Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Nivolumab (new therapeutic indication: renal cell carcinoma, in combination with ipilimumab, first-line treatment)

of 15 August 2019

At its session on 15 August 2019, the Federal Joint Committee (G-BA) resolved to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (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 on DD 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 nivolumab in accordance with the resolution of 21 February 2019:

Nivolumab

Resolution of: 15 August 2019
Entry into force on: 15 August 2019
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 11 January 2019):

OPDIVO in combination with ipilimumab is indicated for first-line treatment of adult patients with intermediate/poor-risk advanced renal cell carcinoma (see Section 5.1).

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

a) Adult patients with untreated advanced renal cell carcinoma with an intermediate risk profile (IMDC score 1–2)

Appropriate comparator therapy:

- Bevacizumab in combination with interferon alfa-2a

  or
- Monotherapy with pazopanib

  or
- Monotherapy with sunitinib

Extent and probability of the additional benefit of nivolumab in combination with ipilimumab compared with sunitinib:

Indication of a considerable additional benefit

b) Adult patients with untreated advanced renal cell carcinoma with a poor risk profile (IMDC score ≥ 3)

Appropriate comparator therapy:

- Sunitinib

  or
- Temsirolimus

Extent and probability of the additional benefit of nivolumab in combination with ipilimumab compared with sunitinib:

Indication of a considerable additional benefit

Study results according to endpoints[1]:

CheckMate 214 study: Nivolumab + ipilimumab vs sunitinib (2nd data cut-off of 6 August 2018)

a) Adult patients with untreated advanced renal cell carcinoma with an intermediate risk profile (IMDC score 1–2)

Mortality

Endpoint	**Nivolumab + ipilimumab**		**Sunitinib**		Nivolumab + ipilimumab vs Sunitinib
	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 (%)*	Hazard Ratio [95% CI] p value[a] Absolute difference (AD)[b]
Overall survival					
	334	n.a. [n.a.; n.a.] *124 (37.1)*	333	34.83 [28.62; n.c.] *159 (47.7)*	0.70 [0.55; 0.88] 0.003 AD: n.c.

Morbidity

Progression-free survival (PFS)[c]					
	334	8.18[d] [6.93; 9.76] *239 (71.6)*	333	8.41[d] [8.02; 9.66] *272 (81.7)*	0.816 [0.685; 0.972] 0.0217 AD: 0.23 months

Endpoint	**Nivolumab + ipilimumab**			**Sunitinib**			Nivolumab + ipilimumab vs Sunitinib
	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	MD [95% CI] p value[f]
Symptomatology							
FKSI-DRS[g]	312	31.52 (3.93)	2.53 (1.06)	304	31.20 (4.41)	1.50 (1.06)	1.03 [0.58; 1.47] < 0.001

(Continuation)

[1] Data from the dossier evaluation of the IQWiG (A19-11) and from the addendum (A19-54) unless otherwise indicated.

							Hedges' g: *0.36* *[0.203; 0.52]*
Health status							
EQ-5D VAS[g]	304	72.70 (24.57)	5.82 (6.59)	301	73.29 (25.49)	1.77 (6.58)	4.06 [1.53; 6.58] 0.002 *Hedges' g:* *0.36* *[0.10; 0.42]*

Endpoint	**Nivolumab + ipilimumab**		**Sunitinib**		Nivolumab + ipilimumab vs Sunitinib
	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 (%)*	Hazard Ratio [95% CI] p value[h] Absolute difference (AD)[b]
Health status (time until confirmed deterioration)[i]					
EQ-5D-VAS MID ≥ 7 mm	334	28.58 [26.32; n.a.] *120 (35.9)*	333	25.59 [20.96; 27.83] *132 (39.6)*	0.78 [0.61; 1.01] 0.057
EQ-5D-VAS MID ≥ 10 mm	334	29.96 [26.51; n.a.] *116 (34.7)*	333	26.25 [23.95; 28.03] *126 (37.8)*	0.80 [0.62; 1.03] 0.086

