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
Ribociclib (new therapeutic indication: breast cancer, HR+, HER2-, early at high risk of recurrence, adjuvant treatment, combination with aromatase inhibitor)

of 5 June 2025

At their session on 5 June 2025, 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 following information shall be added after No. 4 to the information on the benefit assessment of Ribociclib in accordance with the resolution of 20 August 2020:

Ribociclib

Resolution of: 5 June 2025
Entry into force on: 5 June 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 25 November 2024):

Kisqali in combination with an aromatase inhibitor is indicated for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

In pre- or perimenopausal women, or in men, the aromatase inhibitor should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

Therapeutic indication of the resolution (resolution of 5 June 2025):

See new therapeutic indication according to marketing authorisation.

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

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy:

- Tamoxifen (if necessary, in addition with cessation of ovarian function)

or

- abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer)

or

- olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)

or

- an aromatase inhibitor (anastrozole or letrozole or exemestane) in combination with cessation of ovarian function (exemestane only in combination with triptorelin)

Extent and probability of the additional benefit of ribociclib in combination with an aromatase inhibitor versus anastrozole or letrozole:

An additional benefit is not proven.

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy:

- An aromatase inhibitor (anastrozole or letrozole) alone, or, if applicable, tamoxifen if aromatase inhibitors are unsuitable

or

- an aromatase inhibitor (anastrozole or exemestane) in sequence after tamoxifen

or

- olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)

Extent and probability of the additional benefit of ribociclib in combination with an aromatase inhibitor versus anastrozole or letrozole:

An additional benefit is not proven.

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy:

- Tamoxifen

or

- abemaciclib in combination with endocrine therapy (only for patients with node-positive breast cancer)

or

- olaparib as monotherapy or in combination with endocrine therapy (only for patients with germline BRCA1/2-mutations)

Extent and probability of the additional benefit of ribociclib in combination with an aromatase inhibitor versus the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑	Advantage in overall survival.
Morbidity	↑	Advantage in recurrences (recurrence rate, invasive disease-free survival).
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↓	Disadvantages in the endpoints of SAEs, severe AEs and therapy discontinuation due to AEs. In detail, disadvantages in specific AEs.

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
∅: No data available.
n.a.: not assessable

NATALEE study:

- open-label randomised controlled trial
- Ribociclib + anastrozole or letrozole vs anastrozole or letrozole
- Sub-population: premenopausal women

Mortality

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	Median survival time in months [95% CI] *Female patients with event n (%)*	N	Median survival time in months [95% CI] *Female patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
	1115	n.r. 31 (2.8)	1123	n.r. 46 (4.1)	0.63 [0.40; 1.00] 0.049 AD = 1.3%

[1] Data from the dossier assessment of the IQWiG (A24-124) and from the addendum (A25-51), unless otherwise indicated.

Morbidity

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
Recurrences					
Recurrence rate	1115	99 (8.9)	1123	136 (12.1)	0.73 [0.57; 0.93] 0.012 AD = 3.2%
Death due to any cause	1115	4 (0.4)	1123	3 (0.3)	-
Local breast cancer recurrence	1115	4 (0.4)	1123	3 (0.3)	-
Regional invasive breast cancer recurrence	1115	12 (1.1)	1123	18 (1.6)	-
Contralateral invasive breast cancer	1115	3 (0.3)	1123	6 (0.5)	-
Distant recurrence	1115	66 (5.9)	1123	103 (9.2)	-
Secondary primary cancer (not breast cancer)	1115	15 (1.3)	1123	13 (1.2)	-
Invasive disease-free survival (iDFS)	1115	99 (8.9) Median time to event: n.r.	1123	136 (12.1) Median time to event: n.r.	HR: 0.67 [0.52; 0.87] 0.002

