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
Sacituzumab govitecan (breast cancer, triple-negative, at least 2 prior therapies)

of 19 May 2022

At its session on 19 May 2022, 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 Sacituzumab govitecan as follows:

Sacituzumab govitecan

Resolution of: 19 May 2022
Entry into force on: 19 May 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 22 November 2021):

Trodelvy as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease.

Therapeutic indication of the resolution (resolution of 19 May 2022):

See therapeutic indication according to marketing authorisation.

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

Adults with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease

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/or taxane-containing therapy or who are eligible for renewed anthracycline or taxane-containing treatment)

Extent and probability of the additional benefit of Sacituzumab govitecan over Capecitabine, Eribulin or Vinorelbine:

Indication of a major additional benefit

Study results according to endpoints:[1]

Adults with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival
Morbidity	↑	Advantages for fatigue, pain, dyspnoea and disadvantage for diarrhoea
Health-related quality of life	↑	Advantages for physical functioning, role functioning and emotional functioning
Side effects	↑	Advantage for serious AEs as well as, in detail, advantages and 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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

ASCENT study: multicentre, open-label, phase III RCT

- Sacituzumab govitecan vs therapy according to doctor's instructions (capecitabine, eribulin, vinorelbine or gemcitabine)
- Sub-population of patients for whom capecitabine, vinorelbine or eribulin was selected as the active ingredient to be received prior to randomisation in case of allocation to the control arm.
- Data cut-offs used:
    - Data cut-off 1: 11.03.2020 (morbidity, quality of life, side effects)
    - Data cut-off 2: 25.02.2021 (overall survival)

[1] Data from the dossier assessment of the IQWiG (A21-154) and from the addendum (A22-41), unless otherwise indicated.

Mortality

Endpoint	Sacituzumab govitecan		Capecitabine, eribulin, vinorelbine		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 (%)*	Effect estimator [95% CI] p value[a] Absolute difference (AD)[b]
Overall survival					
	221	11.9 [10.2; 14.0] 165 (74.7)	224	6.7 [5.7; 7.5] 190 (84.8)	0.52 [0.42; 0.65] < 0.001 AD: + 5.2 months

Morbidity

Endpoint	Sacituzumab govitecan		Capecitabine, eribulin, vinorelbine		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 (%)*	Effect estimator [95% CI] p value[c] Absolute difference (AD)[b]
Progression-free survival (PFS)[d]					
	221	4.6 [4.0; 5.7] 157 (71.0)	224	1.6 [1.5; 2.5] 148 (66.1)	0.44 [0.34; 0.56] < 0.0001 AD: +4 months
Symptomatology (EORTC QLQ-C30) – time to first deterioration[e]					
Fatigue	211	1.6 [1.4; 2.2] 139 (65.9)	191	1.4 [1.0; 1.5] 110 (57.6)	0.73 [0.57; 0.95] 0.018 AD: +0.2 months
Nausea and vomiting	211	2.1 [1.6; 2.8] 136 (64.5)	191	2.4 [1.6; 3.8] 76 (39.8)	1.22 [0.91; 1.62] 0.194
Pain	211	4.9 [3.5; 6.4] 109 (51.7)	191	2.1 [1.4; 2.8] 84 (44.0)	0.53 [0.39; 0.72] < 0.001 AD: +2.8 months
Dyspnoea	211	6.9 [5.3; n.c.] 82 (38.9)	191	2.8 [1.9; 3.2] 75 (39.3)	0.44 [0.31; 0.61] < 0.001 AD: +4.1 months
Insomnia	211	4.1 [3.0; 6.0] 107 (50.7)	191	3.7 [2.7; n.c.] 62 (32.5)	0.75 [0.53; 1.04] 0.083

