

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
Capivasertib (breast cancer, ER+, HER2-, PIK3CA/AKT1/PTEN
alteration(s), after prior therapy, combination with
fulvestrant)

of 3 April 2025

At their session on 3 April 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. **Annex XII shall be amended in alphabetical order to include the active ingredient
Capivasertib as follows:**

Capivasertib

Resolution of: 3 April 2025

Entry into force on: 3 April 2025

Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 17 June 2024):

TRUQAP is indicated in combination with fulvestrant for the treatment of adult patients with oestrogen receptor (ER)-positive, HER2-negative locally advanced or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN*-alterations following recurrence or progression on or after an endocrine-based regimen.

In pre- or perimenopausal women, TRUQAP plus fulvestrant should be combined with a luteinising hormone releasing hormone (LHRH) agonist.

For men, administration of LHRH agonist according to current clinical practice standards should be considered.

Therapeutic indication of the resolution (resolution of 3 April 2025):

See therapeutic indication according to marketing authorisation.

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

a1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with *PIK3CA/AKT1/PTEN* alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

Appropriate comparator therapy:

- Tamoxifen (only for premenopausal patients who have not received tamoxifen in previous (neo-)adjuvant endocrine therapy; only for postmenopausal patients if aromatase inhibitors are unsuitable)
or
- letrozole
or
- exemestane (only for patients with progression after anti-oestrogen treatment)
or
- anastrozole
or
- fulvestrant
or
- ribociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)
or
- abemaciclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)
or

- palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)
or
- ribociclib in combination with fulvestrant
or
- abemaciclib in combination with fulvestrant
or
- palbociclib in combination with fulvestrant

Extent and probability of the additional benefit of capivasertib in combination with fulvestrant compared with fulvestrant:

An additional benefit is not proven.

- a2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

Appropriate comparator therapy:

- Tamoxifen
or
- palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)

Extent and probability of the additional benefit of capivasertib in combination with fulvestrant compared to the appropriate comparator therapy:

An additional benefit is not proven.

- b1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

Appropriate comparator therapy:

Individualised therapy, taking into account a change of endocrine therapy to

- tamoxifen
- letrozole
- exemestane
- anastrozole
- fulvestrant
- everolimus in combination with exemestane (only for patients without symptomatic visceral metastasis, followed by progression after a non-steroidal aromatase inhibitor)
- ribociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)
- abemaciclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)
- palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)
- ribociclib in combination with fulvestrant
- abemaciclib in combination with fulvestrant

- palbociclib in combination with fulvestrant

Extent and probability of the additional benefit of capivasertib in combination with fulvestrant compared with fulvestrant:

Indication of a considerable additional benefit.

- b2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

Appropriate comparator therapy:

Individualised therapy, taking into account a change of endocrine therapy to

- tamoxifen
- aromatase inhibitor in combination with a GnRH analogue
- fulvestrant
- palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)

Extent and probability of the additional benefit of capivasertib in combination with fulvestrant compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:¹

- a1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

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	↓	Disadvantage in the endpoint of diarrhoea.
Health-related quality of life	↔	No relevant difference for the benefit assessment.
Side effects	↔	No relevant difference for the benefit assessment. 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		

CAPItello 291 study: Capiasertib + fulvestrant **versus** placebo + fulvestrant

Relevant sub-population: Patients with PIK3CA/AKT1/PTEN alteration(s)

Mortality

Endpoint	Capiasertib + fulvestrant		Placebo + fulvestrant		Intervention versus control
	N	Median survival time in months [95% CI] <i>Patients with event n (%)</i>	N	Median survival time in months [95% CI] <i>Patients with event n (%)</i>	Hazard ratio [95% CI] p value Absolute difference (AD) ^a
Overall survival					
	16	n.r. 3 (18.8)	28	n.r. 3 (10.7)	1.09 [0.19; 6.10]; 0.921

¹ Data from the dossier assessment of the IQWiG (A24-105) and from the addendum (A25-26), unless otherwise indicated.