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
Symptomatology (EORTC QLQ-C30)							
Fatigue	1059	29.0 (21.5)	4.1 (0.5)	1004	28.1 (20.7)	1.3 (0.5)	2.81 [1.40; 4.21] < 0.001 0.17 [0.09; 0.26]
Nausea and vomiting	1059	3.3 (9.3)	2.3 (0.2)	1005	3.5 (9.3)	1.3 (0.2)	1.02 [0.39; 1.66] 0.002 0.14 [0.05; 0.23]
Pain	1060	23.1 (22.3)	3.3 (0.5)	1004	21.5 (21.7)	2.5 (0.5)	0.78 [-0.66; 2.23] 0.288
Dyspnoea	1057	10.7 (19.6)	3.5 (0.5)	1004	10.6 (18.6)	2.6 (0.5)	0.93 [-0.34; 2.20] 0.150
Insomnia	1060	33.6 (29.7)	2.7 (0.7)	1005	33.3 (29.9)	2.6 (0.7)	0.09 [-1.74; 1.91] 0.927
Appetite loss	1059	7.8 (18.3)	2.2 (0.4)	1005	7.6 (17.5)	1.7 (0.4)	0.53 [-0.56; 1.63] 0.339
Constipation	1055	10.6 (21.0)	4.6 (0.5)	1004	11.6 (21.7)	3.1 (0.5)	1.54 [0.16; 2.93] 0.029 0.10 [0.01; 0.18]
Diarrhoea	1055	4.6 (13.2)	2.1 (0.3)	1003	4.5 (12.8)	1.7 (0.3)	0.37 [-0.54; 1.27] 0.427
Symptomatology (EORTC QLQ-BR23)							

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
Side effects of systemic therapy	1060	17.9 (13.1)	5.8 (0.4)	1003	17.8 (13.7)	3.3 (0.4)	2.52 [1.53; 3.52] < 0.001 0.22 [0.13; 0.31]
Breast symptoms	1052	21.0 (18.8)	-4.8 (0.4)	1001	20.1 (18.4)	-5.8 (0.4)	1.01 [0.04; 1.99] 0.041 0.09 [0.00; 0.18]
Arm symptoms	1054	24.9 (21.6)	-0.3 (0.4)	1000	24.8 (20.8)	-2.1 (0.5)	1.78 [0.54; 3.03] 0.005 0.12 [0.04; 0.21]
Burden due to hair loss	No suitable data[b]						
Health status (EQ-5D VAS)							
	1051	78.2 (14.7)	-1.2 (0.4)	999	77.6 (15.1)	-0.5 (0.4)	-0.64 [-1.70; 0.41] 0.232

Health-related quality of life

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
EORTC QLQ-C30							
Global health status	1056	73.7 (17.3)	-3.5 (0.4)	1003	74.4 (16.8)	-2.4 (0.4)	-1.16 [-2.31; -0.02] 0.047 - 0.09 [-0.17; -0.00]
Physical functioning	1060	85.9 (14.3)	-1.5 (0.3)	1003	86.3 (13.8)	-0.3 (0.3)	-1.22 [-2.15; -0.30] 0.010 -0.11 [-0.20; -0.03]
Role functioning	1059	83.0 (21.8)	-2.9 (0.5)	1004	83.6 (20.6)	-1.3 (0.5)	-1.64 [-3.06; -0.22] 0.023 -0.10 [-0.19; -0.01]
Emotional functioning	1056	77.6 (20.3)	-5.8 (0.5)	1003	78.5 (19.1)	-5.4 (0.5)	-0.48 [-1.85; 0.89] 0.494
Cognitive functioning	1056	81.4 (20.7)	-6.2 (0.5)	1003	81.6 (20.2)	-5.2 (0.5)	-1.05 [-2.49; 0.38] 0.150
Social functioning	1056	80.4 (24.3)	-0.2 (0.5)	1002	81.7 (22.0)	1.9 (0.5)	-2.08 [-3.52; -0.64] 0.005 -0.12 [-0.21; -0.04]
EORTC QLQ-BR23							
Body image	1060	69.3 (28.1)	2.1 (0.6)	1000	69.6 (27.4)	3.5 (0.6)	-1.35 [-2.98; 0.29] 0.106

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
Sexual functioning	1047	25.6 (23.1)	-5.0 (0.4)	994	25.1 (22.4)	-4.42 (0.46)	-0.57 [-1.82; 0.68] 0.372
Sexual pleasure	No suitable data[c]						
Future prospects	1058	45.3 (31.6)	10.0 (0.7)	997	46.0 (31.5)	11.3 (0.7)	-1.32 [-3.21; 0.58] 0.174

Side effects

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
Total adverse events (presented additionally)					
	1108	1093 (98.6)	1070	964 (90.1)	-
Serious adverse events (SAE)					
	1108	145 (13.1)	1070	105 (9.8)	1.33 [1.05; 1.69] 0.017 AD = 3.3%
Severe adverse events (CTCAE grade ≥ 3)					
	1108	734 (66.2)	1070	200 (18.7)	3.54 [3.11; 4.04] < 0.001 AD = 47.5%
Therapy discontinuation due to adverse events[d]					
	1108	190 (17.1)	1070	60 (5.6)	3.06 [2.32; 4.04]

