Gemeinsamer Bundesausschuss

Resolution

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
Selumetinib (neurofibromatosis (≥ 3 to < 18 years, type 1))

of 3 February 2022

At its session on 3 February 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 on DD. 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 Selumetinib as follows:

Selumetinib

Resolution of: 3 February 2022
Entry into force on: 3 February 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 17 June 2021):

Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and above.

Therapeutic indication of the resolution (resolution of 3 February 2022):

see therapeutic indication according to marketing authorisation

1. Extent of the additional benefit and significance of the evidence

Selumetinib is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The Federal Joint Committee (G-BA) determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5, Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 AM-NutzenV, indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5, Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Paediatric patients aged 3 years and above with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Extent of the additional benefit and significance of the evidence of Selumetinib:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Paediatric patients aged 3 years and above with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	No data available in comparison with the control group.
Morbidity	↑	No data available in comparison with the control group. Advantage in the endpoint "change in tumour volume".
Health-related quality of life	n.a.	No data available in comparison with the control group.
Side effects	n.a.	No data available in comparison with the control group.
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		

SPRINT study: ongoing, open-label, single-arm phase I/II study

Data cut-offs used:

Data cut-off 1: 29 June 2018 (morbidity, quality of life, side effects)

Data cut-off 2: 29 March 2019 (overall survival)

Mortality

No deaths occurred in the study.

Morbidity

Endpoint	Selumetinib	
	N	Patients with event n (%) [95% CI]
Objective response rate (presented additionally)[a]		
NCI POB	50	33 (66)[b] [51.2; 78.8][c]
ICR	50	22 (44)[b] [30.0; 58.7][c]

[1] Data from the dossier assessment of the G-BA (published on the 15. November 2021), unless otherwise indicated.

Endpoint	Selumetinib	
	N	Median time to event in months [95% CI] Patients with event[d] n (%)
Progression-free survival (PFS) (presented additionally)[e]		
NCI POB	50	n.c [n.c.; n.c] 3 (6)
ICR	50	n.c [n.c.; n.c] 11 (22.0)

Endpoint	Selumetinib	
	N	Mean ± standard deviation Median Min – max
Change in tumour volume (best percentage volume reduction achieved)[f]		
Baseline	50	837.11 ± 925.011 487.50 5.6–3820.0
NCI POB	48	-25.28 ± 12.330 -27.85 -54.5 – 2.2
ICR	48	-23.41 ± 13.348 -22.05 -53.7 – 9.5

Endpoint	Selumetinib							
	Before cycle 3		Before cycle 5		Before cycle 9		Before cycle 13	
	N	n (%[g])	N	n (%[g])	N	n (%[g])	N	n (%[g])
Global assessment of clinical change by GIC, age 8 - 18 years								
Tumour pain Improvement [h] Deterioration [i]	26	12 (46.2) n.d.	30	14 (46.7) n.d.	30	16 (53.3) n.d.	29	15 (51.7) n.d.
Total pain Improvement [h] Deterioration [i]	30	9 (30.0) n.d.	30	12 (40.0) n.d.	30	10 (33.3) n.d.	29	12 (41.4) n.d.
Tumour-associated morbidity Improvement [h]	23	-[j] -[j]	29	14 (48.3) n.d.	30	13 (43.3) n.d.	29	17 (58.6) n.d.

Endpoint	Selumetinib							
	Before cycle 3		Before cycle 5		Before cycle 9		Before cycle 13	
	N	n (%[g])	N	n (%[g])	N	n (%[g])	N	n (%[g])
Deterioration [i]								
Global assessment of clinical change by GIC, age 3 - 7 years[k]								
Tumour pain Improvement [h)] Deterioration [i)]	12	1 (8.3) n.d.	13	4 (30.8) n.d.	14	5 (35.7) n.d.	13	6 (46.2) n.d.
Total pain Improvement [h)] Deterioration [i)]	14	2 (14.3) n.d.	13	4 (30.8) n.d.	14	4 (28.6) n.d.	13	5 (38.5) n.d.
Tumour-associated morbidity Improvement [h)] Deterioration [i)]	11	2 (18.2) n.d.	13	3 (23.1) n.d.	14	9 (64.3) n.d.	13	9 (69.2) n.d.