Morbidity

Progression-free survival (PFS) ^b					
	16	11.5 [6.3; n.r.] 11 (68.8)	28	3.7 [1.8; 7.4] 24 (85.7)	0.36 [0.16; 0.77] 0.0078 AD = 7.8 months
Symptomatology					
<i>EORTC QLQ-C30 (time to 1st deterioration)</i>					
Fatigue	14	1.5 [0.9; 11.9] 11 (78.6)	24	2.8 [1.0; n.c.] 14 (58.3)	1.33 [0.56; 3.07]; 0.484
Pain	14	3.3 [1.0; 7.4] 13 (92.9)	24	6.0 [1.0; n.c.] 12 (50.0)	1.86 [0.79; 4.45]; 0.139
Nausea and vomiting	14	6.0 [1.1; 14.7] 11 (78.6)	24	n.r. 9 (37.5)	1.87 [0.71; 5.20]; 0.216
Dyspnoea	14	9.2 [1.0; 14.1] 10 (71.4)	24	3.6 [1.0; n.c.] 12 (50.0)	0.97 [0.39; 2.31]; 0.959
Insomnia	14	6.9 [1.0; 16.6] 10 (71.4)	24	6.5 [1.9; n.c.] 11 (45.8)	1.05 [0.42; 2.57]; 0.901
Appetite loss	14	2.3 [1.0; 15.6] 12 (85.7)	24	8.3 [2.8; n.c.] 10 (41.7)	2.05 [0.83; 5.07]; 0.134
Constipation	14	16.6 [7.4; n.c.] 6 (42.9)	24	12.9 [3.6; n.c.] 6 (25.0)	1.18 [0.33; 3.97]; 0.789
Diarrhoea	14	2.7 [1.0; 3.7] 12 (85.7)	24	12.8 [3.7; n.c.] 8 (33.3)	4.05 [1.54; 11.48]; 0.004 AD = 10.1 months
<i>EORTC QLQ-BR23 (time to 1st deterioration)</i>					
Side effects of systemic therapy	14	2.8 [1.1; 16.6] 10 (71.4)	24	10.2 [3.7; n.c.] 10 (41.7)	2.33 [0.85; 6.61]; 0.092
Chest symptoms	14	12.9 [1.9; n.c.] 7 (50.0)	24	n.r. 7 (29.2)	1.39 [0.43; 4.52]; 0.573
Arm symptoms	14	4.7 [1.0; n.c.] 9 (64.3)	24	2.7 [1.0; 16.5] 14 (58.3)	1.41 [0.55; 3.56]; 0.452
Burden due to hair loss	No suitable data				
PGIS					
	No suitable data				
Health status					

<i>EQ-5D VAS</i>	14	7.5 [1.8; n.c.] 8 (57.1)	24	10.2 [1.9; n.c.] 11 (45.8)	1.42 [0.51; 3.77]; 0.507
<i>PGIC</i>	No suitable data				