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
					< 0.001 AD = 11.5%
Specific adverse events[e]					
Neutropenia (PT, severe AE)	1108	335 (30.2)	1070	9 (0.8)	35.95 [18.64; 69.32] < 0.001 AD = 29.4%
Skin and subcutaneous tissue disorders (SOC, AE)	1108	416 (37.5)	1070	227 (21.2)	1.77 [1.54; 2.03] < 0.001 AD = 16.3%
Respiratory, thoracic and mediastinal disorders (SOC, AE)	1108	339 (30.6)	1070	186 (17.4)	1.76 [1.50; 2.06] < 0.001 AD = 13.2%
Infections and infestations (SOC, severe AE)	1108	57 (5.1)	1070	29 (2.7)	1.90 [1.22; 2.94] 0.004 2.4%
Gastrointestinal disorders (SOC, severe AE)	1108	24 (2.2)	1070	9 (0.8)	2.58 [1.20; 5.51] 0.012 AD = 1.4%
General disorders and administration site conditions (SOC, severe AE)	1108	24 (2.2)	1070	9 (0.8)	2.58 [1.20; 5.51] 0.012 AD = 1.4%
Hepatobiliary toxicity (SMQ, severe AE)	1108	75 (6.8)	1070	21 (2.0)	3.45 [2.14; 5.55] < 0.001 AD = 4.8%

[a] Indication of absolute difference (AD) only in case of statistically significant difference; own calculation.
[b] Only 299 (27%) female patients in the intervention arm vs 256 (23%) female patients in the control arm were included in the evaluation.

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]

[c] Only 630 (57%) female patients in the intervention arm vs 598 (53%) female patients in the control arm were included in the evaluation.
[d] Discontinuation of a therapy component
[e] Selection according to the IQWiG methodology; selection using events occurred in the study, 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; HR = hazard ratio; CI = confidence interval; MD = mean difference; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PT = preferred term; SD = standard deviation; SMD = standardised mean difference; SMQ = standardised MedDRA query; SOC = system organ class; vs = versus

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

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	↑	Advantage in recurrences (recurrence rate, invasive disease-free survival).
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↓	Disadvantages in the endpoints of SAEs, severe AEs and therapy discontinuation due to AEs. In detail, disadvantages in specific AEs.

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
∅: No data available.
n.a.: not assessable

NATALEE study:

- open-label randomised controlled trial
- Ribociclib + anastrozole or letrozole vs anastrozole or letrozole
- Sub-population: postmenopausal women

Mortality

Endpoint	**Ribociclib + anastrozole or letrozole**		**Anastrozole or letrozole**		**Intervention vs control**
	N	Median survival time in months [95% CI] *Female patients with event n (%)*	N	Median survival time in months [95% CI] *Female patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
	1424	n.r. 74 (5.2)	1420	n.r. 75 (5.3)	0.94 [0.68; 1.30] 0.724

Morbidity

Endpoint	**Ribociclib + anastrozole or letrozole**		**Anastrozole or letrozole**		**Intervention vs control**
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
Recurrences					
Recurrence rate	1424	164 (11.5)	1420	203 (14.3)	0.81 [0.67; 0.98] 0.027 AD = 2.8%
Death due to any cause	1424	13 (0.9)	1420	8 (0.6)	-
Local breast cancer recurrence	1424	4 (0.3)	1420	6 (0.4)	-
Regional invasive breast cancer recurrence	1424	13 (0.9)	1420	31 (2.2)	-
Contralateral invasive breast cancer	1424	8 (0.6)	1420	4 (0.3)	-
Distant recurrence	1424	110 (7.7)	1420	142 (10.0)	-

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
Secondary primary cancer (not breast cancer)	1424	24 (1.7)	1420	27 (1.9)	-
Invasive disease-free survival (iDFS)	1424	164 (11.5) Median time to event: n.r.	1420	203 (14.3) median time to event: n.r.	HR: 0.75 [0.61; 0.92] 0.005