Endpoint	Selumetinib	
	N	n (% [95% CI][l])
Worst possible, patient-specified pain PN (NRS-11)[m]		
Baseline MV (SD) Median (min; max)	33	 3.4 (3.2) 3.0 (0.0; 10.0)
Before cycle 3 Improvement by ≥ 2 points[n] Deterioration by ≥ 2 points[o]	31	 13 (41.9 [24.5; 60.9]) 1 (3.2 [0.1; 16.7])
Before cycle 5 Improvement by ≥ 2 points[n] Deterioration by ≥ 2 points[o]	31	 20 (64.5 [45.4; 80.8]) 2 (6.5 [0.8; 21.4])
Before cycle 9 Improvement by ≥ 2 points[n] Deterioration by ≥ 2 points[o]	31	 18 (58.1 [39.1; 75.5]) 0 (0 [0; 11.2])
Before cycle 13 Improvement by ≥ 2 points[n] Deterioration by ≥ 2 points[o]	29	 17 (58.6 [38.9; 76.5]) 0 (0 [0; 11.9])

Endpoint	N	Selumetinib		
		Time [seconds] Median (min; max)	Z-score for time[p] Median (min; max)	Dropped pegs Median (min; max)
Grooved Pegboard Test (presented additionally)				
All participants - dominant hand				
Baseline	25	86.1 (41.0; 164.7)	1.1 (-1.0; 12.4)	1 (0; 6)
Change from baseline				
Before cycle 5	24	1.9 (-96.7; 63.0)	0.06 (-10.7; 4.3)	0 (-4; 11)
Before cycle 9	23	-10.1 (-117.0; 350.4)	-0.54 (-13.0; 33.7)	0 (-4; 11)
Before cycle 13	22	-2.46 (-61.3; 202.4)	-0.35 (-12.2; 19.5)	0 (-3; 6)
All participants - non-dominant hand, N = 25				
Baseline	24	100.1 (46.0; 505.9)	2.2 (-0.9; 39.2)	1 (0; 18)
Change from baseline				
Before cycle 5	23	-7.0 (-217.6; 152.4)	-0.35 (-18.6; 4.5)	-1 (-16; 1)
Before cycle 9	23	-13.2 (-178.4; 92.2)	-1.19 (-9.4; 5.7)	0 (-17; 4)
Before cycle 13	21	-11.7 (-121.9; 134.8)	-0.62 (-11.0; 10.1)	0 (-16; 5)
Participants with unilateral PN – impaired hand; N = 17				
Baseline	16	88.8 (41.0; 505.9)	1.46 (-0.9; 39.2)	1.5 (0; 18)
Change from baseline				
Before cycle 5	16	-6.3 (-205.9; 152.4)	-0.38 (-18.6; 4.5)	-0.5 (-16; 7)
Before cycle 9	15	-1.0 (-102.0; 63.1)	-0.54 (-3.7; 5.7)	-1 (-17; 3)
Before cycle 13	15	-2.7 (-121.9; 70.4)	-0.50 (-11.0; 0.6)	-1 (-16; 2)
Participants with unilateral PN – unimpaired hand; N = 17				
Baseline	17	92.5 (41.0; 300.0)	1.78 (-1.0; 12.4)	1 (0; 8)
Change from baseline				
Before cycle 5	17	-0.01 (-217.6; 63.0)	-0.10 (-10.9; 4.3)	0 (-7; 3)
Before cycle 9	17	-22.8 (-178.4; 350.4)	-1.23 (-13.0; 33.7)	0 (-7; 11)
Before cycle 13	16	-3.6 (-111.0; 202.4)	-0.47 (-12.2; 19.5)	0 (-3; 6)