Endpoint	Sacituzumab govitecan		Capecitabine, eribulin, vinorelbine		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 (%)*	Effect estimator [95% CI] p value[c] Absolute difference (AD)[b]
Appetite loss	211	3.0 [2.1; 4.4] 122 (57.8)	191	2.8 [2.1; 5.5] 71 (37.2)	1.02 [0.75; 1.38] 0.918
Constipation	211	3.6 [2.6; 5.6] 109 (51.7)	191	3.3 [2.1; 4.4] 72 (37.7)	0.85 [0.62; 1.15] 0.285
Diarrhoea	211	2.0 [1.4; 2.6] 134 (63.5)	191	7.2 [3.0; n.c.] 47 (24.6)	2.28 [1.62; 3.20] < 0.001 AD: -5.2 months

Health-related quality of life

Endpoint	Sacituzumab govitecan		Capecitabine, eribulin, vinorelbine		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 (%)*	Effect estimator [95% CI] p value Absolute difference (AD)[a]
EORTC QLQ-C30 - time to first deterioration[f]					
Global health status	211	2.8 [2.1; 3.9] 122 (57.8)	191	3.5 [2.1; 4.4] 70 (36.6)	0.99 [0.73; 1.34] 0.922
Physical functioning	211	5.9 [3.8; 8.3] 100 (47.4)	191	2.1 [1.7; 3.2] 85 (44.5)	0.54 [0.40; 0.73] < 0.001 AD: +3.8 months
Cognitive functioning	211	3.3 [2.8; 4.2] 117 (55.5)	191	2.6 [1.9; 3.2] 74 (38.7)	0.78 [0.58; 1.06] 0.115
Role functioning	211	2.1 [1.6; 3.0] 132 (62.6)	191	1.4 [1.2; 1.8] 104 (54.5)	0.66 [0.50; 0.86] 0.002 AD: +0.7 months
Emotional functioning	211	5.9 [4.9; 9.6] 90 (42.7)	191	n.a. [2.1; n.c.] 58 (30.4)	0.70 [0.49; 0.99] 0.043
Social functioning	211	3.3 [2.3; 4.9] 113 (53.6)	191	2.7 [1.8; 3.5] 82 (42.9)	0.76 [0.56; 1.02] 0.062

Side effects

Endpoint	Sacituzumab govitecan		Capecitabine, eribulin, vinorelbine		Intervention vs control
	N	Median in months [95% CI] *Patients with event n (%)*	N	Median in months [95% CI] *Patients with event n (%)*	Effect estimator [95% CI] p value Absolute difference (AD)[a]
Total adverse events (presented additionally)					
	213	0.1 [0.1; 0.1] 212 (99.5)	192	0.1 [0.1; 0.2] 187 (97.4)	-
Serious adverse events (SAE)					
	213	n.a. 54 (25.4)	192	8.0 [5.6; n.c.] 53 (27.6)	0.67 [0.45; 0.99] 0.041
Severe adverse events (CTCAE grade ≥ 3)					
	213	1.0 [0.9; 1.4] 151 (70.9)	192	1.4 [0.9; 2.3] 122 (63.5)	1.00 [0.78; 1.27] 0.936
Therapy discontinuation due to adverse events					
	213	n.a. 10 (4.7)	192	n.a. 9 (4.7)	0.53 [0.20; 1.39] 0.191
Specific adverse events					
Hand-foot syndrome	No usable data available[g]				
Gastrointestinal toxicity[h]	213	n.a. 29 (13.6)	192	n.a. 10 (5.2)	2.22 [1.08; 4.60] 0.027
Neutropenia[i]	213	3.2 [1.0; 7.9] 115 (54.0)	192	n.a. [3.7; n.c.] 68 (35.4)	1.48 [1.10; 2.01] 0.011
Neuropathy[j]	213	n.a. [16.4; n.c.] 32 (15.0)	192	7.7 [5.3; n.c.] 46 (24.0)	0.35 [0.21; 0.56] < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)[k]	213	1.0 [0.7; 2.2] 136 (63.8)	192	6.1 [3.9; n.c.] 68 (35.4)	1.93 [1.44; 2.59] < 0.001 AD: -5.1 months
General disorders and administration site conditions (SOC, severe AEs)[l]	213	n.a. 17 (8.0)	192	n.a. [6.6; n.c.] 29 (15.1)	0.34 [0.18; 0.64] < 0.001
Metabolism and nutrition	213	n.a. 24 (11.3)	192	n.a. 7 (3.6)	2.54 [1.09; 5.96] 0.026

