Abemaciclib (new therapeutic indication: breast cancer, HR+, HER2-, early at high risk of recurrence, adjuvant treatment, combination with endocrine therapy)

Resolution of: 20 October 2022/ 8 November 2022/ 6 March 2025
Entry into force on: 20 October 2022/ 10 November 2022/ 6 March 2025
Federal Gazette, BAnz AT 08 12 2022 B5/ BAnz AT 02 01 2023 B2/ BAnz AT 25 03 2025 B2

Valid until: patient groups a1) and a2) are limited until 1 July 2026

New therapeutic indication (according to the marketing authorisation of 1 April 2022):

Verzenios in combination with endocrine therapy is indicated for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence.

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

Therapeutic indication of the resolution (resolution of 20 October 2022):

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-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Appropriate comparator therapy:

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

Extent and probability of the additional benefit of abemaciclib in combination with endocrine therapy versus an endocrine therapy:

Hint for a minor additional benefit

a2) Postmenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Appropriate comparator therapy:

- an aromatase inhibitor (anastrozole or letrozole) alone, or, if necessary, tamoxifen if aromatase inhibitors are unsuitable,

  or

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

Extent and probability of the additional benefit of abemaciclib in combination with endocrine therapy versus an endocrine therapy:

An additional benefit is not proven.

a3) Men with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Appropriate comparator therapy:

- Tamoxifen

Extent and probability of the additional benefit of abemaciclib in combination with endocrine therapy versus an endocrine therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a1) Premenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

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 avoiding recurrences (recurrence rate and 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 (CTCAE grade ≥ 3) and 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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

[1] Data from the dossier assessment of the IQWiG (A22-51) and from the addendum (A22-96), unless otherwise indicated.

MONARCH-E study:

- ongoing, open-label, randomised, controlled trial
- Abemaciclib in combination with endocrine therapy **vs** endocrine therapy
- Cohort 1 relevant: high risk of recurrence defined as ≥ 4 positive axillary lymph nodes (pALN) or 1 to 3 pALN in the presence of an additional grade 3 tumour and/or a tumour size of ≥ 5 cm (corresponding to stage IIA to IIIC at the time of diagnosis).

Relevant sub-population: Premenopausal women

Mortality

Endpoint	**Abemaciclib in combination with endocrine therapy**		**Endocrine therapy**		Intervention vs control
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
	553	n.a. [n.c.; n.c.] *17 (3.1)*	535	n.a. [n.c.; n.c.] *11 (2.1)*	1.46 [0.69; 3.13]; 0.322[b, c]

Morbidity

Endpoint	**Abemaciclib in combination with endocrine therapy**		**Endocrine therapy**		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[d]
Recurrences					
Recurrence rate	553	*45 (8.1)*	535	*81 (15.1)*	0.54 [0.38; 0.76]; < 0.001
Local breast cancer recurrence	553	*4 (0.7)*	535	*10 (1.9)*	–
Regional invasive breast cancer recurrence	553	*2 (0.4)*	535	*3 (0.6)*	–
Remote recurrence	553	*36 (6.5)*	535	*62 (11.6)*	–
Contralateral invasive breast cancer	553	*1 (0.2)*	535	*4 (0.7)*	–
Secondary primary cancer (not breast cancer)	553	*2 (0.4)*	535	*3 (0.6)*	–

Death without recurrence	553	*0 (0)*	535	*0 (0)*	–
	N	Median time to event [95% CI] *Patients with event n (%)*	N	Median time to event [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Disease-free survival[e]	553	n.a. [n.c.; n.c.] *45 (8.1)*	535	n.a. [n.c.; n.c.] *81 (15.1)*	0.52 [0.36; 0.74]; < 0.001[b, c]

Endpoint	**Abemaciclib in combination with endocrine therapy**			**Endocrine therapy**			Intervention vs control
	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	Difference Δ [95% CI]; p value; SMD [95% CI]
Symptomatology (FACIT fatigue)[h]							
	476	40.35 (9.18)	-0.86 (0.28)	467	40.33 (8.84)	0.75 (0.28)	-1.60 [-2.39; -0.82]; < 0.001; -0.26 [-0.39; -0.13]
Health status (EQ-5D VAS)[i]							
	478	77.47 (15.05)	1.92 (0.47)	471	78.50 (15.39)	0.75 (0.28)	-0.59 [-1.91; 0.73]; 0.380