Health-related quality of life

<i>EORTC QLQ-C30 (time to 1st deterioration)</i>					
Global health status	14	1.5 [1.0; n.c.] 10 (71.4)	24	3.6 [1.9; 7.4] 16 (66.7)	1.50 [0.62; 3.47]; 0.384
Physical functioning	14	4.6 [3.7; n.c.] 9 (64.3)	24	6.4 [2.8; n.c.] 12 (50.0)	0.83 [0.32; 2.05]; 0.632
Role functioning	14	7.3 [1.1; 11.1] 10 (71.4)	24	2.8 [1.8; 6.5] 15 (62.5)	0.80 [0.34; 1.83]; 0.627
Emotional functioning	14	12.0 [6.4; n.c.] 6 (42.9)	24	n.r. 8 (33.3)	0.98 [0.32; 2.88]; 0.974
Cognitive functioning	14	6.5 [1.1; 16.5] 10 (71.4)	24	2.7 [1.8; n.c.] 15 (62.5)	0.78 [0.32; 1.83]; 0.573
Social functioning	14	n.r. 6 (42.9)	24	1.9 [1.0; 7.9] 15 (62.5)	0.50 [0.17; 1.30]; 0.177
<i>EORTC QLQ-BR23 (time to 1st deterioration)</i>					
Body image	14	4.6 [1.9; n.c.] 8 (57.1)	24	2.8 [1.8; n.c.] 13 (54.2)	1.26 [0.47; 3.20]; 0.626
Sexual activity	14	n.r. 4 (28.6)	24	n.r. 4 (16.7)	1.34 [0.31; 5.72]; 0.684
Sex pleasure	No suitable data ^c				
Future prospects	14	n.r. 5 (35.7)	24	6.5 [1.8; n.c.] 12 (50.0)	0.65 [0.20; 1.82]; 0.447

Side effects

Total adverse events (presented additionally)					
	16	0.1 [0.0; 0.3] 16 (100)	28	0.5 [0.5; 1.8] 22 (78.6)	–
Serious adverse events (SAE)					
	16	n.r. 3 (18.8)	28	16.0 [16.0; n.c.] 2 (7.1)	1.96 [0.31; 12.26]; 0.474
Severe adverse events (CTCAE grade 3 or 4)					
	16	n.r. 7 (43.8)	28	17.5 [14.0; n.c.] 2 (7.1)	3.46 [0.85; 14.03]; 0.083

Therapy discontinuation due to adverse events					
	No suitable data				
Specific adverse events					
PRO-CTCAE	No suitable data				
Diarrhoea (PT, AEs)	16	1.1 [0.1; 9.2] 11 (68.8)	28	n.r. 3 (10.7)	10.47 [3.31; 33.10]; < 0.001
Maculopapular rash (PT, AEs)	16	n.r. 6 (37.5)	28	n.r. 0 (0)	21.64 [3.92; 119.57]; < 0.001
Stomatitis (PT, AEs)	16	n.r. 4 (25.0)	28	n.r. 0 (0)	13.39 [1.76; 101.87]; 0.012
Gastrointestinal disorders (SOC, severe AEs ^d)	16	n.r. 3 (18.8)	28	n.r. 0 (0)	17.25 [1.61; 184.64]; 0.019
<p>a Indication of absolute difference (AD) only in case of statistically significant difference; own calculation b Information of the pharmaceutical company c No baseline or post-baseline score was available in 81% and 93% of patients respectively. d Operationalised as CTCAE grade \geq 3</p> <p>Abbreviations used: AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR = hazard ratio; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PRO-CTCAE = patient-reported outcome – CTCAE; PT = preferred term; QLQ-BR23 = Quality of Life Questionnaire – Breast Cancer 23; QLQ-C30 = Quality of Life Questionnaire – Core 30; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale</p>					

- a2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

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		

- b1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival.
Morbidity	↓↓	Disadvantages in the endpoints of appetite loss, diarrhoea and nausea and vomiting. Advantage in the endpoint of constipation.
Health-related quality of life	↔	No relevant difference for the benefit assessment. Disadvantage in social functioning.
Side effects	↓↓	Disadvantage for severe AEs and in detail disadvantages for 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		

CAPItello 291 study:

- Capivasertib + fulvestrant **versus** placebo + fulvestrant

FAKTION study:

- Capivasertib + fulvestrant **versus** placebo + fulvestrant
- Only data on overall survival and PFS, subject to meta-analytic evaluation

Relevant sub-population: Patients with PIK3CA/AKT1/PTEN alteration(s)

Mortality

Endpoint	Capivasertib + fulvestrant		Placebo + fulvestrant		Intervention versus control
	N	Median survival time in months [95% CI] <i>Patients with event n (%)</i>	N	Median survival time in months [95% CI] <i>Patients with event n (%)</i>	Hazard ratio [95% CI] p value Absolute difference (AD) ^a
Overall survival					
CAPItello-291	156	n.r. 41 (26.3)	124	n.r. 46 (37.1)	0.65 [0.42; 0.99]; 0.044 ^b
FAKTION ^c	39	38.9 [23.3; 0.7] 25 (64.1)	37	20.0 [14.8; 31.4] 32 (86.5)	0.46 [0.27; 0.79]; 0.005 ^d AD = 18.9 months
Total ^e	0.57 [0.41; 0.79]; n.d.				