Health-related quality of life

Endpoint	**Nivolumab + ipilimumab**			**Sunitinib**			Nivolumab + ipilimumab vs Sunitinib
	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	MD [95% CI] p value[f]
FACT-G total score[g]							
	309	84.50 (13.73)	5.43 (3.00)	303	82.98 (15.07)	1.78 (3.00)	3.64 [2.05; 5.24]; < 0.001

(Continuation)

							Hedges' g: *0.36* *[0.201; 0.52]*
FACT-G sub-scales[g] (presented additionally)							
Physical well-being	312	24.33 (3.97)	1.80 (1.14)	306	24.29 (4.27)	−0.24 (1.14)	2.03 [1.53; 2.54]
Emotional well-being	311	17.67 (4.29)	1.84 (0.91)	306	16.93 (4.76)	1.49 (0.90)	0.35 [−0.07; 0.78]
Functional well-being	312	19.70 (5.90)	1.95 (1.27)	306	19.50 (6.04)	0.96 (1.27)	0.99 [0.34; 1.65]
Social well-being	312	22.77 (5.58)	0.56 (1.07)	307	22.32 (5.32)	0.12 (1.07)	0.43 [−0.12; 0.99]

Side effects

Endpoint	**Nivolumab + ipilimumab**		**Sunitinib**		Nivolumab + ipilimumab vs sunitinib
	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 (%)*	Hazard Ratio [95% CI] p value[a] Absolute difference (AD)[b]
Adverse events (presented additionally)[j]					
	333	0.26 [0.23; 0.33] *329 (98.8)*	329	0.26 [0.20; 0.30] *325 (98.8)*	-
Serious adverse events (SAE)[j]					
	333	9.13 [5.88; 12.29] *192 (57.7)*	329	20.83 [14.95; 31.01] *145 (44.1)*	1.38 [1.11; 1.71] 0.004 AD: 11.7 months
Severe adverse events (CTCAE grade 3–4)[j]					
	333	4.21 [3.06; 5.32] *244 (73.3)*	329	2.14 [1.91; 2.86] *260 (79.0)*	0.66 [0.55; 0.79] < 0.001 AD: 2.07 months
Therapy discontinuation because of adverse events[k]					
	333	n.a. [37.82; n.c.] *95 (28.5)*	329	n.a. [n.a.; n.a.] *61 (18.5)*	1.51 [1.09; 2.09] 0.012 AD: n.c.

(Continuation)

Immune-mediated adverse events					
No usable data					
Specific adverse events					
Gastrointestinal disorders (SOC, AE)	333	no data available *238 (71.5)*	329	no data available *287 (87.2)*	0.46 [0.39; 0.55] no data available
Pruritus (PT, AE)	333	no data available *126 (37.8)*	329	no data available *38 (11.6)*	3.85 [2.68; 5.54] no data available
Rash (PT, AE)[l]	333	no data available *88 (26.4)*	329	no data available *57 (17.3)*	1.57 [1.12; 2.20] no data available
Hand-foot syndrome (PT, severe AE [CTCAE Grade 3–4])	333	no data available *1 (0.3)*	329	no data available *25 (7.6)*	0.04 [0.01; 0.28] no data available
Myalgia (PT, AE)	333	no data available *51 (15.3)*	329	no data available *23 (7.0)*	2.27 [1.39; 3.72] no data available
Epistaxis (PT, AE)	333	no data available *5 (1.5)*	329	no data available *46 (14.0)*	0.09 [0.03; 0.22] no data available
Reduced appetite (PT, AE)	333	no data available *66 (19.8)*	329	no data available *95 (28.9)*	0.62 [0.45; 0.85] no data available
Taste disorder (PT, AE)	333	no data available *22 (6.6)*	329	no data available *109 (33.1)*	0.16 [0.10; 0.25] no data available
Endocrine disorders (SOC, severe AE [CTCAE-Grade 3–4])	333	no data available *22 (6.6)*	329	no data available *1 (0.3)*	2.6 [3.05; > 99.99] no data available
Hypertension (PT, severe AE [CTCAE-Grade 3–4])	333	no data available *9 (2.7)*	329	no data available *58 (17.6)*	0.13 [0.07; 0.27] no data available
Blood and lymphatic system disorders (SOC, severe AE [CTCAE-Grade 3–4])	333	no data available *14 (4.2)*	329	no data available *44 (13.4)*	0.30 [0.17; 0.55] no data available