Health-related quality of life

Endpoint	Abemaciclib in combination with endocrine therapy			Endocrine therapy			Intervention vs control
	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	Difference Δ [95% CI]; p value; SMD [95% CI]
FACT-B (total score)[j]							
	489	106.47 (17.11)	-1.53 (0.54)	477	105.86 (17.26)	1.13 (0.55)	-2.67 [< -4.18; -1.15]; < 0.001; -0.22 [-0.35; -0.10]
FACT-G (total score)[k] (presented additionally)							
	490	83.37 (13.41)	-1.70 (0.44)	477	82.84 (13.77)	0.32 (0.44)	−2.02 [−3.24; −0.80]; 0.001; -0.21 [-0.33; -0.08]

Side effects

Endpoint	Abemaciclib in combination with endocrine therapy		Endocrine therapy		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[d]
Total adverse events (presented additionally)					
	553	*543 (98.2)*	535	*465 (86.9)*	–
Serious adverse events (SAE)					
	553	*63 (11.4)*	535	*39 (7.3)*	1.56 [1.07; 2.29]; 0.021
Severe adverse events (CTCAE grade 3 or 4)					
	553	*244 (44.1)*	535	*73 (13.6)*	3.23 [2.56; 4.08]; < 0.001
Therapy discontinuation due to adverse events[l]					
	553	*69 (12.5)*	535	*6 (1.1)*	11.13 [4.87; 25.41]; < 0.001
Specific adverse events					

Neutropenia (severe AEs[m])	553	*42 (7.6)*	535	*6 (1.1)*	6.77 [2.90; 15.80]; < 0.001
General disorders and administration site conditions (SOC, AEs)	553	*310 (56.1)*	535	*165 (30.8)*	1.82 [1.57; 2.11]; < 0.001
Eye disorders (SOC, AEs)	553	*78 (14.1)*	535	*32 (6.0)*	2.36 [1.59; 3.50]; < 0.001
Respiratory, thoracic and mediastinal disorders (SOC, AEs)	553	*157 (28.4)*	535	*74 (13.8)*	2.05 [1.60; 2.63]; < 0.001
Gastrointestinal disorders (SOC, AEs)	553	*496 (89.7)*	535	*177 (33.1)*	2.71 [2.40; 3.07]; < 0.001
Diarrhoea (PT, severe AEs[m])	553	*30 (5.4)*	535	*2 (0.4)*	14.51 [3.49; 60.42]; < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)	553	*220 (39.8)*	535	*107 (20.0)*	1.99 [1.63; 2.42]; < 0.001
Blood and lymphatic system disorders (SOC, severe AEs)	553	*62 (11.2)*	535	*8 (1.5)*	7.50 [3.63; 15.51]; < 0.001
Hepatic events (CMQ, severe AEs)[n]	553	*14 (2.5)*	535	*1 (0.2)*	13.54 [1.79; 102.64]; < 0.001

[a] Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
[b] Effect and CI: Cox proportional hazards model; p value: log-rank test
[c] p value: z test
[d] IQWiG's own calculation, unconditional exact test (CSZ method according to Martín Andrés et al.[2])
[e] For individual components, see Recurrences
[f] Those in the premenopausal patient population without a switch to unapproved endocrine therapy (553 vs 535) for whom usable data were available at baseline and at least one further survey time point
[g] MMRM: the change in the score compared to the start of the study is modelled. Independent variables are: Value at the start of the study, treatment, visit, treatment*visit. Although, according to the pharmaceutical company, the analysis formally only takes into account all visits at which at least 25% of all patients in both treatment groups have values for the change in score, this does not lead to a loss of data in the present case; no time point is affected. The changes per arm and the effect refer to the entire observation period.
[h] Higher (increasing) values mean better symptomatology; positive effects mean an advantage for the intervention (scale range 0 to 52).
[i] Higher (increasing) values mean better health status; positive effects mean an advantage for the intervention (scale range 0 to 100).
[j] Result is composed of the FACT-G and the BCS subscale. Higher (increasing) values mean better health-related quality of life; positive effects mean an advantage for the intervention (scale range 0 to 148). No evaluations of the BCS subscale are available.
[k] Result is composed of the FACT-G subscales (EWB, FWB, PWB, SWB). Higher (increasing) values mean better health-related quality of life; positive effects mean an advantage for the intervention (scale range 0 to 108). No evaluations of the subscales are available.
[l] Discontinuation of at least one of the medicines
[m] Operationalised as CTCAE grade ≥ 3
[n] includes the PTs ALT increased and AST increased