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
Symptomatology (EORTC QLQ-C30)							
Fatigue	1325	26.6 (20.3)	2.8 (0.4)	1263	27.4 (20.9)	2.7 (0.4)	0.05 [-1.13; 1.22] 0.939
Nausea and vomiting	1325	3.1 (9.2)	2.0 (0.2)	1263	3.2 (9.0)	1.1 (0.2)	0.88 [0.33; 1.44] 0.002 0.12 [0.05; 0.20]
Pain	1328	21.3 (21.8)	3.0 (0.5)	1263	21.3 (22.2)	4.5 (0.5)	-1.52 [-2.82; -0.21] 0.022 -0.09 [-0.17; -0.01]
Dyspnoea	1322	11.1 (19.0)	3.5 (0.4)	1260	12.5 (20.9)	3.4 (0.4)	0.11 [-1.08; 1.30] 0.853
Insomnia	1322	30.2 (29.6)	2.2 (0.5)	1261	29.3 (28.5)	3.4 (0.6)	-1.22

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
							[-2.75; 0.30] 0.116
Appetite loss	1325	8.1 (18.5)	1.1 (0.4)	1261	8.9 (19.2)	0.6 (0.4)	0.47 [-0.51; 1.44] 0.349
Constipation	1323	10.9 (20.8)	4.1 (0.4)	1263	11.3 (21.5)	1.3 (0.4)	2.78 [1.57; 3.98] < 0.001 0.18 [0.10; 0.26]
Diarrhoea	1322	5.8 (14.4)	1.2 (0.3)	1259	5.4 (14.2)	1.8 (0.3)	-0.58 [-1.36; 0.20] 0.144
Symptomatology (EORTC QLQ-BR23)							
Side effects of systemic therapy	1329	16.0 (13.5)	4.2 (0.3)	1257	16.2 (13.7)	3.0 (0.3)	1.22 [0.37; 2.07] 0.005 0.11 [0.03; 0.19]
Breast symptoms	1322	18.9 (17.8)	-5.5 (0.3)	1259	19.8 (18.7)	-5.5 (0.3)	0.01 [-0.87; 0.89] 0.981
Arm symptoms	1323	22.2 (20.6)	0.3 (0.4)	1261	24.0 (21.7)	-0.3 (0.4)	0.58 [-0.58; 1.74] 0.329
Burden due to hair loss	No suitable data[b]						
Health status (EQ-5D VAS)							
	1323	78.6 (14.9)	-1.6 (0.3)	1259	78.2 (14.8)	-1.3 (0.3)	-0.27 [-1.13; 0.59] 0.540

Health-related quality of life

Endpoint	Ribociclib + anastrozole or letrozole			Anastrozole or letrozole			Intervention vs control
	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	N	Value at the start of the study MV (SD)	Mean change in the course of study MV (SE)	MD [95% CI] p value SMD if applicable [95% CI]
EORTC QLQ-C30							
Global health status	1322	74.0 (17.7)	-2.8 (0.4)	1258	73.2 (18.4)	-2.4 (0.4)	-0.43 [-1.40; 0.54] 0.388
Physical functioning	1326	84.5 (15.2)	-2.2 (0.3)	1264	83.5 (15.5)	-2.8 (0.3)	0.64 [-0.27; 1.56] 0.168
Role functioning	1325	84.8 (21.0)	-3.0 (0.4)	1264	84.3 (21.5)	-3.5 (0.4)	0.57 [-0.63; 1.78] 0.353
Emotional functioning	1323	80.4 (19.6)	-2.8 (0.4)	1259	80.6 (19.5)	-3.8 (0.4)	0.98 [-0.14; 2.10] 0.088
Cognitive functioning	1322	85.2 (18.7)	-4.5 (0.4)	1260	84.0 (19.4)	-5.1 (0.4)	0.62 [-0.50; 1.75] 0.278
Social functioning	1323	85.9 (20.4)	0.4 (0.3)	1259	84.6 (22.2)	0.5 (0.3)	-0.05 [-0.90; 0.80] 0.911
EORTC QLQ-BR23							
Body image	1327	74.3 (25.9)	2.7 (0.5)	1254	74.3 (26.4)	2.1 (0.5)	0.57 [-0.76; 1.90] 0.401
Sexual functioning	1297	18.3 (21.7)	-1.9 (0.4)	1221	16.8 (21.2)	-2.1 (0.4)	0.12 [-0.88; 1.13] 0.808
Sexual pleasure	No suitable data[c]						
Future prospects	1327	52.2 (31.2)	9.1 (0.5)	1252	51.3 (31.7)	8.1 (0.5)	0.94 [-0.55; 2.43] 0.215

