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
Talazoparib (new therapeutic indication: prostate cancer, metastatic, castration-resistant, in combination with enzalutamide)

of 15 August 2024

At its session on 15 August 2024, 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 Talazoparib in accordance with the resolution of 20 November 2020:

Talazoparib

Resolution of: 15 August 2024
Entry into force on: 15 August 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 5 January 2024):

Talzenna is indicated in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated.

Therapeutic indication of the resolution (resolution of 15 August 2024):

See new therapeutic indication according to marketing authorisation.

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

a) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have not received prior therapy for mCRPC

Appropriate comparator therapy:

- Abiraterone acetate in combination with prednisone or prednisolone (only for patients whose disease is progressive during or after docetaxel-containing chemotherapy; only for patients with asymptomatic or mildly symptomatic disease after failure of androgen deprivation therapy, in whom chemotherapy is not yet clinically indicated)
  or
- enzalutamide (only for patients whose disease progresses during or after chemotherapy with docetaxel; only for patients with asymptomatic or mildly symptomatic disease after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated)
  or
- olaparib as monotherapy (only for patients with BRCA1/2 mutations (germline and/or somatic) whose disease is progressive after previous treatment that included a new hormonal agent)
  or
- olaparib in combination with abiraterone acetate and prednisone or prednisolone (only for patients with BRCA mutations and for patients without BRCA mutations with symptomatic disease progression)

Extent and probability of the additional benefit of talazoparib in combination with enzalutamide compared with enzalutamide:

a1) Adults without HRR deficiency

Hint for a lesser benefit.

a2) Adults with HRR deficiency

An additional benefit is not proven.

b) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have received prior therapy for mCRPC

Appropriate comparator therapy:

Patient-individual therapy with selection of:

- abiraterone acetate in combination with prednisone or prednisolone (only for patients whose disease is progressive during or after docetaxel-containing chemotherapy),
- enzalutamide (only for patients whose disease progresses during or after chemotherapy with docetaxel),
- olaparib in combination with abiraterone acetate and prednisone or prednisolone and
- olaparib as monotherapy (only for patients with BRCA1/2 mutations (germline and/or somatic) whose disease is progressive after previous treatment that included a new hormonal agent)

taking into account the previous therapy/ therapies and the BRCA1/2 mutational status.

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

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have not received prior therapy for mCRPC

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A24-22) unless otherwise indicated.

a1) Adults without HRR deficiency

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	↓	Disadvantages in the symptom scales "nausea and vomiting", "fatigue", "dyspnoea" and "appetite loss"
Health-related quality of life	↓	Disadvantages in the functional scales "global health status", "physical functioning" and "role functioning"
Side effects	↓	Disadvantages in severe AEs, SAEs and therapy discontinuation due to AEs. In detail, disadvantages in some 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		

a2) Adults with HRR deficiency

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment
Morbidity	↔	Advantages in the symptom scales "pain" and "symptoms of the urinary tract"; Disadvantages in the symptom scales "nausea and vomiting", "fatigue", "dyspnoea" and "appetite loss"; overall, no relevant difference for the benefit assessment
Health-related quality of life	↔	In the overall assessment of all the results, no relevant difference for the benefit assessment; a positive effect was observed for the "physical functioning" functional scale
Side effects	↓	Disadvantages in severe AEs, SAEs and therapy discontinuation due to AEs. In detail, disadvantages in some 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

TALAPRO-2 study (2-part)

Part 2 of the study: ongoing, double-blind, randomised phase III study consisting of 3 cohorts

Talazoparib + enzalutamide **vs** enzalutamide

Relevant sub-population: Evaluation cohorts 1 (patients without HRR deficiency) and 2 (patients with HRR deficiency) without overlap

FDA data cut-off from 28 March 2023

Mortality

Endpoint	**Talazoparib + enzalutamide**		**Enzalutamide**		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[a] Absolute difference (AD)[b]
Overall survival					
without HRR deficiency	317	n.r. [37.0; n.c.] 125 (39.4)	319	38.7 [35.0; n.c.] 133 (41.7)	0.93 [0.73; 1.18]; 0.538
with HRR deficiency	200	41.9 [34.5; n.c.] 60 (30.0)	199	30.8 [26.8; 38.8] 76 (38.2)	0.67 [0.47; 0.94]; 0.018
				Total[c]:	0.84 [0.69; 1.02]; 0.076