a Hazard ratio and CI: Cox Proportional Hazards Model, p value: Log rank test; stratified according to IMDC score (1 to 2, 3 to 6) and region (US, Canada/Western Europe/Northern Europe, Rest of World) in accordance with IVRS
b Absolute difference given only in the case of a statistically significant difference; own calculation
c Information from the dossier of the pharmaceutical company in accordance with investigator. No confirmation of the radiological findings by the IRRC was made for this data cut-off.
d Median survival time according to Kaplan-Meier. The 2-sided 95% CI was calculated using a log-log transformation (according to Brookmeyer and Crowley).
e Number of patients included in the evaluation to calculate the effect estimate; values at the start of study may be based on other patient numbers.
f MV and SE (change per treatment group) as well as MD, CI, and p value (group comparison): MMRM
g A positive change compared with the start of study means an improvement.
h HR and CI: Cox Proportional Hazards Model, p value: Log rank test; stratified according to IMDC score (1 to 2, 3 to 6) and region (US, Canada/Western Europe/Northern Europe, Rest of World) in accordance with IVRS and adjusted for value to baseline
i Confirmed deterioration is considered if the values remain deteriorated by at least 7 or 10 points or if no data is available after deterioration. Patients whose values improve again into the non-clinically relevant range are censored. The analysis includes all the time points collected, including the follow-up time points.
j 100 days of follow-up without recording the progress of the underlying disease
k 30 days of follow-up without recording the progress of the underlying disease
l The PT maculopapular rash (AE) shows a significant difference between treatment groups to the detriment of nivolumab + ipilimumab.

Abbreviations used:
CI: confidence interval; CTCAE: Common Terminology Criteria for Adverse Events; EQ-5D: European Quality of Life Questionnaire – 5 Dimensions; FACT-G: Functional Assessment of Cancer Therapy – General; FKSI-DRS: Functional Assessment of Cancer Therapy – Kidney Symptom Index – Disease related Symptoms; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; IRRC: Independent Radiology Review Committee; IVRS: Information from the speech dialogue system; MD: mean difference; MMRM: mixed model with repeated measurements; MV: mean value; 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; RR: relative risk; SOC: system organ class; SD: standard deviation; SE: Standard error; VAS: visual analogue scale; vs: versus

b) Adult patients with untreated advanced renal cell carcinoma with a poor risk profile (IMDC score ≥ 3)

Mortality

Endpoint	**Nivolumab + ipilimumab**		**Sunitinib**		Nivolumab + ipilimumab vs Sunitinib
	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 (%)*	Hazard Ratio [95% CI] p value[a] Absolute difference (AD)[b]
Overall survival					
	91	21.45 [15.08; 27.33] *58 (63.7)*	89	9.72 [6.24; 14.32] *68 (76.4)*	0.58 [0.41; 0.83]; 0.003 AD: 11.73 months

Morbidity

Progression-free survival (PFS)[c]					
	91	6.26[d] [3.12; 10.74] *73 (80.2)*	89	4.27[d] [2.89; 5.72] *84 (94.4)*	0.599 [0.433; 0.829] 0.0018 AD: 1.99 months