Abbreviations used:

AD = absolute difference; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BCS = Breast Cancer Specific Subscale; CMQ = Customised MedDRA Query; CTCAE = Common Terminology Criteria for Adverse Events; EWB = emotional well-being; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy - Fatigue; FACT-B = Functional Assessment of Cancer Therapy - Breast; FACT-G = Functional Assessment of Cancer Therapy - General; FWB = functional well-being; HR = hazard ratio; IDFS = invasive-disease-free survival; CI = confidence interval; MD = mean difference; MMRM = mixed model with repeated measures; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.a. = not achieved; PT = preferred term; PWB = physical well-being; RCT = randomised controlled trial; RR = relative risk; SD = standard deviation; SE = standard error; SMD = standardised mean difference; SOC = system organ class; SAE = serious adverse event; SWB = social/family well-being; AE = adverse event; VAS = visual analogue scale; vs = versus

a2) Postmenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

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 avoiding recurrences (recurrence rate and 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 (CTCAE grade ≥ 3) and discontinuation due to AEs. In detail, mainly 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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

MONARCH-E study:

- ongoing, open-label, randomised, controlled trial
- Abemaciclib in combination with endocrine therapy vs endocrine therapy
- Cohort 1 relevant: high risk of recurrence defined as ≥ 4 positive axillary lymph nodes (pALN) or 1 to 3 pALN in the presence of an additional grade 3 tumour and/or a tumour size of ≥ 5 cm (corresponding to stage IIA to IIIC at the time of diagnosis).

Relevant sub-population: Postmenopausal women

Mortality

Endpoint	**Abemaciclib in combination with endocrine therapy**		**Endocrine therapy**		Intervention vs control
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
	1284	n.a. [n.c.; n.c.] *54 (4.2)*	1264	n.a. [n.c.; n.c.] *58 (4.6)*	0.94 [0.65; 1.36]; 0.738[b, c]

Morbidity

Endpoint	**Abemaciclib in combination with endocrine therapy**		**Endocrine therapy**		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[d]
Recurrences					
Recurrence rate	1284	*122 (9.5)*	1264	*165 (13.1)*	0.73 [0.58; 0.91]; 0.005
Local breast cancer recurrence	1284	*13 (1.0)*	1264	*12 (0.9)*	–
Regional invasive breast cancer recurrence	1284	*8 (0.6)*	1264	*12 (0.9)*	–
Remote recurrence	1284	*74 (5.8)*	1264	*117 (9.3)*	–
Contralateral invasive breast cancer	1284	*3 (0.2)*	1264	*7 (0.6)*	–

Secondary primary cancer (not breast cancer)	1284	*13 (1.0)*	1264	*12 (0.9)*	–
Death without recurrence	1284	*14 (1.1)*	1264	*9 (0.7)*	–
	N	Median time to event [95% CI] *Patients with event n (%)*	N	Median time to event [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Disease-free survival[e]	1284	n.a. [n.c.; n.c.] *122 (9.5)*	1264	n.a. [n.c.; n.c.] *165 (13.1)*	0.74 [0.58; 0.93]; 0.010[b, c]

Endpoint	**Abemaciclib in combination with endocrine therapy**			**Endocrine therapy**			Intervention vs control
	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	Difference Δ [95% CI]; p value; SMD [95% CI]
Symptomatology (FACIT fatigue)[h]							
	1075	40.22 (9.39)	-1.16 (0.19)	1077	39.54 (9.58)	0.47 (0.19)	-1.63 [< -2.16; -1.10]; < 0.001; -0.26 [-0.34; -0.17]
Health status (EQ-5D VAS)[i]							
	1090	78.16 (16.34)	-0.21 (0.31)	1092	78.53 (14.92)	1.25 (0.31)	−1.46 [−2.33; −0.59]; 0.001; -0.14 [-0.23; -0.06]