Endpoint	Sacituzumab govitecan		Capecitabine, eribulin, vinorelbine		Intervention vs control
	N	Median in months [95% CI] *Patients with event n (%)*	N	Median in months [95% CI] *Patients with event n (%)*	Effect estimator [95% CI] p value Absolute difference (AD)[a]
disorders (SOC, severe AEs)					
Respiratory, thoracic and mediastinal disorders (SOC, severe AEs)	213	n.a. 14 (6.6)	192	n.a. 26 (13.5)	0.29 [0.15; 0.58] < 0.001

a Effect, CI and p value: Cox proportional hazards model or log-rank test, each stratified by region, number of previous chemotherapies and existing brain metastases at the start of the study
b Effect, CI and p value: Cox proportional hazards model or log-rank test, each not stratified, unless otherwise stated.
c Indication of absolute difference (AD) only in case of statistically significant difference; own calculation
d Information from the dossier of the pharmaceutical company
e An increase by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100)
f A decrease by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100)
g Operationalised as palmar-plantar erythrodysaesthesia syndrome (PT, AEs), no usable results; the pharmaceutical company does not provide time-to-event analyses.
h Operationalised as SOC gastrointestinal disorders (SOC, severe AEs), with PT diarrhoea as the most common manifestation.
i Operationalised by the pharmaceutical company's predefined compilation of the PTs neutropenia, neutrophil count decreased, febrile neutropenia, each severe AEs
j Operationalised by the pharmaceutical company's predefined compilation of the PTs gait disorder, hypaesthesia, muscular weakness, peripheral neuropathy, paraesthesia, peripheral sensory neuropathy, AEs in each case
k Among others, the PT alopecia as the most frequent manifestation, < 10% for the PTs dry skin and maculopapular rash
l Including fatigue as the most common manifestation

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30; 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.a. = not achieved; PT = preferred term; SOC = system organ class; SAE: serious adverse event; AE: adverse event; vs = versus

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

Adults with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease

approx. 1,150 – 2,370 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 Trodelvy (active ingredient: sacituzumab govitecan) at the following publicly accessible link (last access: 13 April 2022):

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

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

It must be administered in an environment where full resuscitation equipment is immediately available.

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Sacituzumab govitecan	€ 167,239.06
Appropriate comparator therapy:	
Capecitabine monotherapy	
Capecitabine	€ 2,454.96
Vinorelbine monotherapy	
Vinorelbine	€ 7,063.14 - € 8,515.64
Eribulin monotherapy	
Eribulin	€ 39,892.63
Anthracycline or taxane-containing therapy	
Taxanes	
Docetaxel	€ 21,738.69
Nab-paclitaxel	€ 32,594.55
Paclitaxel	
Paclitaxel	€ 16,647.10
Additionally required SHI services	€ 248.46

Designation of the therapy	Annual treatment costs/ patient
Total	€ 16,895.56
Anthracyclines	
Doxorubicin	€ 1,311.35 - € 4,227.96
Doxorubicin, PEG-liposomal (PLD)	€ 42,508.31
Epirubicin	€ 1,929.96 - € 3,747.68

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

Other SHI services:

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	52.1	€ 4,212.00
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
Doxorubicin, PEG-liposomal (PLD)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	13.0	€ 1,053.00
Epirubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	6 - 8	€ 486 - € 648
Paclitaxel	Surcharge for production of a parenteral preparation	€ 81	1	17.4	€ 1,409.40

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	containing cytostatic agents				
nab-paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 19 May 2022.

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

Berlin, 19 May 2022

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

Prof. Hecken