

Resolution
by the Federal Joint Committee
on an amendment to the Pharmaceutical Directive (AM-RL):
Appendix XII – Resolutions on the benefit assessment of pharmaceuticals
with new active ingredients, in accordance with the German Social Code,
Book Five (SGB V), section 35a
Cabazitaxel

from 29 March 2012

In its session on 29 March 2012, the Federal Joint Committee resolved to amend the Pharmaceutical Directive (AM-RL) version published 18 December 2008/22 January 2009 (Federal Gazette, number 49a of 31 March 2009), last amended on 29 March 2012 (Federal Gazette, AT 2 May 2012 B3), as follows:

I.

Appendix XII shall be amended in alphabetical order to include the active ingredient cabazitaxel:

Cabazitaxel

Therapeutic indication:

Jevtana[®] in combination with prednisone or prednisolone is indicated for the treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.

1. Additional benefit of the pharmaceutical over appropriate comparator

a) Patients with hormone-refractory metastatic prostate cancer whose disease has progressed on or after a docetaxel-based chemotherapy regimen and for whom an additional regimen of docetaxel is not advisable.

Appropriate comparator: palliative treatment with dexamethasone, prednisone, prednisolone or methylprednisolone, as well as best supportive care (e.g. appropriate pain therapy).

Best supportive care (BSC) is understood to be the therapy that provides the best possible individual supportive treatment for the patient to relieve symptoms and improve quality of life.

Extent and probability of additional benefit over best supportive care: Indication of a minor additional benefit.

Study results according to endpoints:

	Effect estimates [95% CI] Cabazitaxel + prednisone + BSC vs. mitoxantrone + prednisone + BSC	Result/incident rate Absolute difference (AD)	p-value
Mortality			
Overall survival ¹	HR 0.70 [0.59; 0.83]	Median: 15.1 vs. 12.7 months AD = 2.4 months	<0.001
Morbidity			
Pain ² change in present pain intensity (PPI) score	OR ³ 0.94 [0.70; 1.25]	improved: 21.3 vs. 18.2% unchanged: 46.2 vs. 49.7% worsened: 32.4 vs. 32.1%	0.658
Health-related quality of life			
	No applicable data available in the dossier submitted by the pharmaceutical company ¹		
Side effects			
Neutropenia degree $\geq 3^{1,4}$	RR ⁵ 1.41 [1.28; 1.56]	81.7% vs. 58.0%	<0.001
AE ²	RR ⁵ 1.08 [1.04; 1.13]	95.7% vs. 88.4%	<0.001

	Effect estimates [95%-CI] Cabazitaxel + prednisone + BSC vs. mitoxantrone + prednisone + BSC	Result/incident rate, absolute difference (AD)	p-value
AE of CTCAE degrees 3 to 5 ²	RR ⁵ 1.46 [1.25; 1.70]	57.4% vs. 39.4%	<0.001
SAE ²	RR ⁵ 1.88 [1.49; 2.38]	39.1% vs. 20.8%	<0.001
Termination due to AE ²	RR ⁵ 2.19 [1.47; 3.27]	18.3% vs. 8.4%	<0.001
AE leading to death ^{1,6}	RR ⁵ 2.57 [1.09; 6.08]	4.9% vs. 1.9%	<0.05

Abbreviations used: CTCAE = common terminology criteria for adverse events, HR = hazard ratio, CI = confidence interval, OR = odds ratio, PPI = present pain intensity scale (McGill-Melzack), RR = relative risk, (S)AE = (serious) adverse event

¹ Data from the dossier submitted by the pharmaceutical company

² Data from the benefit assessment conducted by the Institute for Quality and Efficiency in Health Care (IQWiG) A11-24 for cabazitaxel, page 24 f.

³ Logistic regression (IQWiG calculation)

⁴ Severity degree ≥ 3 neutropenia based on laboratory values

⁵ Incident rate (IQWiG calculation/own calculation)

⁶ Not including deaths resulting from progression of disease (reported as AE)

- b) Patients with hormone-refractory metastatic resistant prostate cancer whose disease has progressed after a docetaxel-based chemotherapy regimen, but for whom appropriate chemotherapy with docetaxel may be advisable
Appropriate comparator: docetaxel in combination with prednisone or prednisolone (docetaxel retherapy).

Extent and probability of additional benefit over docetaxel retherapy: as the necessary proof documents for the benefit assessment were not submitted in their entirety, an additional benefit over the appropriate comparator is considered not proved (SGB V, section 35a, paragraph 1, sentence 5).

2. Number of patients and criteria for defining patients eligible for treatment

Target population: approx. 6,300 patients

- a) "Best supportive care" patient group
Proportion of target population: 80 to 90%
Number of patients: 5,040 to 5,670 patients
- b) "Docetaxel retherapy" patient group,
percentage of target population: 10 to 20%
Number of patients: 630 to 1,260 patients

3. Requirements for quality-assured administration

The administration of cabazitaxel should be limited to facilities specialized in the administering cytotoxic substances, and be conducted only by a physician experienced in the use of antineoplastic chemotherapy (Jevtana[®] product information, section 4.2). Special care must be taken in the diagnosis of patients with ECOG (Eastern Cooperative Oncology Group) performance status greater than 1. The specifications outlined in the product information are to be followed.