Endpoint	**Nivolumab + ipilimumab**			**Sunitinib**			Nivolumab + ipilimumab vs Sunitinib
	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	MD [95% CI] p value[f]
Symptomatology							
FKSI-DRS[g]	80	27.80 (5.19)	3.52 (1.36)	76	26.72 (5.79)	2.70 (1.37)	0.82 [−0.30; 1.94]; 0.149
Health status							
EQ-5D VAS[g]	78	63.38 (24.43)	15.02 (7.32)	74	58.98 (25.96)	13.71 (7.35)	1.31 [−3.58; 6.20]; 0.598

(Continuation)

Endpoint	Nivolumab + ipilimumab		Sunitinib		Nivolumab + ipilimumab vs Sunitinib
	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 (%)*	Hazard Ratio [95% CI] p value[h] Absolute difference (AD)[b]
Health status (time until confirmed deterioration)[i]					
EQ-5D-VAS MID ≥ 7 mm	91	26.32 [21.42; n.a.] *29 (31.9)*	89	21.91 [15.05; n.a.] *23 (25.8)*	0.64 [0.36; 1.13] 0.122
EQ-5D-VAS MID ≥ 10 mm	91	26.32 [21.42; n.a.] *29 (31.9)*	89	21.91 [15.05; n.a.] *22 (24.7)*	0.67 [0.38; 1.21] 0.184

Health-related quality of life

Endpoint	Nivolumab + ipilimumab			Sunitinib			Nivolumab + ipilimumab vs Sunitinib
	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	N[e]	Values at start of study MV (SD)	Mean change in the course of study MV[f] (SE)	MD [95% CI] p value[f]
FACT-G total score[g]							
	80	76.15 (17.37)	6.53 (3.57)	77	72.67 (15.96)	4.54 (3.59)	2.00 [−1.74; 5.73]; 0.293
FACT-G sub-scales[g] **(presented additionally)**							
Physical well-being	80	20.68 (5.55)	2.96 (1.42)	77	20.44 (5.39)	0.72 (1.42)	2.24 [0.99; 3.49]
Emotional well-being	80	17.23 (4.58)	1.08 (1.11)	77	16.06 (4.65)	0.98 (1.12)	0.10 [−0.85; 1.05]
Functional well-being	80	15.52 (7.31)	2.84 (1.51)	77	14.00 (7.03)	2.07 (1.52)	0.77 [−0.70; 2.25]
Social well-being	80	22.71 (3.97)	1.08 (1.28)	77	22.16 (5.26)	1.90 (1.28)	−0.82 [−1.90; 0.26]

(Continuation)

Side effects

Endpoint	Nivolumab + ipilimumab		Sunitinib		Nivolumab + ipilimumab vs Sunitinib
	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 (%)*	Hazard Ratio [95% CI] p value[a] Absolute difference (AD)[b]
Adverse events (presented additionally)[j]					
	90	0.26 [0.16; 0.39] *90 (100.0)*	87	0.23 [0.16; 0.30] *86 (98.9)*	-
Serious adverse events (SAE)[j]					
	90	4.53 [2.92; 6.60] *60 (66.7)*	87	4.24 [2.60; 6.28] *57 (65.5)*	0.89 [0.62; 1.29] 0.551
Severe adverse events (CTCAE grade 3–4)[j]					
	90	2.76 [1.58; 4.86] *71 (78.9)*	87	1.35 [0.85; 2.10] *76 (87.4)*	0.57 [0.41; 0.81] 0.001 AD: 1.41 months
Therapy discontinuation because of adverse events[k]					
	90	n.a. *23 (25.6)*	87	19.71 [15.21; n.c.] *25 (28.7)*	0.73 [0.41; 1.29] 0.272
Immune-mediated adverse events					
No usable data					
Specific adverse events					
Stomatitis (PT, AE)	90	no data available *2 (2.2)*	87	no data available *15 (17.2)*	0.12 [0,03; 0,51] no data available
Fever (PT, AE)	90	no data available *26 (28.9)*	87	no data available *9 (10.3)*	2.71 [1.26; 5.80] no data available
Mucositis (PT, AE)	90	no data available *1 (1.1)*	87	no data available *25 (28.7)*	0.03 [0.00; 0.21] no data available
Epistaxis (PT, AE)	90	no data available *1 (1.1)*	87	no data available *9 (10.3)*	0.09 [0.01; 0.74] no data available