Morbidity

Endpoint	Talazoparib + enzalutamide		Enzalutamide		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Progression-free survival (PFS) according to BCIR[2]					
Study cohort 1 (all-comers)	402	n.r. [27.47; n.r.] 151 (37.6)	403	21.95 [16.62; 25.13] 191 (47.4)	0.63 [0.51; 0.78]; < 0.0001
Study cohort 2 (HRR-deficient)	200	n.r. [21.88; n.r.] 66 (33.0)	199	13.80 [11.01; 16.69] 104 (52.3)	0.45 [0.33; 0.61]; < 0.0001

Endpoint	Talazoparib + enzalutamide		Enzalutamide		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Symptomatic bone fracture					
without HRR deficiency	317	n.r. 30 (9.5)	319	n.r. 21 (6.6)	1.43 [0.82; 2.49]; 0.209
with HRR deficiency	200	n.r. 19 (9.5)	199	n.r. 14 (7.0)	1.17 [0.59; 2.34]; 0.651
				Total[c]	1.32 [0.86; 2.04]; 0.207
Spinal cord compression					
without HRR deficiency	317	n.r. 17 (5.4)	319	n.r. 19 (6.0)	0.88 [0.46; 1.69]; 0.701
with HRR deficiency	200	n.r. 12 (6.0)	199	n.r. 12 (6.0)	0.88 [0.39; 1.96]; 0.755
				Total[c]	0.88 [0.53; 1.46]; 0.621

[2] Data on talazoparib from module 4 of the pharmaceutical company from 02.02.2024

Worst pain (BPI-SF question 3 – time to first confirmed deterioration[d])					
without HRR deficiency	No suitable data[e]				
with HRR deficiency	No suitable data[e]				
Impairment due to pain (BPI-SF question 9a-g – time to first confirmed deterioration[f])					
without HRR deficiency	No suitable data[e]				
with HRR deficiency	No suitable data[e]				
Symptomatology (EORTC QLQ-C30 – time to 1st deterioration[g])					
Fatigue					
without HRR deficiency	311	1.9 [1.9; 2.8] 239 (76.8)	314	3.7 [2.8; 4.6] 226 (72.0)	1.26 [1.05; 1.52]; 0.012
with HRR deficiency	197	2.8 [1.9; 3.7] 138 (70.1)	197	3.7 [2.3; 4.6] 127 (64.5	1.10 [0.86; 1.41]; 0.401
				Total[c]	1.20 [1.03; 1.39]; 0.016
Nausea and vomiting					
without HRR deficiency	311	9.2 [5.6; 16.3] 159 (51.1)	314	34.0 [17.5; n.c.] 122 (8.9)	1.54 [1.22; 1.95]; < 0.001
with HRR deficiency	197	10.6 [7.4; 19.4] 91 (46.2)	197	13.8 [8.3; 27.7] 79 (40.1)	1.11 [0.82; 1.51]; 0.500
				Total[c]	1.36 [1.13; 1.64]; 0.001
Pain					
Effect modification by the characteristic HRR gene mutational status					
without HRR deficiency	311	7.4 [4.7; 9.2] 186 (59.8)	314	9.3 [7.4; 11.7] 179 (57.0)	1.09 [0.89; 1.34]; 0.397
with HRR deficiency	197	9.3 [6.5; 15.6] 108 (54.8)	197	5.6 [3.7; 6.6] 121 (61.4)	0.64 [0.49; 0.83]; < 0.001
				Total[c]	0.89 [0.76; 1.05]; 0.166
				Interaction[h]	**0.002**