Morbidity

Progression-free survival (PFS)^f					
CAPItello-291	156	6.1 [5.5; 7.9] 124 (79.5)	124	2.6 [1.9; 3.6] 106 (85.5)	0.52 [0.40; 0.68]; < 0.0001 AD = 3.5 months
FAKTION	-	-	-	-	0.44 [0.26; 0.73]
Total	0.50 [0.40; 0.64]				
Symptomatology					
<i>EORTC QLQ-C30 (time to 1st deterioration)</i>					
Fatigue	139	1.8 [1.8; 2.7] 101 (72.7)	98	1.9 [1.8; 2.7] 64 (65.3)	1.04 [0.76; 1.44]; 0.808
Pain	139	3.3 [2.7; 4.6] 86 (61.9)	98	2.7 [1.9; 5.6] 56 (57.1)	0.86 [0.61; 1.22]; 0.397
Nausea and vomiting	139	1.9 [1.8; 3.6] 96 (69.1)	98	3.7 [2.7; 11.0] 47 (48.0)	1.57 [1.11; 2.26]; 0.015 AD = 1.8 months
Dyspnoea	139	7.4 [4.6; 10.2] 68 (48.9)	98	5.6 [2.9; n.c.] 44 (44.9)	0.83 [0.57; 1.23]; 0.374

Insomnia	139	9.3 [5.6; 13.0] 61 (43.9)	98	6.5 [3.0; n.c.] 41 (41.8)	0.74 [0.49; 1.12]; 0.152
Appetite loss	139	2.8 [1.9; 3.6] 87 (62.6)	98	7.3 [4.5; 10.1] 43 (43.9)	1.66 [1.15; 2.42]; 0.009 AD = 4.5 months
Constipation	139	15.6 [11.1; n.c.] 43 (30.9)	98	9.1 [3.7; n.c.] 37 (37.8)	0.63 [0.40; 0.99]; 0.044 AD = 6.5 months
Diarrhoea	139	1.0 [1.0; 1.8] 112 (80.6)	98	10.2 [3.9; n.c.] 33 (33.7)	4.11 [2.79; 6.25]; < 0.001 AD = 9.2 months
<i>EORTC QLQ-BR23 (time to 1st deterioration)</i>					
Side effects of systemic therapy	136	5.7 [3.6; 7.4] 69 (50.7)	98	6.4 [4.6; 16.5] 36 (36.7)	1.33 [0.88; 2.02]; 0.193
Chest symptoms	136	n.r. 41 (30.1)	98	n.r. 26 (26.5)	0.78 [0.47; 1.32]; 0.359
Arm symptoms	136	3.7 [2.8; 5.5] 78 (57.4)	98	4.5 [1.9; 5.6] 49 (50.0)	0.92 [0.64; 1.33]; 0.678
Burden due to hair loss	No suitable data				
<i>PGIS</i>					
	No suitable data				
Health status					
<i>EQ-5D VAS</i>	136	6.4 [3.6; n.c.] 62 (45.6)	97	8.3 [4.6; 13.8] 39 (40.2)	1.07 [0.71; 1.61]; 0.768
<i>PGIC</i>	No suitable data				