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Pruritus (PT, AE)	90	no data available *22 (24.4)*	87	no data available *7 (8.0)*	2.94 [1.25; 6.95] no data available
Hand-foot syndrome (PT, severe AE [CTCAE Grade 3–4])	90	no data available *0 (0)*	87	no data available *7 (8.0)*	RR: -[l] 0.007[m]
Taste disorder (PT, AE)	90	no data available *7 (7.8)*	87	no data available *24 (27.6)*	0.22 [0.09; 0.51] no data available
Respiratory, thoracic, and mediastinal disorders (SOC, SAE)	90	no data available *8 (8.9)*	87	no data available *17 (19.5)*	0.34 [0.15; 0.82] no data available
Hypothyroidism (PT, AE)	90	no data available *5 (5.6)*	87	no data available *16 (18.4)*	0.23 [0.08; 0.63] no data available
Gastrointestinal disorders (SOC, severe AE [CTCAE Grade 3–4])	90	no data available *7 (7.8)*	87	no data available *17 (19.5)*	0.38 [0.16; 0.92] no data available
Thrombocyto-penia (PT, severe AE [CTCAE-Grade 3–4])	90	no data available *0 (0)*	87	no data available *7 (8.0)*	RR: –[l] 0.007[m]
Hypertension (PT, severe AE [CTCAE-Grade 3–4])	90	no data available *4 (4.4)*	87	no data available *11 (12.6)*	0.20 [0.05; 0.71] no data available

a Hazard ratio and CI: Cox Proportional Hazards Model, p value: Log rank test; stratified according to IMDC score (1 to 2, 3 to 6) and region (US, Canada/Western Europe/Northern Europe, Rest of World) in accordance with IVRS
b Absolute difference given only in the case of a statistically significant difference; own calculation
c Information from the dossier of the pharmaceutical company in accordance with investigator. No confirmation of the radiological findings by the IRRC was made for this data cut-off.
d Median survival time according to Kaplan-Meier. The 2-sided 95% CI was calculated using a log-log transformation (according to Brookmeyer and Crowley).
e Number of patients included in the evaluation to calculate the effect estimate; values at the start of study may be based on other patient numbers.
f MV and SE (change per treatment group) as well as MD, CI, and p value (group comparison): MMRM
g A positive change compared with the start of study means an improvement.
h HR and CI: Cox Proportional Hazards Model, p value: Log rank test; stratified according to IMDC score (1 to 2, 3 to 6) and region (US, Canada/Western Europe/Northern Europe, Rest of World) in accordance with IVRS and adjusted for value to baseline
i Confirmed deterioration is considered if the values remain deteriorated by at least 7 or 10 points or if no data is available after deterioration. Patients whose values improve again into the non-clinically relevant range are censored. The analysis includes all the time points collected, including the follow-up time points.
j 100 days of follow-up without recording the progress of the underlying disease
k 30 days of follow-up without recording the progress of the underlying disease

(Continuation)

l No representation of effect estimation and CI because not informative
m In the case of 0 events, the HR was not calculable; the RR, CI (asymptotic) and p value (unconditional exact test, CSZ method according to Andrés and Mato, 1994) were used; in the calculation, the correction factor 0.5 was used in both study arms.

