

Talazoparib

Resolution of: 20 November 2020
Entry into force on: 20 November 2020
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Valid until: unlimited

Therapeutic indication (according to the marketing authorisation of 20 June 2019):

Talzenna is indicated as monotherapy for the treatment of adult patients with germline BRCA1/2-mutations, who have HER2-negative locally advanced or metastatic breast cancer. Patients should have been previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced, or metastatic setting unless patients were not suitable for these treatments (see Section 5.1). Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy.

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

Adult patients with HER2-negative, locally advanced or metastatic breast cancer with BRCA1/2 mutations in the germline; after prior therapy with an anthracycline and/or a taxane in the (neo)adjuvant or metastatic setting or not suitable for these treatments

Appropriate comparator therapy:

– Capecitabine

or

– Eribulin

or

– Vinorelbine

or

– An anthracycline- or taxane-containing therapy (only for patients who have not yet received anthracycline- and taxane-containing therapy or who are suitable for renewed anthracycline- or taxane-containing therapy)

Extent and probability of the additional benefit of talazoparib compared with capecitabine or vinorelbine or eribulin:

Hint for a considerable additional benefit

Study results according to endpoints:¹

¹ Data from the dossier assessment of the IQWiG (A20-48) and the addendum (A20-89) unless otherwise indicated.

Adult patients with HER2-negative, locally advanced or metastatic breast cancer with BRCA1/2 mutations in the germline; after prior therapy with an anthracycline and/or a taxane in the (neo)adjuvant or metastatic setting or not suitable for these treatments

EMBRACA study: Talazoparib vs chemotherapy according to the doctor's instructions (capecitabine or vinorelbine or eribulin or gemcitabine)

Study design: RCT, open, parallel

Relevant sub-population: Talazoparib vs chemotherapy according to the doctor's instructions with the use of capecitabine or vinorelbine or eribulin

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↔	No difference relevant for the benefit assessment.
Morbidity	↑	Advantages in pain, insomnia, loss of appetite, and chest symptoms
Health-related quality of life	↑	Advantages in health status, physical, social, and emotional functioning, role functioning, and body image
Side effects	↑	Advantage in the endpoint severe AE (CTCAE grade 3 or 4)
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		

Mortality

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value
Mortality					
Overall survival	266	19.6 [16.7; 22.7] 199 (74.8)	130	19.8 [17.6; 22.4] 97 (74.6)	0.86 [0.67; 1.10]; 0.236

Morbidity

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
Progression-free survival (PFS) ^b					
	266	8.5 [7.1; 9.2] 173 (65)	130	5.6 [3.3; 8.2] 74 (56.9)	0.541 [0.41; 0.72]; < 0.0001 2.9 months
Symptomatology					
<i>EORTC QLQ-C30 symptom scales – time to first deterioration^c</i>					
Fatigue	243	2.1 [1.5; 2.8] 166 (68.3)	104	1.5 [1.4; 1.9] 69 (66.3)	0.74 [0.55; 0.99]; 0.043 0.6 months
Nausea and vomiting	243	3.8 [2.3; 7.5] 139 (57.2)	104	3.0 [1.5; 11.3] 51 (49.0)	0.93 [0.66; 1.30]; 0.659
Pain	243	5.7 [4.0; 9.7] 130 (53.5)	104	2.9 [1.6; 4.9] 61 (58.7)	0.55 [0.40; 0.75]; < 0.001 2.8 months
Dyspnoea	243	8.4 [5.6; 10.8] 122 (50.2)	104	7.8 [5.1; n.c.] 36 (34.6)	0.99 [0.67; 1.45]; 0.94
Insomnia	243	10.4 [7.0; 17.1] 109 (44.9)	104	3.2 [1.8; 8.1] 53 (51.0)	0.54 [0.38; 0.76]; < 0.001 7.2 months
Loss of appetite	243	7.4 [4.9; 11.9] 128 (52.7)	104	2.3 [1.5; 4.2] 58 (55.8)	0.60 [0.44; 0.84]; 0.002 5.1 months
Constipation	243	7.2 [5.7; 10.1] 118 (48.6)	104	10.1 [3.7; n.c.] 37 (35.6)	1.03 [0.70; 1.50]; 0.884
Diarrhoea	243	10.7 [8.2; 16.0] 103 (42.4)	104	n.a. [3.5; n.c.] 34 (32.7)	0.79 [0.53; 1.19]; 0.256