Side effects

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
Total adverse events (presented additionally)					
	1409	1376 (97.7)	1362	1183 (86.9)	-
Serious adverse events (SAE)					
	1409	229 (16.3)	1362	162 (11.9)	1.37 [1.13; 1.65] < 0.001 AD = 4.4%
Severe adverse events (CTCAE grade ≥ 3)					
	1409	883 (62.7)	1362	280 (20.6)	3.05 [2.73; 3.41] < 0.001 AD = 42.1%
Therapy discontinuation due to adverse events[d]					
	1409	340 (24.1)	1362	68 (5.0)	4.83 [3.77; 6.20] < 0.001 AD = 19.1%
Specific adverse events[e]					
Neutropenia (PT, severe AE)	1409	374 (26.5)	1362	4 (0.3)	90.38 [33.84; 241.39] < 0.001 AD = 26.2%
Gastrointestinal disorders (SOC, AEs)	1409	760 (53.9)	1362	384 (28.2)	1.91 [1.74; 2.11] < 0.001 AD = 25.7%
Skin and subcutaneous tissue disorders (SOC, AE)	1409	536 (38.0)	1362	274 (20.1)	1.89 [1.67; 2.14] < 0.001 AD = 17.9%
Respiratory, thoracic and	1409	34 (2.4)	1362	16 (1.2)	2.05 [1.14; 3.70]

Endpoint	Ribociclib + anastrozole or letrozole		Anastrozole or letrozole		Intervention vs control
	N	*Female patients with event n (%)*	N	*Female patients with event n (%)*	RR [95% CI] p value Absolute difference (AD)[a]
mediastinal disorders (SOC, AE)					0.015 AD = 1.2%
Infections and infestations (SOC, severe AE)	1409	89 (6.3)	1362	51 (3.7)	1.69 [1.21; 2.36] 0.002 AD = 2.6%
Nervous system disorders (SOC, severe AE)	1409	40 (2.8)	1362	16 (1.2)	2.42 [1.36; 4.29] 0.002 AD = 1.6%
Fatigue (PT, severe AE)	1409	15 (1.1)	1362	3 (0.2)	4.83 [1.40; 16.66] 0.006 AD = 0.9%
Hepatobiliary toxicity (SMQ, severe AE)	1409	142 (10.1)	1362	21 (1.5)	6.54 [4.16; 10.27] < 0.001 AD = 8.6%
Nephrotoxicity (SMQ, severe AE)	1409	7 (0.5)	1362	0 (0)	14.50 [0.83; 253.63] 0.009 AD = 0.5%

[a] Indication of absolute difference (AD) only in case of statistically significant difference; own calculation.
[b] Only 356 (25%) female patients in the intervention arm vs 351 (25%) female patients in the control arm were included in the evaluation.
[c] Only 583 (41%) female patients in the intervention arm vs 513 (36%) female patients in the control arm were included in the evaluation.
[d] Discontinuation of a therapy component
[e] Selection according to the IQWiG methodology; selection using events occurred in the study, 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; HR = hazard ratio; CI = confidence interval; MD = mean difference; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PT = preferred term; SD = standard deviation; SMD = standardised mean difference; SMQ = standardised MedDRA query; SOC = system organ class; vs = versus

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

No data available.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.

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
∅: No data available.
n.a.: not assessable

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

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Approx. 940 – 4,020 female patients

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Approx. 2770 – 11860 female patients

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Approx. 20 – 80 male 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 Kisqali (active ingredient: ribociclib) at the following publicly accessible link (last access: 22 April 2025):

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

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

4. Treatment costs

Annual treatment costs:

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ribociclib in combination with an aromatase inhibitor	
1st to 3rd treatment year	
Ribociclib	€ 30,143.23
Anastrozole	€ 143.63
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 30,286.86 - € 30,568.71
LHRH agonist[2]	€ 1,851.93 - € 2,629.25
Appropriate comparator therapy:	
Tamoxifen (if necessary, in addition with cessation of ovarian function)	
1st to at least 5th treatment year	
Tamoxifen	€ 91.10
If applicable, LHRH agonist[2]	€ 1,906.92 - € 2,629.25
Total	€ 72.34 - € 2,701.59
Abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer)	
1st to 2nd treatment year	
Abemaciclib	€ 25,977.05
Tamoxifen	€ 91.10
Anastrozole	€ 143.63