Endpoint	N	Selumetinib		
		Time [seconds] Median (min; max)	Z-score for time[p] Median (min; max)	Dropped pegs Median (min; max)
Participants with bilateral PN – dominant hand; N = 8				
Baseline	8	88.9 (51.0; 137.0)	1.93 (-0.1; 6.8)	0 (0; 1)
Change from baseline				
Before cycle 5	7	-14.0 (-36.0; 3.0)	-0.57 (-3.5; 0.3)	0 (-1; 1)
Before cycle 9	7	-12.0 (-33.8; 84.0)	-0.55 (-3.3; 3.4)	0 (-1; 1)
Before cycle 13	6	-18.6 (-43.1; 84.0)	-1.28 (-4.1; 11.3)	0 (-1; 0)
Participants with bilateral PN – non-dominant hand; N = 8				
Baseline	8	94.2 (46.0; 209.8)	2.14 (-0.2; 6.2)	0 (0; 4)
Change from baseline				
Before cycle 5	7	-2.0 (-55.7; 26.0)	-0.18 (-2.2; 1.2)	0 (-2; 1)
Before cycle 9	7	4.9 (-98.9; 92.2)	0.44 (-3.2; 4.2)	0 (-1; 3)
Before cycle 13	6	5.67 (-12.9; 134.8)	0.92 (-1.2; 10.1)	1 (-1; 5)

Endpoint	PROMIS patient-reported Mobility[q] N = 24		PROMIS patient-reported Upper extremities[q] N = 24	
	N	LSM [95% CI]; p value	N	LSM [95% CI]; p value
PROMIS				
Baseline MV (SD)	23	46.57 (6.54)	22	45.95 (12.91)
Change from baseline				
Before cycle 3	21	0.69 [-2.44; 3.82], 0.65	21	0.34 [-2.64; 3.32], 0.81
Before cycle 5	22	1.83 [-0.69; 4.35], 0.15	21	-0.09 [-2.10; 1.92], 0.93
Before cycle 9	22	1.01 [-2.06; 4.08], 0.50	21	-1.40 [-4.82; 2.03], 0.40
Before cycle 13	20	1.75 [-0.70; 4.19], 0.15	19	1.76 [-0.88; 4.39], 0.18

Endpoint	**Eye affected by PN HOTV (logMAR) N = 10**		**Eye not affected by PN HOTV (logMAR) N = 10**	
	N	**Patients with event n (%)[r]**	**N**	**Patients with event n (%)[r]**
Visual acuity				
Baseline MV (SD) [logMAR]	5	0.54 (0.38)	7	0.01 (0.11)
Before cycle 13 Improvement by ≥ 0.2 logMAR Deterioration by ≥ 0.2 logMAR	4	0 (0) 2 (50)	6	0 (0) 1 (16.7)
Before cycle 25 Improvement by ≥ 0.2 logMAR Deterioration by ≥ 0.2 logMAR	4	0 (0) 1 (25)	6	0 (0) 1 (16.7)

Endpoint	**Selumetinib**	
	N	Patients with event n (%) [95% CI]
Exophthalmos[st] (presented additionally)[u]		
Right eye	7	1(14.3) [0.4; 57.9]
Left eye	7	2 (28.6) [3.7; 71.0]
Side affected by PN	7	2 (28.6) [3.7; 71.0]
Side not affected by PN	7	1(14.3) [0.4; 57.9]

Endpoint	**Selumetinib**	
	N	Patients with event n (%)
Symptom checklist		
Tiredness/ fatigue Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	17 (38.6) 13 (29.5)

Endpoint	Selumetinib	
	N	Patients with event n (%)
Sleep disorders Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 17 (38.6) 6 (13.6)
Reduced appetite Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 10 (22.7) 6 (13.6)
Increased appetite Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 10 (22.7) 10 (22.7)
Headaches Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 16 (36.4) 6 (13.6)
Visual disorders Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 5 (11.4) 1 (2.3)
Impaired hearing Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 3 (6.8) 4 (9.1)
Sores in the mouth Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 5 (11.4) 6 (13.6)
Difficulty swallowing Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 5 (11.4) 1 (2.3)
Choking Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 6 (13.6) 0
Snoring Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 15 (34.1) 3 (6.8)
Waking up frequently at night Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 17 (38.6) 7 (15.9)
Cough Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 17 (38.6) 8 (18.2)
Wheezing Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 5 (11.4) 1 (2.3)