4. Costs of treatment

- a) "Best supportive care" patient group

Duration of treatment:

Description of therapy	Mode of treatment	Number of treatments per patient per year ¹	Duration per treatment (days)	Number of treatment days per patient per year
Pharmaceutical evaluated				
Cabazitaxel	Every 3 weeks, 1 x 50 mg	17 cycles ¹	1	17
Prednisolone	ongoing, 2 x 5 mg daily	ongoing	365	365
Appropriate comparator				
Prednisolone	ongoing, 1 x 5 mg daily	ongoing	365	365

¹ Standardized calculation for one year

Consumption:

Description of therapy	Strength	Number/amount per pack	Average annual consumption
Pharmaceutical evaluated			
Cabazitaxel	40 mg/ml	1 x 60 mg/1.5 ml	17 packs
Prednisolone	5 mg	100 tablets ¹	730 tablets
Appropriate comparator			
Prednisolone	5 mg	100 tablets ¹	365 tablets

¹ Largest pack

Costs:

Cost of pharmaceutical:

Description of therapy	Cost (pharmacy retail price)	Cost after legally mandated rebates ^{1,2}
Pharmaceutical evaluated		
Cabazitaxel	€5,443.79/pack	€4,738.54 (€2.05 ¹ ; €703.20 ²)
Prednisolone	€14.61 ³ /100 tablets	€12.23 (€2.05 ¹ ; €0.33 ²)
Appropriate comparator		
Prednisolone	€14.61 ³ /100 tablets	€12.23 (€2.05 ¹ ; €0.33 ²)

¹ Rebate in accordance with SGB V, section 130² Rebate in accordance with SGB V, section 130a³ Reference price

"Lauer-Taxe", effective 1 March 2012

Costs for additional, necessary statutory health insurance (SHI) benefits:

Description of therapy	Additional necessary SHI expense items			
	Description	Frequency	Number per patient/year	Cost per unit
Pharmaceutical evaluated				
Cabazitaxel	Premedication antihistamine, i.v.: diphenhydramine, 25 mg	1 x 25 mg per cycle	17 cycles	€0.79
	Premedication corticosteroid, i.v.: dexamethasone, 8 mg	1 x 8 mg per cycle	17 cycles	€1.68
	Premedication H ₂ antagonist, i.v.: ranitidine, 50 mg	1 x 50 mg per cycle	17 cycles	€2.46
	Prophylaxis antiemetic, oral: ondansetron, 8 mg	10 x 8 mg per cycle	17 cycles	€77.94
	Prophylaxis G-CSF ¹ : filgrastim, 41.5 million U	n/a	17 cycles	€182.52 per administration day

¹ Additional SHI expense items necessary only for certain patient groupsAnnual treatment costs¹:

Description of therapy	Annual treatment costs per patient
Pharmaceutical evaluated	€82,053.24
Appropriate comparator	€44.64

¹ Does not include the costs for additional SHI expense items necessary only for certain patient groups

b) "Docetaxel retherapy" patient group

Duration of treatment:

Description of therapy	Mode of treatment	Number of treatments per patient per year ¹	Duration per treatment (days)	Number of treatment days per patient per year
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Pharmaceutical evaluated

Cabazitaxel	Every 3 weeks, 1 x 50 mg	17 cycles ¹	1	17
Prednisolone	ongoing, 2 x 5 mg daily	ongoing	365	365

Appropriate comparator

Docetaxel	Every 3 weeks, 1 x 150 mg	17 cycles ¹	1	17
Prednisolone	ongoing, 2 x 5 mg daily	ongoing	365	365

¹ Standardized calculation for one year

Consumption:

Description of therapy	Strength	Number/amount per pack	Average annual consumption
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Pharmaceutical evaluated

Cabazitaxel	40 mg/ml	1 x 60 mg/1.5 ml	17 packs
Prednisolone	5 mg	100 tablets ¹	730 tablets

Appropriate comparator

Docetaxel	10 mg/ml	1 x 160 mg/16 ml	17 packs
Prednisolone	5 mg	100 tablets ¹	730 tablets

¹ Largest pack

Costs:

Cost of pharmaceutical:

Description of therapy	Cost (pharmacy retail price)	Cost after legally mandated rebates ^{1,2}
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Pharmaceutical evaluated

Cabazitaxel	€5,443.79/pack	€4,738.54 (€2.05 ¹ ; €703.20 ²)
Prednisolone	€14.61 ³ /100 tablets	€12.23 (€2.05 ¹ ; €0.33 ²)

Appropriate comparator

Docetaxel	€1,555.73/1 pack	€1,480.31 (€2.05 ¹ ; €73.37 ²)
Prednisolone	€14.61 ³ /100 tablets	€12.23 (€2.05 ¹ ; €0.33 ²)

¹ Rebate in accordance with SGB V, section 130

² Rebate in accordance with SGB V, section 130a

³ Reference price

"Lauer-Taxe", effective 1 March 2012

Costs for additional, necessary statutory health insurance (SHI) benefits:

None

Annual treatment costs:

Description of therapy	Annual treatment costs per patient
Pharmaceutical evaluated	€80,644.46
Appropriate comparator	€25,254.55

II.

This resolution takes effect on the day of its publication in the internet on the website of the Federal Joint Committee on 29 March 2012.

The justification for this resolution will be published on the website of the Federal Joint Committee at www.g-ba.de.

Berlin, 29 March 2012

The Federal Joint Committee in
accordance with SGB V, section 91

The Chair
Hess