Dyspnoea					
without HRR deficiency	311	6.4 [4.9; 9.3] 183 (58.8)	314	16.4 [10.3; 23.0] 151 (48.1)	1.43 [1.16; 1.78]; 0.001
with HRR deficiency	197	8.3 [5.6; 13.8] 99 (50.3)	197	9.2 [5.6; 13.9] 91 (46.2)	1.02 [0.77; 1.36]; 0.883
				Total[c]	1.27 [1.07; 1.50]; 0.007
Insomnia					
without HRR deficiency	311	11.1 [8.4; 15.7] 157 (50.5)	314	9.1 [5.6; 15.7] 163 (51.9)	0.91 [0.73; 1.14]; 0.414
with HRR deficiency	197	16.6 [10.2; 24.9] 86 (43.7)	197	10.2 [5.6; 17.4] 91 (46.2)	0.82 [0.61; 1.10]; 0.168
				Total[c]	0.88 [0.73; 1.05]; 0.145
Appetite loss					
without HRR deficiency	311	5.6 [4.0; 9.2] 187 (60.1)	314	15.7 [11.1; 21.2] 155 (49.4)	1.44 [1.17; 1.78]; < 0.001
with HRR deficiency	197	7.4 [4.7; 11.9] 104 (52.8)	197	11.1 [7.5; 13.8] 96 (48.7)	1.09 [0.82; 1.44]; 0.573
				Total[c]	1.30 [1.10; 1.54]; 0.002
Constipation					
without HRR deficiency	311	11.0 [7.3; 15.7] 156 (50.2)	314	18.5 [11.1; 25.0] 139 (44.3)	1.17 [0.93; 1.47]; 0.176
with HRR deficiency	197	15.7 [7.5; 24.0] 89 (45.2)	197	11.1 [7.4; 19.4] 87 (44.2)	0.91 [0.67; 1.22]; 0.512
				Total[c]	1.07 [0.89; 1.28]; 0.488
Diarrhoea					
without HRR deficiency	311	34.1 [21.2; n.c.] 116 (37.3)	314	26.1 [21.2; n.c.] 116 (36.9)	0.92 [0.71; 1.19]; 0.520
with HRR deficiency	197	19.3 [14.1; 27.6] 77 (39.1)	197	26.1 [19.4; n.c.] 58 (29.4)	1.23 [0.88; 1.74]; 0.229
				Total[c]	1.02 [0.83; 1.26]; 0.830

Symptomatology (EORTC QLQ-PR25 – time to 1st deterioration[g])					
Symptoms of the urinary tract					
Effect modification by the characteristic HRR gene mutational status					
without HRR deficiency	311	24.9 [13.9; 32.3] 136 (43.7)	314	32.2 [19.3; n.c.] 119 (37.9)	1.10 [0.86; 1.40]; 0.455
with HRR deficiency	197	32.3 [23.0; n.c.] 62 (31.5)	197	15.6 [9.5; 21.7] 76 (38.6)	0.58 [0.41; 0.82]; 0.002
				Total[c]	0.89 [0.73; 1.09]; 0.252
				Interaction[h]	**0.003**
Bowel symptoms					
without HRR deficiency	311	n.r. [30.8; n.c.] 98 (31.5)	314	n.r. [34.4; n.c.] 83 (26.4)	1.16 [0.87; 1.55]; 0.320
with HRR deficiency	197	n.r. [28.6; n.c.] 49 (24.9)	197	n.r. [27.9; n.c.] 51 (25.9)	0.75 [0.51; 1.12]; 0.154
				Total[c]	1.00 [0.79; 1.26]; 0.971
Hormone treatment-related symptoms					
without HRR deficiency	311	9.3 [7.4; 12.6] 162 (52.1)	314	12.5 [8.3; 21.9] 148 (47.1)	1.12 [0.90; 1.40]; 0.326
with HRR deficiency	197	9.3 [5.6; 15.6] 96 (48.7)	197	7.4 [4.7; 11.0] 92 (46.7)	0.86 [0.64; 1.15]; 0.306
				Total[c]	1.02 [0.85; 1.21]; 0.845
Incontinence aid					
without HRR deficiency	No suitable data[i]				
with HRR deficiency	No suitable data[i]				
Health status (EQ-5D VAS – time to 1st deterioration[j])					

without HRR deficiency	311	12.0 [6.5; 21.3] 157 (50.5)	314	15.7 [8.4; 21.4] 151 (48.1)	1.05 [0.84; 1.31]; 0.685
with HRR deficiency	197	16.1 [7.5; 30.4] 88 (44.7)	197	9.2 [7.3; 12.0] 96 (48.7)	0.76 [0.57; 1.01]; 0.062
				Total[c]	0.93 [0.78; 1.11]; 0.416