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
<i>EORTC QLQ-BR23 symptom scales – time to first deterioration^c</i>					
Side effects of the systemic therapy	243	9.3 [5.8; 12.5] 119 (49.0)	104	3.5 [2.1; 10.6] 50 (48.1)	0.65 [0.46; 0.92]; 0.013 5.8 months
Symptoms in the chest area	243	37.4 [23.5; n.c.] 59 (24.3)	104	12.5 [8.8; n.c.] 29 (27.9)	0.54 [0.34; 0.86]; 0.008 24.9 months
Symptoms in the arm area	243	6.9 [4.2; 14.9] 122 (50.2)	104	3.9 [2.1; 11.9] 49 (47.1)	0.70 [0.50; 0.99]; 0.044 3 months
Burden of hair loss	No usable data				

Health-related quality of life

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
<i>EORTC QLQ-C30 functional scales – time to first deterioration^d</i>					
Global health status	243	5.7 [3.8; 7.8] 130 (53.5)	104	3.3 [2.1; 5.0] 55 (52.9)	0.61 [0.44; 0.85]; 0.003 2.4 months
Physical functioning	243	9.3 [7.7; 14.9] 109 (44.9)	104	2.8 [2.1; 6.6] 53 (51.0)	0.51 [0.36; 0.72]; < 0.001 6.5 months
Role functioning	243	4.6 [3.5; 6.6] 135 (55.6)	104	1.7 [1.1; 3.0] 64 (61.5)	0.56 [0.41; 0.77]; < 0.001 2.9 months
Cognitive functioning	243	4.4 [3.0; 7.5] 141 (58.0)	104	2.8 [1.7; 3.7] 56 (53.8)	0.71 [0.51; 0.98]; 0.038 1.6 months

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
Emotional functioning	243	10.7 [6.4; 24.3] 101 (41.6)	104	3.5 [2.3; 9.9] 49 (47.1)	0.54 [0.38; 0.77]; < 0.001 7.2 months
Social functioning	243	8.2 [4.9; 12.5] 122 (50.2)	104	2.3 [1.6; 4.9] 54 (51.9)	0.60 [0.43; 0.84]; 0.003 5.9 months
<i>EORTC QLQ-BR23 functional scales – time to first deterioration^d</i>					
Body image	243	17.7 [11.5; n.c.] 88 (36.2)	104	4.9 [2.8; n.c.] 42 (40.4)	0.56 [0.38; 0.81]; 0.002 12.8 months
Sexual functioning	243	32.8 [7.5; n.c.] 92 (37.9)	104	14.0 [3.6; n.c.] 33 (31.7)	0.95 [0.63; 1.42]; 0.799
Sexual enjoyment	No usable data				
Future perspective	243	n.a. [24.8; n.c.] 68 (28.0)	104	n.a. [6.1; n.c.] 27 (26.0)	0.70 [0.44; 1.11]; 0.129

Side effects

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
Adverse events (presented additionally)					
	265	0.2 [0.1; 0.3] 261 (98.5)	114	0.1 [0.1; 0.2] 111 (97.4)	–
Serious adverse events (SAE)					
	265	20.7 [15.3; 31.1] 95 (35.8)	114	n.a. [6.7; n.c.] 33 (28.9)	0.75 [0.49; 1.13]; 0.162

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
Severe adverse events (CTCAE grade 3 or 4)					
	265	3.5 [2.8; 4.0] 183 (69.1)	114	2.0 [1.3; 3.5] 72 (63.2)	0.73 [0.55; 0.97]; 0.027 1.5 months
Therapy discontinuation because of adverse events					
	265	n.a. 21 (7.9)	114	n.a. 10 (8.8)	0.59 [0.27; 1.27]; 0.169
Specific adverse events					
Myelodysplastic syndrome ^e (PT, CTCAE-grade ≥ 3)	265	0 (0)	114	0 (0)	n.c.
Acute myeloid leukaemia ^f (PT, CTCAE grade ≥ 3)	265	0 (0)	114	0 (0)	n.c.
Hand-foot syndrome (PT, AEs) ^g	265	n.a. 4 (1.5)	114	n.a. 28 (24.6)	0.05 [0.02; 0.14]; < 0.001
Anaemia (PT, CTCAE grade ≥ 3)	265	18.1 [11.6; n.c.] 103 (38.9)	114	n.a. 5 (4.4)	7.23 [2.93; 17.79]; < 0.001
Thrombocytopenia (PT, CTCAE grade ≥ 3)	265	n.a. 22 (8.3)	114	n.a. 1 (0.9)	8.34 [1.12; 61.98]; 0.013
Neutropoenia (PT, CTCAE grade ≥ 3)	265	n.a. 50 (18.9)	114	n.a. 26 (22.8)	0.61 [0.38; 0.99]; 0.044
Diarrhoea (PT, CTCAE grade ≥ 3)	265	n.a. 2 (0.8)	114	n.a. [11.8; n.c.] 6 (5.3)	0.12 [0.02; 0.58]; 0.002
Skin and subcutaneous tissue disorders (SOC, CTCAE grade ≥ 3)	265	n.a. 2 (0.8)	114	n.a. [16.5; n.c.] 8 (7.0)	0.04 [0.01; 0.32]; < 0.001