Endpoint	Selumetinib	
	N	Patients with event n (%)
Breathing difficulties Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 3 (6.8) 1 (2.3)
Chest pain Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 1 (2.3) 3 (6.8)
Palpitation/ cardiac flutter Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 3 (6.8) 2 (4.5)
Shortness of breath on exertion Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 9 (20.5) 3 (6.8)
Shortness of breath at rest Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 2 (4.5) 0
Swelling of the feet/hands Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 0 6 (13.6)
Abdominal pain Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 10 (22.7) 10 (22.7)
Heartburn Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 2 (4.5) 2 (4.5)
Nausea Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 8 (18.2) 10 (22.7)
Vomiting Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 3 (6.8) 5 (11.4)
Diarrhoea Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 5 (11.4) 10 (22.7)
Constipation Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 5 (11.4) 6 (13.6)
Faecal incontinence Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 4 (9.1) 3 (6.8)

Endpoint	Selumetinib	
	N	Patients with event n (%)
Pain when urinating Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 4 (9.1) 3 (6.8)
Increased urinary frequency / increased urge to urinate Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 6 (13.6) 2 (4.5)
Urinary hesitancy Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 3 (6.8) 2 (4.5)
Urinary incontinence Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 6 (13.6) 2 (4.5)
Weakness Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 15 (34.1) 2 (4.5)
Muscle pain Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 16 (36.4) 4 (9.1)
Dizziness Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 4 (9.1) 5 (11.4)
Numbness Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 3 (6.8) 0
Tingling Improvement[v] for visit before cycle 13 Deterioration[w] for visit before cycle 13	44	 6 (13.6) 0

Health-related quality of life

Endpoint	Selumetinib	
	N	Effect estimator
Changes in PedsQL total value[x], age 8 - 18 years		
Baseline MV (SD) Median (min; max)	33	73.9 (20.7) 81.8 (13.0; 96.7)
Change from baseline		LSM [95% CI]; p value
Before cycle 3	31	6.55 [2.81; 10.28]; 0.001
Before cycle 5	31	4.68 [0.34; 9.02], 0.04
Before cycle 9	31	5.29 [0.74; 9.84], 0.02
Before cycle 13	29	6.68 [1.34; 12.03], 0.02
Changes in PedsQL total value, age 3 - 7 years[z]		
Baseline MV (SD) Median (min; max)	n.d.	n.d.
Change from baseline		LSM [95% CI]; p value
Before cycle 3	16	5 (31.3 [11.0; 58.7]), n.d.
Before cycle 5	15	4 (26.7 [7.8; 55.1]), n.d.
Before cycle 9	16	7 (43.8 [19.8; 70.1]), n.d.
Before cycle 13	15	8 (53.3 [26.6; 78.7]), n.d.

Side effects

Endpoint	Selumetinib	
	N	Patients with event n (%)
Total adverse events (presented additionally)		
	50	48 (98)
Serious adverse events (SAE)		
	50	12 (24)
Severe adverse events (CTCAE grade ≥ 3)		
	50	31 (62)
Therapy discontinuation due to adverse events[a1]		
	50	6 (12)

Endpoint	Selumetinib	
	N	Patients with event n (%)
SAE with an incidence ≥ 5%		
Infections and infestations	50	6 (12)
Gastrointestinal disorders	50	3 (6)
AE CTCAE grade 3 or higher with incidence ≥ 5% **SOC** PT		
Gastrointestinal disorders	50	**12 (24)**
Diarrhoea	50	8 (16)
Vomiting	50	3 (6)
Investigations, examinations	50	**10 (20)**
Weight increased	50	3 (6)
Creatine phosphokinase in the blood increased	50	3 (6)
Infections and infestations	50	**9 (18)**
Paronychia	50	3 (6)
Skin and subcutaneous tissue disorders	50	**5 (10)**
Respiratory, thoracic and mediastinal disorders	50	**4 (8)**
Hypoxia	50	4 (8)
General disorders and administration site conditions	50	**4 (8)**
Pyrexia	50	4 (8)
Nervous system disorders	50	**3 (6)**
Injury, poisoning and procedural complications	50	**3 (6)**