Health-related quality of life

<i>EORTC QLQ-C30 (time to 1st deterioration)</i>					
Global health status	139	4.6 [2.7; 7.4] 77 (55.4)	98	3.7 [2.6; n.c.] 45 (45.9)	1.13 [0.78; 1.65]; 0.557
Physical functioning	139	5.5 [3.8; 13.9] 68 (48.9)	98	4.5 [2.8; 7.4] 49 (50.0)	0.81 [0.56; 1.18]; 0.276
Role functioning	139	2.8 [1.9; 3.7] 88 (63.3)	98	2.7 [1.8; 4.6] 59 (60.2)	0.91 [0.65; 1.29]; 0.589
Emotional functioning	139	7.3 [4.6; n.c.] 63 (45.3)	98	4.7 [3.6; 9.7] 45 (45.9)	0.79 [0.54; 1.18]; 0.257
Cognitive functioning	139	3.7 [2.8; 12.8] 71 (51.1)	98	3.6 [2.6; 4.6] 51 (52.0)	0.90 [0.63; 1.30]; 0.569
Social functioning	139	2.0 [1.8; 3.7] 92 (66.2)	98	4.7 [2.8; n.c.] 45 (45.9)	1.55 [1.08; 2.24]; 0.02

					AD = 2.7 months
<i>EORTC QLQ-BR23 (time to 1st deterioration)</i>					
Body image	136	10.1 [3.7; n.c.] 59 (43.4)	98	10.1 [4.6; n.c.] 36 (36.7)	1.05 [0.69; 1.61]; 0.818
Sexual activity	136	n.r. 28 (20.6)	98	n.r. 20 (20.4)	0.74 [0.41; 1.35]; 0.314
Sex pleasure	No suitable data ^g				
Future prospects	136	n.r. 53 (39.0)	98	9.1 [4.6; n.c.] 34 (34.7)	1.02 [0.66; 1.59]; 0.943

Side effects

Total adverse events (presented additionally)					
	156	0.1 [0.1; 0.3] 152 (97.4)	123	0.5 [0.5; 0.7] 105 (85.4)	–
Serious adverse events (SAE)					
	156	n.r. 28 (17.9)	123	n.r. 12 (9.8)	1.57 [0.83; 2.97]; 0.164
Severe adverse events (CTCAE grade 3 or 4)^h					
	156	n.r. 62 (39.7)	123	n.r. 20 (16.3)	2.33 [1.51; 3.61]; < 0.001
Therapy discontinuation due to adverse events					
	No suitable data				
Specific adverse events					
PRO-CTCAE	No suitable data				
Diarrhoea (PT, AEs)	156	0.4 [0.2; 0.5] 119 (76.3)	123	n.r. 25 (20.3)	4.89 [3.50; 6.82]; < 0.001
Maculopapular rash (PT, AEs)	156	n.r. 30 (19.2)	123	n.r. 2 (1.6)	4.90 [2.44; 9.84]; < 0.001
Stomatitis (PT, AEs)	156	n.r. 24 (15.4)	123	n.r. 6 (4.9)	2.72 [1.32; 5.59]; 0.007
Nausea (PT, AEs)	156	n.r. 55 (35.3)	123	n.r. 17 (13.8)	2.35 [1.47; 3.75]; < 0.001
Maculopapular rash (PT, severe AEs ^h)	156	n.r. 11 (7.1)	123	n.r. 0 (0)	6.12 [1.86; 20.07]; 0.003
Diarrhoea (PT, severe AEs ^h)	156	n.r. 18 (11.5)	123	n.r. 1 (0.8)	4.77 [1.92; 11.85]; < 0.001
a Indication of absolute difference (AD) only in case of statistically significant difference; own calculation b HR, CI and p value: Cox model (binding treatment according to Efron) and log-rank test, both stratified by liver metastases yes vs no; prior therapy with CDK4/6 inhibitors yes vs no					

c For the FAKTION study, data are only available for the overall survival endpoint. The study is no longer presented for the other endpoints.