Abbreviations used:
CI: confidence interval; CTCAE: Common Terminology Criteria for Adverse Events; EQ-5D: European Quality of Life Questionnaire – 5 Dimensions; FACT-G: Functional Assessment of Cancer Therapy – General; FKSI-DRS: Functional Assessment of Cancer Therapy – Kidney Symptom Index – Disease related Symptoms; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; IRRC: Independent Radiology Review Committee; IVRS: Information from the speech dialogue system; MD: mean difference; MMRM: mixed model with repeated measurements; MV: mean value; 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; RR: relative risk; SOC: system organ class; SD: standard deviation; SE: Standard error; VAS: visual analogue scale; vs: versus

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

a) Adult patients with untreated advanced renal cell carcinoma with an intermediate risk profile (IMDC score 1–2)

approx. 1,760–1,790 patients

b) Adult patients with untreated advanced renal cell carcinoma with a poor risk profile (IMDC score ≥ 3)

approx. 350–1,060 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 OPDIVO® (active ingredient: nivolumab) at the following publicly accessible link (last access: 25 June 2019):

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

Only specialists in internal medicine, haematology, and oncology with experience treating patients with advanced renal cell carcinoma, specialists in internal medicine and nephrology, and doctors from other specialisms participating in the oncology agreement may initiate and monitor treatment with nivolumab in combination with ipilimumab.

In accordance with the specifications of the EMA regarding additional measures for risk minimisation, the pharmaceutical company must provide training material for doctors as well as a patient card. The training and information material shall include, in particular, instructions on how to deal with the immune-mediated adverse reactions potentially occurring with nivolumab. Patients treated with nivolumab must be informed about the risks of treatment with nivolumab.

The CheckMate 214 (CA209-214) study exclusively investigated patients with renal cell carcinoma with clear cell histology. No data are available for patients with non-clear-cell renal cell carcinoma.

4. Treatment costs

Annual treatment costs:

a) Adult patients with untreated advanced renal cell carcinoma with an intermediate risk profile (IMDC score 1–2)

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Nivolumab in combination with ipilimumab	
Initial treatment	
Nivolumab	€ 11,719.92
Ipilimumab	€ 28,762.32
Total	€ 40,482.24
Follow-up treatment	
Nivolumab	€ 58,599.60
Initial treatment + total follow-up treatment	€ 99,081.84
Appropriate comparator therapy:	
Bevacizumab in combination with interferon alfa-2a	
Bevacizumab	€ 82,929.60
Interferon alfa-2a	€ 15,468.70
Total	€ 98,398.30
Monotherapies	
Pazopanib	€ 54,402.40
Sunitinib	€ 50,799.62

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2019)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/patient/ year
Medicinal product to be assessed:					
Nivolumab in combination with ipilimumab					
Nivolumab (follow-up treatment with nivolumab in 14-day cycle)	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	24	€ 1,704

(Continuation)

Nivolumab (follow-up treatment with nivolumab in 28-day cycle)	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	14	€ 994
Ipilimumab	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	4	€ 284
Total					€ 1,278 – € 1,988
Appropriate comparator therapy:					
Bevacizumab	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	26	€ 1,846

b) Adult patients with untreated advanced renal cell carcinoma with a poor risk profile (IMDC score ≥ 3)

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Nivolumab in combination with ipilimumab	
Initial treatment	
Nivolumab	€ 11,719.92
Ipilimumab	€ 28,762.32
Total	€ 40,482.24
Follow-up treatment	
Nivolumab	€ 58,599.60
Initial treatment + total follow-up treatment	€ 99,081.84
Appropriate comparator therapy:	
Sunitinib	€ 50,799.62
Temsirolimus	€ 58,039.80

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2019)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/patient/ year
Medicinal product to be assessed:					
Nivolumab in combination with ipilimumab					
Nivolumab (follow-up treatment with nivolumab in 14-day cycle)	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	24	€ 1,704
Nivolumab (follow-up treatment with nivolumab in 28-day cycle)	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	14	€ 994
Ipilimumab	Surcharge for the preparation of parenteral solutions with monoclonal antibodies	€ 71	1	4	€ 284
Total					€ 1,278 – € 1,988
Appropriate comparator therapy:					
Temsirolimus	Surcharge for the preparation of parenteral preparations containing cytostatic agents	€ 81	1	52	€ 4,212

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 15 August 2019.

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

Berlin, 15 August 2019

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

Prof Hecken