Endpoint	Talazoparib		Chemotherapy according to the doctor's instructions ^a		Intervention vs control
	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	N	Median time to event in months [95% CI] <i>Patients with event n (%)</i>	HR [95% CI] p value Absolute difference (AD) ^a
Eye disorders (SOC, AEs)	265	n.a. 35 (13.2)	114	20.0 [20.0; n.c.] 21 (18.4)	0.38 [0.21; 0.68]; < 0.001
Paresthesia (PT, AEs)	265	n.a. 13 (4.9)	114	n.a. 14 (12.3)	0.23 [0.10; 0.53]; < 0.001
<p>a Absolute difference (AD) given only in the case of a statistically significant difference; own calculation</p> <p>b Data from dossier on talazoparib Module 4A from 21 February 2019, data cut-off of 15 September 2017.</p> <p>c An increase of the respective score by at least 10 points was regarded as a clinically relevant deterioration.</p> <p>d A decrease of the respective score by at least 10 points was regarded as a clinically relevant deterioration.</p> <p>e For MDS, the pharmaceutical company considers the SMQ MDS, which is not a sufficiently specific operationalisation for the present benefit assessment. The SMQ MDS results show that 1 (0.4%) patient in the talazoparib arm and no patient in the chemotherapy arm experienced a severe event (CTCAE grade ≥ 3).</p> <p>f The pharmaceutical company states that the SMQ AML is to be considered although it is not an SMQ according to MedDRA but rather a compilation of PTs predefined by the pharmaceutical company, which does not represent a sufficiently specific operationalisation for the present benefit assessment. In the compilation of PTs to AML considered by the pharmaceutical company, no patient in the talazoparib arm and one (0.9%) patient in the chemotherapy arm experienced a severe event (CTCAE grade ≥ 3).</p> <p>g 1 (0.4 %) patient in the talazoparib arm and 3 (2.6%) patients in the chemotherapy arm had a severe hand-foot syndrome (CTCAE grade ≥ 3).</p>					
<p>Abbreviations used:</p> <p>AD = absolute difference; AML = acute myeloid leukaemia; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organization for Research and Treatment of Cancer; HR = hazard ratio; CI = confidence interval; MDS = myelodysplastic syndrome; MedDRA = Medical Dictionary for Regulatory Activities; n = number of patients with (at least one) event; N= number of patients evaluated; n.c = not calculable; n.a. = not achieved; PT = preferred term; QLQ-BR23 = Quality of Life Questionnaire – Breast Cancer 23; QLQ-C30 = Quality of Life Questionnaire Cancer-30; SMQ = standardised MedDRA query; SOC = system organ class; SAE = serious adverse event; AE = adverse event</p>					

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

Adult patients with HER2-negative, locally advanced or metastatic breast cancer with BRCA1/2 mutations in the germline; after prior therapy with an anthracycline and/or a taxane in the (neo)adjuvant or metastatic setting or not suitable for these treatments

approx. 410–1,830 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 Talzenna (active ingredient: talazoparib) at the following publicly accessible link (last access: 27 August 2020):

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

The selection of patients for breast cancer treatment with Talzenna should be based on the detection of a pathogenic or suspected pathogenic *BRCA* germline mutation using a validated test procedure by an experienced laboratory.

4. Treatment costs

Annual treatment costs:

Adult patients with HER2-negative, locally advanced or metastatic breast cancer with BRCA1/2 mutations in the germline; after prior therapy with an anthracycline and/or a taxane in the (neo)adjuvant or metastatic setting or not suitable for these treatments

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Talazoparib	€ 80,482.62
Appropriate comparator therapy:	
Capecitabine	€ 2,382.37
Vinorelbine	€ 6,861.61 – 8,271.54
Eribulin	€ 38,822.71
Anthracycline- or taxane-containing therapy	
Docetaxel	€ 23,377.77
Doxorubicin	€ 2,028.85 – 3,042.05
Pegylated liposomal doxorubicin (PLD)	€ 41,162.29
Epirubicin	€ 4,552.70 – 5,007.97
Paclitaxel	€ 16,258.56
Additionally required SHI services	€ 224.22
Total:	€ 16,482.78
nab-paclitaxel	€ 31,632.33

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 November 2020

Other services covered by SHI funds:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Vinorelbine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	52	€ 4,212

Eribulin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2	34.8	€ 2,818.80
Docetaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Doxorubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	5–11	€ 405 – 891
Pegylated liposomal doxorubicin (PLD)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	13	€ 1,053
Epirubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	10–16	€ 810 – 1,296
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
nab-paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40