Endpoint	Selumetinib	
	N	Patients with event n (%)
Adverse Events of Special Interest (AESI) Preferred terms with incidence ≥ 5%		
Muscle-related effects	50	**43 (86)**
Creatine phosphokinase in the blood increased	50	38 (76)
Creatinine increased	50	14 (28)
Hypocalcaemia	50	12 (24)
Musculoskeletal pain	50	3 (6)
Rash, non-acneiform	50	**35 (70)**
Pruritus	50	23 (46)
Rash	50	3 (6)
Rash, maculopapular	50	18 (36)
Rash, acneiform	50	**25 (50)**
Acneiform dermatitis	50	25 (50)
Effects of oral mucositis	50	**25 (50)**
Stomatitis	50	25 (50)
Diseases of the nail	50	**23 (46)**
Paronychia	50	23 (46)
Effects of leukopenia	50	**22 (44)**
Decreased lymphocyte counts	50	10 (20)
Decreased neutrophil counts	50	16 (32)
Decreased leucocyte counts	50	10 (20)
Effects of erythropenia	50	**21 (42)**
Anaemia	50	21 (42)
Effects of heart failure	50	**18 (36)**
Decreased ejection fraction	50	11 (22)
Oedema, peripheral	50	6 (12)
Retinal effects	50	**8 (16)**
Blurred vision	50	4 (8)

Endpoint	Selumetinib	
	N	Patients with event n (%)
Effects of thrombocytopenia	50	**6 (12)**
Platelet count decreased	50	6 (12)

[a] Data from the selumetinib module 4A dossier.
[b] Percentages refer to the FAS.
[c] Confidence intervals were calculated using the Clopper-Pearson method for binomial distributions.
[d] Progression according to REiNS criteria.
[e] Data from the selumetinib module 4A dossier.
[f] Data from the selumetinib module 4A dossier.
[g] Percentage based on all subjects who responded.
[h] Response categories "very much better" or "much better".
[i] For deteriorations, no analysis aggregated across response categories was provided.
[j] No presentation as return rate below 70%.
[k] Data from G-BA Amendment.
[l] Percentage based on all subjects who responded; confidence intervals were calculated using the Clopper-Pearson method for binomial distributions.
[m] Scale range from 0 "no pain" to 10 for "worst pain imaginable".
[n] At baseline, 11 study participants (33.3%) had a score < 2 and therefore, could not improve by 2 points.
[o] At baseline, 4 study participants (12.1 %) had a score > 8 and, therefore, could not deteriorate by 2 points.
[p] Age (and gender)-standardised Z-score.
[q] Shown are T-scores based on the US general population with a mean of 50 and a standard deviation of 10. Higher values correspond to better physical functioning.
[r] Percentage based on patients without missing data for the respective study visit.
[s] Patients with PN of the eye socket; responders above n/N* (%) [95% CI]
[t] Improvement by 2 mm.
[u] Data from the selumetinib module 4A dossier.
[v] Improvement by at least one response category.
[w] Deterioration by at least one response category.
[x] Higher values represent a higher quality of life.
[y] LSM, CI and p value adjusted for study visit, baseline value, age, number of morbidities at baseline and baseline x study visit interaction using MMRM.
[z] Data from G-BA Amendment.
[a1] Study participants received study medication until the occurrence of disease progression, unacceptable AEs, withdrawal of consent, or decision of the medical investigator, whichever occurred earlier.

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; GIC = Global Impression of Change; ICR = Independent Centralised Review; n.d. = no data available; CI = confidence interval; logMAR = Logarithm of the Minimum Angle of Resolution; LSM = Least Square Mean; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; NCI POB = Paediatric Oncology Branch of the National Cancer Institute; PedsQL = Pediatric Quality of Life Inventory; PN = plexiform neurofibroma; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = standard deviation

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

Paediatric patients aged 3 years and above with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

approx. 510 to 740 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 Koselugo (active ingredient: selumetinib) at the following publicly accessible link (last access: 23 December 2021):

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

Treatment with selumetinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with NF1-related tumours, or specialists in paediatrics and adolescent medicine specialising in neuropaediatrics, paediatric haematology and oncology.

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

4. Treatment costs

Annual treatment costs:

Paediatric patients aged 3 years and above with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Selumetinib	€ 114,913.50 – € 343,721.23

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 January 2022)

Costs for additionally required SHI services: not applicable

II. Entry into force

1. **The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 3 February 2022.**

2. **The period of validity of the resolution is limited to 1 July 2023.**

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

Berlin, 3 February 2022

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

Prof. Hecken