d HR, CI and p value: Cox model, adjusted according to log-rank test, stratified by mutational status, AI resistance primary or secondary and disease measurable or immeasurable

e HR and AI calculated from meta-analysis, fixed-effect model

f Information of the pharmaceutical company

g No baseline or post-baseline score was available in 83% and 81% of patients respectively.

h Operationalised as CTCAE grade ≥ 3

Abbreviations used:

AD = absolute difference; 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.c. = not calculable; n.r. = not reached; PRO-CTCAE = patient-reported outcome – CTCAE; PT = preferred term; QLQ-BR23 = Quality of Life Questionnaire – Breast Cancer 23; QLQ-C30 = Quality of Life Questionnaire – Core 30; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale

b2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

There are no assessable data.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.c.	There are no assessable data.
Morbidity	n.c.	There are no assessable data.
Health-related quality of life	n.c.	There are no assessable data.
Side effects	n.c.	There are no assessable data.
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) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

approx. 75 – 7,965 patients

a2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

approx. 1 – 70 patients

b1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

approx. 410 – 18,550 patients

b2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

approx. 5 – 160 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 Truqap (active ingredient: capivasertib) at the following publicly accessible link (last access: 5 February 2025):

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

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

Patients with ER-positive, HER2-negative advanced breast cancer should be selected for treatment with capivasertib based on the presence of one or more PIK3CA/AKT1/PTEN alteration(s), which should be detected using a CE-marked IVD with the appropriate intended use. If a CE-marked IVD is not available, an alternative validated test must be used.

4. Treatment costs

Annual treatment costs:

a1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Capivasertib	€ 92,010.81
Fulvestrant	€ 4,505.48
Total:	€ 96,516.29
Appropriate comparator therapy:	
<i>Anti-oestrogens</i>	
Tamoxifen	€ 72.34
Fulvestrant	€ 4,183.66
<i>Non-steroidal aromatase inhibitors</i>	
Anastrozole	€ 134.23
Letrozole	€ 170.12
<i>Steroidal aromatase inhibitors</i>	
Exemestane	€ 425.48
<i>Ribociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Ribociclib	€ 29,658.94
Anastrozole	€ 134.23
Letrozole	€ 170.12
Ribociclib + anastrozole Total:	€ 29,793.17
Ribociclib + letrozole Total:	€ 29,829.06
<i>Abemaciclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Abemaciclib	€ 25,977.05
Anastrozole	€ 134.23
Letrozole	€ 170.12
Abemaciclib + anastrozole Total:	€ 26,111.28
Abemaciclib + letrozole Total:	€ 26,147.17
<i>Palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Palbociclib	€ 23,124.01
Anastrozole	€ 134.23
Letrozole	€ 170.12
Palbociclib + anastrozole Total:	€ 23,258.24
Palbociclib + letrozole Total:	€ 23,294.13

Designation of the therapy	Annual treatment costs/ patient
<i>Ribociclib in combination with fulvestrant</i>	
Ribociclib	€ 29,658.94
Fulvestrant	€ 4,505.48
Total:	€ 34,164.42
<i>Abemaciclib in combination with fulvestrant</i>	
Abemaciclib	€ 25,977.05
Fulvestrant	€ 4,183.66
Total:	€ 30,160.71
<i>Palbociclib in combination with fulvestrant</i>	
Palbociclib	€ 23,124.01
Fulvestrant	€ 4,505.48
Total:	€ 27,629.49

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2025)

Costs for additionally required SHI services: not applicable

- a2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Capivasertib	€ 92,010.81
Fulvestrant	€ 4,505.48
Total:	€ 96,516.29
Appropriate comparator therapy:	
<i>Anti-oestrogens</i>	
Tamoxifen	€ 72.34
<i>Palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Palbociclib	€ 23,124.01
Anastrozole	€ 134.23
Letrozole	€ 170.12
Palbociclib + anastrozole Total:	€ 23,258.24
Palbociclib + letrozole Total:	€ 23,294.13

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2025)