Health-related quality of life

Endpoint	Abemaciclib in combination with endocrine therapy			Endocrine therapy			Intervention vs control
	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	N[f]	Values at the start of the study MV (SD)	Change MV[g] (SE)	Difference Δ [95% CI]; p value; SMD [95% CI]
FACT-B (total score)[j]							
	1105	108.31 (18.20)	-2.08 (0.37)	1110	107.72 (17.91)	-0.10 (0.37)	-1.98 [< -3.00; -0.96]; < 0.001; -0.16 [-0.25; -0.08]
FACT-G (total score)[k] (presented additionally)							
	1107	84.38 (14.38)	-2.29 (0.30)	1110	83.96 (14.16)	-0.75 (0.29)	-1.54 [< -2.35; -0.72]; < 0.001; -0.16 [-0.24; -0.07]

Side effects

Endpoint	Abemaciclib in combination with endocrine therapy		Endocrine therapy		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[d]
Total adverse events (presented additionally)					
	1283	*1260 (98.2)*	1265	*1119 (88.5)*	–
Serious adverse events (SAE)					
	1283	*200 (15.6)*	1265	*123 (9.7)*	1.60 [1.30; 1.98]; < 0.001
Severe adverse events (CTCAE grade 3 or 4)					
	1283	*645 (50.3)*	1265	*213 (16.8)*	2.99 [2.61; 3.41]; < 0.001
Therapy discontinuation due to adverse events[l]					
	1283	*282 (22.0)*	1265	*14 (1.1)*	19.86 [11.68; 33.78]; < 0.001

Specific adverse events					
Neutropenia (PT, severe AEs[m])	1283	*257 (20.0)*	1265	*7 (0.6)*	36.20 [17.15; 76.39]; < 0.001
Alopecia (PT, AEs)	1283	*150 (11.7)*	1265	*34 (2.7)*	4.35 [3.02; 6.26]; < 0.001
Arthralgia (PT, AEs)	1283	*342 (26.7)*	1265	*488 (38.6)*	0.69 [0.62; 0.77]; < 0.001
Dizziness (PT, AEs)	1283	*137 (10.7)*	1265	*83 (6.6)*	1.63 [1.25; 2.11]; < 0.001
Eye disorders (SOC, AEs)	1283	*195 (15.2)*	1265	*66 (5.2)*	2.91 [2.23; 3.81]; < 0.001
Gastrointestinal disorders (SOC, AEs)	1283	*1142 (89.0)*	1265	*408 (32.3)*	2.76 [2.54; 3.00]; < 0.001
Diarrhoea (PT, severe AEs[m])	1283	*125 (9.7)*	1265	*2 (0.2)*	61.62 [15.28; 248.59]; < 0.001
Fatigue (PT, severe AEs[m])	1283	*34 (2.7)*	1265	*2 (0.2)*	16.76 [4.04; 69.62]; < 0.001
Hypocalcaemia (PT, severe AEs[m])	1283	*18 (1.4)*	1265	*5 (0.4)*	3.55 [1.32; 9.53]; 0.007
Blood and lymphatic system disorders (SOC, severe AEs[m])	1283	*209 (16.3)*	1265	*13 (1.0)*	15.85 [9.10; 27.61]; < 0.001
Hepatic events (CMQ, severe AEs[m])[n]	1283	*45 (3.5)*	1265	*11 (0.9)*	4.03 [2.10; 7.76]; 0.001
Venous thromboembolism (CMQ, severe AEs[m])[o]	1283	*14 (1.1)*	1265	*4 (0.3)*	3.45 [1.14; 10.46]; 0.020
ILD / pneumonitis (SMQ, SAE)	1283	*7 (0.5)*	1265	*1 (0.1)*	6.90 [0.85; 56.02]; 0.036

[a] Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
[b] Effect and CI: Cox proportional hazards model; p value: log-rank test
[c] p value: z test