Health-related quality of life

Endpoint	**Talazoparib + enzalutamide**		**Enzalutamide**		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
EORTC QLQ-C30 – time to 1st deterioration[k]					
Global health status					
Effect modification by the characteristic HRR gene mutational status					
without HRR deficiency	311	3.7 [2.9; 4.7] 213 (68.5)	314	7.6 [6.4; 9.4] 189 (60.2)	1.32 [1.09; 1.61]; 0.005
with HRR deficiency	197	6.4 [4.6; 8.4] 116 (58.9)	197	6.5 [3.7; 8.3] 111 (56.3)	0.94 [0.72; 1.22]; 0.649
				Total[c]	1.17 [1.001; 1.37]; 0.049
				Interaction[h]	**0.042**
Physical functioning					
Effect modification by the characteristic HRR gene mutational status					
without HRR deficiency	311	5.6 [3.7; 7.4] 211 (67.8)	314	8.3 [6.5; 13.7] 184 (58.6)	1.30 [1.07; 1.59]; 0.009
with HRR deficiency	197	8.3 [5.6; 10.3] 108 (54.8)	197	5.6 [4.5; 7.5] 117 (59.4)	0.76 [0.59; 0.99]; 0.043
				Total[c]	1.07 [0.91; 1.25]; 0.424

				Interaction[h]	**0.001**
Role functioning					
Effect modification by the characteristic HRR gene mutational status					
without HRR deficiency	311	5.5 [3.7; 6.5] 218 (70.1)	314	7.4 [5.6; 9.2] 181 (57.6)	1.32 [1.08; 1.60]; 0.006
with HRR deficiency	197	7.4 [4.8; 10.2] 114 (57.9)	197	6.5 [4.5; 9.2] 111 (56.3)	0.88 [0.68; 1.15]; 0.351
				Total[c]	1.14 [0.98; 1.34]; 0.100
				Interaction[h]	**0.015**
Emotional functioning					
without HRR deficiency	311	17.5 [9.2; 28.6] 143 (46.0)	314	23.1 [17.5; 31.5] 132 (42.0)	1.12 [0.88; 1.42]; 0.360
with HRR deficiency	197	13.6 [8.2; 21.1] 86 (43.7)	197	9.3 [8.2; 15.6] 90 (45.7)	0.82 [0.61; 1.10]; 0.187
				Total[c]	0.99 [0.82; 1.19]; 0.912
Cognitive functioning					
without HRR deficiency	311	4.6 [2.8; 6.5] 208 (66.9)	314	4.6 [3.7; 6.4] 195 (62.1)	1.06 [0.87; 1.29]; 0.551
with HRR deficiency	197	5.7 [3.7; 9.2] 113 (57.4)	197	4.6 [2.8; 6.5] 113 (57.4)	0.85 [0.66; 1.11]; 0.232
				Total[c]	0.98 [0.84; 1.14]; 0.781
Social functioning					
without HRR deficiency	311	4.6 [3.7; 6.5] 199 (64.0)	314	8.9 [6.4; 11.7] 180 (57.3)	1.18 [0.96; 1.44]; 0.107
with HRR deficiency	197	6.5 [4.7; 10.6] 110 (55.8)	197	7.4 [5.5; 12.0] 100 (50.8)	1.01 [0.77; 1.33]; 0.912
				Total[c]	1.12 [0.95; 1.31]; 0.184
EORTC QLQ-PR25 – time to 1st deterioration[k]					

Sexual activity					
without HRR deficiency	311	n.r. [26.7; n.c.] 103 (33.1)	314	n.r. 89 (28.3)	1.19 [0.89; 1.58]; 0.237
with HRR deficiency	197	n.r. 52 (26.4)	197	n.r. 43 (21.8)	1.07 [0.71; 1.60]; 0.751
				Total[c]	1.15 [0.91; 1.45]; 0.247
Sexual functioning					
without HRR deficiency	No suitable data[i]				
with HRR deficiency	No suitable data[i]				

