxel		Trastuzumab + docetaxel		Intervention vs Control
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Overall survival[a]					
	107	8 (7.5)	107	6 (5.6)	1.33 [0.48; 3.71] 0.682[b]

Morbidity

Endpoint	Pertuzumab + trastuzumab + docetaxel		Trastuzumab + docetaxel		Intervention vs Control
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
pathological complete remission[c,d]	107	42 (39.3)	107	23 (21.5)	1.83 [1.19; 2.81] 0.0042[e]

Breast conserving surgery[f]	107	27 (25.2)	107	25 (23.4)	1.08 [0.48; 3.71] 0.819[b]
Recurrence rate	101[g]	14 (13.9)	103[g]	18 (17.5)	0.79 [0.42; 1.51] 0.532b

Endpoint	**Pertuzumab + trastuzumab + docetaxel**		**Trastuzumab + docetaxel**		Intervention vs Control
	N	Median in months [95% CI] *Patients with event n (%)*	N	Median in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value
Disease-free survival	101[g]	67.2[67.2; 72.2] *15 (14.9)*	103[g]	n. a. *18 (17.5)*	0.60 [0.28; 1.27] 0.185

Health-related quality of life

Not surveyed

Side effects

Endpoint	**Pertuzumab + trastuzumab + docetaxel**		**Trastuzumab + docetaxel**		Intervention vs Control
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Adverse events (presented additionally)					
	107	105 (98.1)	107	107 (100.0)	not applicable
Serious adverse events (SAEs)					
	107	22 (20.6)	107	21 (19.6)	1.05 [0.61; 1.79] 0.922[b]
Severe adverse events (CTCAE grade 3 or 4)					
	107	78 (72.9)	107	87 (81.3)	0.90 [0.77; 1.04] 0.151[b]
Therapy discontinuation due to adverse events					
	107	6 (5.6)	107	0 (0)	-[h] 0.014[b]

[a] Data on overall mortality was not systematically collected after disease progression, recurrence, or discontinuation. Where data were available, they were recorded.
[b] Exact unconditional test (CSZ method)
[c] Not used to derive an additional benefit
[n] Information from the dossier of the pharmaceutical company
[e] Cochran-Mantel-Haenszel test
[f] Data cut-off of 22.12.2009
[g] Number of patients who underwent surgery
[h] Effect estimator (RR) with 95% CI not precisely estimable
Abbreviations used: CTCAE: Common Terminology Criteria for Adverse Events; HR: Hazard ratio; CI Confidence interval; n: Number of patients evaluated; n: Number of patients with event; 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. 2,690 to 3,450 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 Phesgo (active ingredient: pertuzumab/trastuzumab) at the following publicly accessible link (last access: 7 April 2021):
https://www.ema.europa.eu/en/documents/product-information/phesgo-epar-product-information_de.pdf

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

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

4. Treatment costs

Annual treatment costs:

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Pertuzumab / trastuzumab	€17,805.63 - € 33,044.88
Docetaxel	€ 3,270.36 - € 8,005.77
Paclitaxel	€ 2,829.84 - € 5,659.68
Doxorubicin	€ 522.39 - € 1,918.38
Epirubicin	€ 963.54 - € 2,806.50

Designation of the therapy	Annual treatment costs/patient
Total:	
Pertuzumab/trastuzumab + docetaxel	€ 21,075.99 - € 41,050.65
Pertuzumab/trastuzumab + paclitaxel	€ 20,635.47 - € 38,704.56
Additionally required SHI services	€ 80.01 - € 136.39
Pertuzumab/trastuzumab + docetaxel + doxorubicin	€ 21,598.38 - € 42,969.03
Pertuzumab/trastuzumab + paclitaxel + doxorubicin *Additionally required SHI services*	€ 21,157.86 - € 40,622.94 € 80.01 - € 136.39
Pertuzumab/trastuzumab + paclitaxel + epirubicin *Additionally required SHI services*	€ 21,599.01 - € 41,511.06 € 80.01 - € 136.39
Pertuzumab/trastuzumab + docetaxel + epirubicin	€ 22,039.53 - € 43,857.15
Appropriate comparator therapy:	
Trastuzumab 3-weekly	€ 6,865.37 - € 12,988.67
Trastuzumab weekly	€ 7,420.70 - € 14,099.33
Docetaxel	€ 3,270.36 - € 8,005.77
Paclitaxel	€ 2,829.84 - € 5,659.68
Doxorubicin	€ 522.39 - € 1,918.38
Epirubicin	€ 963.54 - € 2,806.50
Total:	
Trastuzumab + docetaxel	€ 10,135.73 - € 20,994.44
Trastuzumab + paclitaxel *Additionally required SHI services*	€ 10,250.54- € 19,759.01 € 80.01 - € 136.39
Trastuzumab + docetaxel + doxorubicin	€ 10,658.12 - € 22,912.82
Trastuzumab + paclitaxel + doxorubicin *Additionally required SHI services*	€ 10,772.93 - € 21,677.39 € 80.01 - € 136.39
Trastuzumab + paclitaxel + epirubicin *Additionally required SHI services*	€ 11,214.08 - € 22,565.51 € 80.01 - € 136.39
Trastuzumab + docetaxel + epirubicin	€ 11,099.27- € 23,800.94

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2021)

Other SHI services:

Designation of therapy	Type of service	Costs/ unit	Number / cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed					
Pertuzumab/ trastuzumab	not applicable				
Docetaxel	b	€ 81	1	3 - 6	€ 243 - € 486
Paclitaxel	b	€ 81	1	3 - 6	€ 243 - € 486
Doxorubicin	b	€ 81	1	3 - 6	€ 243 - € 486
Epirubicin	b	€ 81	1	3 - 6	€ 243 - € 486
Appropriate comparator therapy					
Trastuzumab	a	€ 71	1	3 - 18	€ 213 - € 1,278
Docetaxel	b	€ 81	1	3 - 6	€ 243 - € 486
Paclitaxel	b	€ 81	1	3 - 6	€ 243 - € 486
Doxorubicin	b	€ 81	1	3 - 6	€ 243 - € 486
Epirubicin	b	€ 81	1	3 - 6	€ 243 - € 486
a: Surcharge for the preparation of a parenteral solution containing monoclonal antibodies b: Surcharge for the preparation of a parenteral preparation containing cytostatic agents					

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 15 July 2021.

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

Berlin, 15 July 2021

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

Prof. Hecken