[d] IQWiG's own calculation, unconditional exact test (CSZ method according to Martin Andrés et al.[2])
[e] For individual components, see Recurrences
[f] Those in the premenopausal patient population without a switch to unapproved endocrine therapy (553 vs 535) for whom usable data were available at baseline and at least one further survey time point
[g] MMRM: the change in the score compared to the start of the study is modelled. Independent variables are: Value at the start of the study, treatment, visit, treatment*visit. Although, according to the pharmaceutical company, the analysis formally only takes into account all visits at which at least 25% of all patients in both treatment groups have values for the change in score, this does not lead to a loss of data in the present case; no time point is affected. The changes per arm and the effect refer to the entire observation period.
[h] Higher (increasing) values mean better symptomatology; positive effects mean an advantage for the intervention (scale range 0 to 52).
[i] Higher (increasing) values mean better health status; positive effects mean an advantage for the intervention (scale range 0 to 100).
[j] Result is composed of the FACT-G and the BCS subscale. Higher (increasing) values mean better health-related quality of life; positive effects mean an advantage for the intervention (scale range 0 to 148). No evaluations of the BCS subscale are available.
[k] Result is composed of the FACT-G subscales (EWB, FWB, PWB, SWB). Higher (increasing) values mean better health-related quality of life; positive effects mean an advantage for the intervention (scale range 0 to 108). No evaluations of the subscales are available.
[l] Discontinuation of at least one of the medicines
[m] Operationalised as CTCAE grade ≥ 3
[m] Includes the PTs ALT increased and AST increased
[o] Includes the PTs pulmonary embolism and deep vein thrombosis

Abbreviations used:
AD = absolute difference; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BCS = Breast Cancer Specific Subscale; CMQ = Customised MedDRA Query; CTCAE = Common Terminology Criteria for Adverse Events; EWB = emotional well-being; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy - Fatigue; FACT-B = Functional Assessment of Cancer Therapy - Breast; FACT-G = Functional Assessment of Cancer Therapy - General; FWB = functional well-being; HR = hazard ratio; IDFS = invasive-disease-free survival; CI = confidence interval; MD = mean difference; MMRM = mixed model with repeated measures; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.a. = not achieved; PT = preferred term; PWB = physical well-being; RCT = randomised controlled trial; RR = relative risk; SD = standard deviation; SE = standard error; SMD = standardised mean difference; SOC = system organ class; SAE = serious adverse event; SWB = social/family well-being; AE = adverse event; VAS = visual analogue scale; vs = versus

[2] Martín Andrés A, Silva Mato A. Choosing the optimal unconditioned test for comparing two independent proportions. Computat Stat Data Anal 1994; 17(5): 555-574. https://dx.doi.org/10.1016/0167-9473(94)90148-1.

a3) Men with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

MONARCH-E study:

- ongoing, open-label, randomised, controlled trial
- Abemaciclib in combination with endocrine therapy vs endocrine therapy
- Cohort 1 relevant: high risk of recurrence defined as ≥ 4 positive axillary lymph nodes (pALN) or 1 to 3 pALN in the presence of an additional grade 3 tumour and/or a tumour size of ≥ 5 cm (corresponding to stage IIA to IIIC at the time of diagnosis).

Relevant sub-population: Men

Mortality

Endpoint	Abemaciclib in combination with endocrine therapy		Endocrine therapy		Intervention vs control
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
	10	n.a. [15.95; n.c.] *2 (20.0)*	9	n.a. [n.c.; n.c.] *0 (0)*	–

Morbidity

Endpoint	**Abemaciclib in combination with endocrine therapy**		**Endocrine therapy**		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value
Recurrences					
Recurrence rate	10	*2 (20.0)*	9	*1 (11.1)*	–
Local breast cancer recurrence	10	*0 (0)*	9	*1 (11.1)*	–
Regional invasive breast cancer recurrence	10	*0 (0)*	9	*0 (0)*	–
Remote recurrence	10	*2 (20.0)*	9	*0 (0)*	–
Contralateral invasive breast cancer	10	*0 (0)*	9	*0 (0)*	–
Secondary primary cancer (not breast cancer)	10	*0 (0)*	9	*0 (0)*	–
Death without recurrence	10	*0 (0)*	9	*0 (0)*	–
	N	Median time to event [95% CI] *Patients with event n (%)*	N	Median time to event [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Disease-free survival[b]	10	n.a. [9.93; n.c.] *2 (20.0)*	9	n.a. [21.76; n.c.] *1 (11.1)*	–
Symptomatology (FACIT fatigue)					
	No usable data available.				
Health status (EQ-5D VAS)					
	No usable data available.				

Health-related quality of life

Endpoint	Abemaciclib in combination with endocrine therapy		Endocrine therapy		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value
FACT-B, FACT-ES					
	No usable data available.				