Side effects

Endpoint	**Talazoparib + enzalutamide**		**Enzalutamide**		Intervention vs control
	N	Median in months [95% CI] *Patients with event n (%)*	N	Median in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Adverse events in total					
without HRR deficiency	314	0.6 [0.5; 0.9] 310 (98.7)	317	1.0 [0.8; 1.2] 301 (95.0)	
with HRR deficiency	198	0.5 [0.5; 0.7] 196 (99.0)	199	0.6 [0.5; 0.8] 194 (97.5)	
Serious adverse events (SAE)					
without HRR deficiency	314	35.3 [25.0; n.c.] 133 (42.4)	317	40.5 [40.5; 46.5] 90 (28.4)	1.51 [1.15; 1.97]; 0.002
with HRR deficiency	198	44.4 [33.9; 44.4] 67 (33.8)	199	n.r. [32.7; n.c.] 42 (21.1)	1.39 [0.94; 2.04]; 0.098
				Total[c]	1.47 [1.18; 1.83]; < 0.001
Severe adverse events (CTCAE grade 3 or 4)					

without HRR deficiency	314	3.7 [3.3; 4.6] 249 (79.3)	317	21.4 [17.6; 29.0] 145 (45.7)	2.40 [1.95; 2.94]; < 0.001
with HRR deficiency	198	4.7 [4.1; 6.6] 137 (69.2)	199	23.7 [17.6; n.c.] 81 (40.7)	2.00 [1.52; 2.64]; < 0.001
				Total[c]	2.25 [1.91; 2.65]; < 0.001
Therapy discontinuation due to adverse events					
without HRR deficiency	314	n.r. 70 (22.3)	317	n.r. 38 (12.0)	1.78 [1.20; 2.64]; 0.004
with HRR deficiency	198	44.4 [n. c.] 23 (11.6)	199	n.r. 16 (8.0)	1.12 [0.58; 2.13]; 0.740
				Total[c]	1.57 [1.12; 2.20]; 0.009
Specific adverse events					
MDS (PT, AEs)					
without HRR deficiency	No suitable data				
with HRR deficiency	No suitable data				
AML (PT, AEs)					
without HRR deficiency	No suitable data				
with HRR deficiency	No suitable data				
Dizziness (PT, AEs)					
Effect modification by the characteristic HRR gene mutational status					
without HRR deficiency	314	n.r. 44 (14.0)	317	n.r. 15 (4.7)	2.85 [1.59; 5.13]; < 0.001
with HRR deficiency	198	n.r. 20 (10.1)	199	n.r. 16 (8.0)	1.16 [0.60; 2.24]; 0.657
				Total[c]	1.92 [1.24; 2.97]; 0.004
				Interaction[h]	**0.046**

Infections and infestations (SOC, SAEs)					
without HRR deficiency	314	n.r. 25 (8.0)	317	n.r. 10 (3.2)	2.26 [1.09; 4.71]; 0.025
with HRR deficiency	198	n.r. 13 (6.6)	199	n.r. 8 (4.0)	1.30 [0.54; 3.14]; 0.565
				Total[c]	1.80 [1.03; 3.16]; 0.040
Anaemia (PT, severe AEs)					
without HRR deficiency	314	19.3 [9.2; 38.2] 157 (50.0)	317	n.r. 12 (3.8)	16.76 [9.31; 30.15]; < 0.001
with HRR deficiency	198	36.0 [20.3; n.c.] 83 (41.9)	199	n.r. 9 (4.5)	10.27 [5.16; 20.44]; < 0.001
				Total[c]	13.63 [8.72; 21.31]; < 0.001
Investigations (SOC, severe AEs)					
without HRR deficiency	314	n.r. 97 (30.9)	317	n.r. 22 (6.9)	4.79 [3.01; 7.60]; < 0.001
with HRR deficiency	198	n.r. [35.9; n.c.] 55 (27.8)	199	n.r. 17 (8.5)	3.22 [1.87; 5.56]; < 0.001
				Total[c]	4.05 [2.85; 5.77]; < 0.001

[a] Cox proportional hazards model; for cohort 1 (without HRR mutation) unadjusted, for cohort 2 (with HRR mutation) adjusted by stratification factor prior therapy with taxanes or therapy with novel hormonal active ingredients (yes vs no)
[b] Data on absolute difference (AD) only in the case of statistically significant difference; own calculation
[c] IQWiG calculation by means of a meta-analysis using a fixed effect
[d] An increase in score by ≥ 2 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 10).
[e] The written statement procedure showed that the endpoints "worst pain" and "impairment due to pain" were not operationalised as "time to first deterioration" but as "time to first confirmed deterioration", contrary to the information in the pharmaceutical company's dossier; however, these data cannot be interpreted without the information on first deterioration.
[f] An increase in score by ≥ 15% of the scale range compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 10).
[g] An increase in score by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).
[h] IQWIG calculation by means of the Q-test from a meta-analysis using a fixed effect
[i] For about 50% and 91% of patients, respectively, no incontinence aid or sexual functioning survey was available at the start of the study. At least this percentage of patients was not included in the evaluation.