[2] Goserelin, leuprorelin or triptorelin

Designation of the therapy	Annual treatment costs/ patient
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 26,049.39 - € 26,402.53
LHRH agonist[2]	€ 1,906.92 - € 2,629.25
Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)	
1st treatment year	
Olaparib as monotherapy	
Olaparib	€ 60,277.20
Olaparib in combination with endocrine therapy	
Olaparib	€ 60,277.20
Tamoxifen	€ 91.10
Anastrozole	€ 143.63
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 60,349.54 - € 60,702.68
LHRH agonist[2]	€ 1,906.92 - € 2,629.25
An aromatase inhibitor (anastrozole, letrozole or exemestane) in combination with cessation of ovarian function (exemestane only in combination with triptorelin)	
1st to 5th treatment year	
Anastrozole	€ 143.63
LHRH agonist[2]	€ 1,906.92 - € 2,629.25
Total	€ 2,050.55 - € 2,772.88
1st to 5th treatment year	
Letrozole	€ 176.59
LHRH agonist[2]	€ 1,906.92 - € 2,629.25
Total	€ 2,083.51 - € 2,805.84
1st to 5th treatment year	
Exemestane	€ 425.48
Triptorelin	€ 2,629.25
Total	€ 3,054.73

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 May 2025)

Costs for additionally required SHI services: not applicable

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ribociclib in combination with an aromatase inhibitor	
1st to 3rd treatment year	
Ribociclib	€ 30,143.23
Anastrozole	€ 143.63
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 30,286.86 - € 30,568.71
Appropriate comparator therapy:	
Aromatase inhibitor (anastrozole or letrozole) alone, or, if applicable, tamoxifen if aromatase inhibitors are unsuitable	
1st to 5th treatment year	
Anastrozole	€ 143.63
1st to 5th treatment year	
Letrozole	€ 176.59
1st to at least 5th treatment year	
Tamoxifen[3]	€ 91.10
Aromatase inhibitor (anastrozole or exemestane) in sequence after tamoxifen	
Anastrozole in sequence after tamoxifen	
Up to the 2nd or 3rd treatment year	
Tamoxifen	€ 91.10
From the 3rd or 4th up to the 5th treatment year	
Anastrozole	€ 143.63
Exemestane in sequence after tamoxifen	
Up to the 2nd or 3rd treatment year	
Tamoxifen	€ 72.34
From the 3rd or 4th up to the 5th treatment year	
Exemestane	€ 425.48
Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)	
1st treatment year	

[3] If aromatase inhibitors are unsuitable.

Designation of the therapy	Annual treatment costs/ patient
Olaparib as monotherapy	
Olaparib	€ 60,277.20
Olaparib in combination with endocrine therapy	
Olaparib	€ 60,277.20
Tamoxifen	€ 91.10
Anastrozole	€ 143.63
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 60,349.54 - € 60,702.68

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 May 2025)

Costs for additionally required SHI services: not applicable

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ribociclib in combination with an aromatase inhibitor	
1st to 3rd treatment year	
Ribociclib	€ 30,143.23
Anastrozole	€ 143.63
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 30,286.86 - € 30,568.71
Appropriate comparator therapy:	
Tamoxifen	
1st to at least 5th treatment year	
Tamoxifen	€ 91.10
Abemaciclib in combination with endocrine therapy (only for patients with node-positive breast cancer)	
1st to 2nd treatment year	
Abemaciclib	€ 25,977.05
Tamoxifen	€ 91.10
Anastrozole	€ 143.63
Letrozole	€ 176.59

Designation of the therapy	Annual treatment costs/ patient
Exemestane	€ 425.48
Total	€ 26,049.39 - € 26,402.53
Olaparib as monotherapy or in combination with endocrine therapy (only for male patients with germline BRCA1/2-mutations)	
1st treatment year	
Olaparib as monotherapy	
Olaparib	€ 60,277.20
Olaparib in combination with endocrine therapy	
Olaparib	€ 60,277.20
Tamoxifen	€ 91.10
Anastrozole	€ 143.63
Letrozole	€ 176.59
Exemestane	€ 425.48
Total	€ 60,349.54 - € 60,702.68

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 May 2025)

Costs for additionally required SHI services: not applicable

5. Designation of 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 the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

- No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

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

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

- No medicinal product with new active ingredients 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 5 June 2025.

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

Berlin, 5 June 2025

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

Prof. Hecken