Side effects

Endpoint	Abemaciclib in combination with endocrine therapy		Endocrine therapy		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value
Total adverse events (presented additionally)					
	10	*10 (100.0)*	9	*9 (100.0)*	–
Serious adverse events (SAE)					
	10	*3 (30.0)*	9	*1 (11.1)*	–
Severe adverse events (CTCAE grade 3 or 4)					
	10	*4 (40.0)*	9	*2 (22.2)*	–
Therapy discontinuation due to adverse events[f]					
	10	*2 (20.0)*	9	*0 (0)*	–
Specific adverse events					
Neutropenia (PT, severe AEs[c])	10	*2 (20.0)*	9	*0 (0)*	–
Diarrhoea (PT, severe AEs[c])	10	*0 (0)*	9	*0 (0)*	–

[a] Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
[b] For individual components, see Recurrences
[C] Operationalised as CTCAE grade ≥ 3

Abbreviations used:
AD = absolute difference; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CMQ = Customised MedDRA Query; CTCAE = Common Terminology Criteria for Adverse Events; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy - Fatigue; FACT-B = Functional Assessment of Cancer Therapy - Breast; FACT-ES = Functional Assessment of Cancer Therapy - Endocrine Symptoms; HR = hazard ratio; IDFS = invasive disease-free survival; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.a. = not achieved; PT = preferred term; RCT =

randomised controlled trial; SOC = system organ class; RR = relative risk; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

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

a1) Premenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

approx. 2,360 - 4,130 patients

a2) Postmenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

approx. 4,470 - 5,220 patients

a3) Men with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

approx. 75 - 80 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 Verzenios (active ingredient: abemaciclib) at the following publicly accessible link (last access: 27 June 2022):

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

Treatment with abemaciclib 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:

The annual treatment costs shown refer to the first year of treatment.

a1) Premenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Abemaciclib + tamoxifen	
Abemaciclib	€ 23,637.40
Tamoxifen	€ 72.20
Total	€ 23,709.60
GnRH agonist[3]	€ 1,851.84 - € 2,237.26
Appropriate comparator therapy:	
Tamoxifen	€ 72.20
GnRH agonist[3]	€ 1,851.84 - € 2,237.26

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 October 2022)

Costs for additionally required SHI services: not applicable

a2) Postmenopausal women with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Abemaciclib + anastrozole	
Abemaciclib	€ 23,637.40
Anastrozole	€ 190.09
Total	€ 23,827.49
Abemaciclib + letrozole	
Abemaciclib	€ 23,637.40
Letrozole	€ 176.44
Total	€ 23,813.84
Abemaciclib + tamoxifen[4]	
Abemaciclib	€ 23,637.40

[3] Leuprorelin or goserelin
[4] If aromatase inhibitors are unsuitable.

Designation of the therapy	Annual treatment costs/ patient
Tamoxifen	€ 72.20
Total	€ 23,709.60
Abemaciclib + anastrozole in sequence after abemaciclib + tamoxifen[5]	
Abemaciclib + tamoxifen	
Abemaciclib + tamoxifen	€ 23,637.40
Tamoxifen	€ 72.20
Total	€ 23,709.60
Abemaciclib + exemestane in sequence after abemaciclib + tamoxifen[5]	
Abemaciclib + tamoxifen	
Abemaciclib	€ 23,637.40
Tamoxifen	€ 72.20
Total	€ 23,709.60
Appropriate comparator therapy:	
Anastrozole	€ 190.09
Letrozole	€ 176.44
Tamoxifen[4]	€ 72.20
Anastrozole in sequence after tamoxifen[5]	
Tamoxifen	€ 72.20
Exemestane in sequence after tamoxifen[5]	
Tamoxifen	€ 72.20

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 October 2022)

Costs for additionally required SHI services: not applicable

[5] According to the marketing authorisations, the switch to anastrozole and exemestane is indicated after 2 to 3 years of initial adjuvant therapy with tamoxifen. Treatment with abemaciclib should be given for 2 years. Accordingly, no costs are presented for anastrozole and exemestane.

a3) Men with hormone receptor-positive, HER2-negative early-stage breast cancer at high risk of recurrence

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Abemaciclib + tamoxifen	
Abemaciclib	€ 23,637.40
Tamoxifen	€ 72.20
Total	€ 23,709.60
Appropriate comparator therapy:	
Tamoxifen	€ 72.20

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 October 2022)

Costs for additionally required SHI services: not applicable