Costs for additionally required SHI services: not applicable

b1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Capivasertib	€ 92,010.81
Fulvestrant	€ 4,505.48
Total:	€ 96,516.29
Appropriate comparator therapy:	
<i>Anti-oestrogens</i>	
Tamoxifen	€ 72.34
Fulvestrant	€ 4,183.66
<i>Non-steroidal aromatase inhibitors</i>	
Anastrozole	€ 134.23
Letrozole	€ 170.12
<i>Steroidal aromatase inhibitors</i>	
Exemestane	€ 425.48
<i>Everolimus in combination with exemestane</i>	
Everolimus	€ 4,878.23
Exemestane	€ 425.48
Total:	€ 5,303.71
<i>Ribociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Ribociclib	€ 29,658.94
Anastrozole	€ 134.23
Letrozole	€ 170.12
Ribociclib + anastrozole Total:	€ 29,802.57
Ribociclib + letrozole Total:	€ 29,793.17
<i>Abemaciclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Abemaciclib	€ 25,977.05
Anastrozole	€ 134.23
Letrozole	€ 170.12
Abemaciclib + anastrozole Total:	€ 26,111.28
Abemaciclib + letrozole Total:	€ 26,147.17

Designation of the therapy	Annual treatment costs/ patient
<i>Palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Palbociclib	€ 23,124.01
Anastrozole	€ 134.23
Letrozole	€ 170.12
Palbociclib + anastrozole Total:	€ 23,258.24
Palbociclib + letrozole Total:	€ 23,294.13
<i>Ribociclib in combination with fulvestrant</i>	
Ribociclib	€ 29,658.94
Fulvestrant	€ 4,505.48
Total:	€ 34,164.42
<i>Abemaciclib in combination with fulvestrant</i>	
Abemaciclib	€ 25,977.05
Fulvestrant	€ 4,183.66
Total:	€ 30,160.71
<i>Palbociclib in combination with fulvestrant</i>	
Palbociclib	€ 23,124.01
Fulvestrant	€ 4,505.48
Total:	€ 27,307.67

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 2025)

Costs for additionally required SHI services: not applicable

b2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alterations, with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Capivasertib	€ 92,010.81
Fulvestrant	€ 4,505.48
Total:	€ 96,516.29
Appropriate comparator therapy:	
<i>Anti-oestrogens</i>	
Tamoxifen	€ 72.34
Fulvestrant	€ 4,183.66
<i>aromatase inhibitor in combination with a GnRH analogue</i>	

Designation of the therapy	Annual treatment costs/ patient
Aromatase inhibitors	€ 143.63 - € 425.48
GnRH analogue	€ 2,049.41 - € 2,582.75
Total:	€ 2,193.04 - € 3,008.23 ²
<i>Palbociclib in combination with a non-steroidal aromatase inhibitor (anastrozole, letrozole)</i>	
Palbociclib	€ 23,124.01
Anastrozole	€ 134.23
Letrozole	€ 170.12
Palbociclib + anastrozole Total:	€ 23,258.24
Palbociclib + letrozole Total:	€ 23,294.13

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 March 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) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage
 - 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.
- a2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), following disease recurrence on or after (neo-)adjuvant endocrine therapy, no previous treatment in locally advanced or metastatic stage
 - 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.
- b1) Women with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage

² The range is based on the combinations of active ingredients referenced in the publication by DiLauro et al. (2015): anastrozole and leuprorelin (lower limit) and exemestane and goserelin (upper limit): Di Lauro et al. Role of gonadotropin-releasing hormone analogues in metastatic male breast cancer: results from a pooled analysis. J Hematol Oncol. 2015 May 17;8:53

- 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.
- b2) Men with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with PIK3CA/AKT1/PTEN alteration(s), with disease progression on or after endocrine therapy which occurred in locally advanced or metastatic stage
- 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.

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 3 April 2025.

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

Berlin, 3 April 2025

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

Prof. Hecken