The pharmaceutical company's approach does not ensure that the burden of patients who only develop incontinence or limitation of the sexual function in the course of treatment is assessed.

[j] A decrease by ≥ 15% of the scale range compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).

[k] A decrease in score by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).

Abbreviations used:
AD = absolute difference; AML = acute myeloid leukaemia; BPI-SF = Brief Pain Inventory - Short Form; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR = hazard ratio; HRR = homologous recombination repair; 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; PT = preferred term; QLQ-C30 = Quality of Life Questionnaire – Core 30; QLQ-PR25 = Quality of Life Questionnaire – Prostate 25; SOC = system organ class; VAS = visual analogue scale; vs = versus

b) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have received prior therapy for mCRPC

No data are available to allow an assessment of the additional benefit.

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

a) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have not received prior therapy for mCRPC

and

b) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have received prior therapy for mCRPC

approx. 9,400 to 12,200 patients in total

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 Talzenna (active ingredient: talazoparib) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 6 August 2024):

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

Treatment with talazoparib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology as well as specialists in urology and further doctors from other professional groups participating in the Oncology Agreement who are experienced in the treatment of patients with prostate cancer.

Medicinal castration with a GnRH agonist or antagonist should be continued during the treatment of patients who have not been surgically castrated.

4. Treatment costs

Annual treatment costs:

a) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have not received prior therapy for mCRPC

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Talazoparib + enzalutamide + GnRH analogues	
Talazoparib	€ 42,285.25
Enzalutamide	€ 40,687.07
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 84,256.02- € 85,310.18
Appropriate comparator therapy:	
Abiraterone acetate + prednisone or prednisolone + GnRH analogues	
Abiraterone acetate	€ 1,456.96
Prednisone or prednisolone	€ 55.85 - € 70.19

Designation of the therapy	Annual treatment costs/ patient
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 2,796.51- € 3,865.01
Enzalutamide + GnRH analogues	
Enzalutamide	€ 40,687.07
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 41,970.77- € 43,024.93
Olaparib as monotherapy + GnRH analogues	
Olaparib	€ 58,564.51
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 59,848.21- € 60,902.37
Olaparib + abiraterone acetate + prednisone or prednisolone + GnRH analogues	
Olaparib	€ 58,564.51
Abiraterone acetate	€ 1,456.96
Prednisone or prednisolone	€ 55.85 - € 70.19
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 61,361.02- € 62,429.52

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2024)

Costs for additionally required SHI services: not applicable

b) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have received prior therapy for mCRPC

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Talazoparib + enzalutamide + GnRH analogues	
Talazoparib	€ 42,285.25
Enzalutamide	€ 40,687.07
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 84,256.02- € 85,310.18
Appropriate comparator therapy:	
Abiraterone acetate + prednisone or prednisolone + GnRH analogues	
Abiraterone acetate	€ 1,456.96
Prednisone or prednisolone	€ 55.85 - € 70.19

Designation of the therapy	Annual treatment costs/ patient
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 2,796.51- € 3,865.01
Enzalutamide + GnRH analogues	
Enzalutamide	€ 40,687.07
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 41,970.77- € 43,024.93
Olaparib as monotherapy + GnRH analogues	
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Olaparib + abiraterone acetate + prednisone or prednisolone + GnRH analogues	
Olaparib	€ 58,564.51
Abiraterone acetate	€ 1,456.96
Prednisone or prednisolone	€ 55.85 - € 70.19
GnRH analogues	€ 1,283.70 - € 2,337.86
Total	€ 61,361.02- € 62,429.52

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2024)

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:

a) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have not received prior therapy for mCRPC

- 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.

b) Adults with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have received prior therapy for mCRPC

– 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 15 August 2024.

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

Berlin, 15 August 2024

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

Prof. Hecken