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
Selumetinib (reassessment of an orphan drug after exceeding the EUR 30 million limit: neurofibromatosis type 1 (≥ 3 to < 18 years))

dated 7 May 2026

At their session on 7 May 2026, 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. In Annex XII, the information on the active ingredient Selumetinib in the version of the resolution of 21 December 2023 (Federal Gazette, BAnz AT 06.02.2024 B5) shall be replaced by the following information:

Selumetinib

Resolution of: 7 May 2026
Entry into force on: 7 May 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 24 October 2025):

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

Therapeutic indication of the resolution (resolution of 7 May 2026):

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 older.

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

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

Appropriate comparator therapy for selumetinib as monotherapy:

- Best supportive care

Extent and probability of the additional benefit of selumetinib compared to best supportive care:

Hint for a non-quantifiable additional benefit.

Study results according to endpoints:[1]

Paediatric patients aged 3 years and older 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.	There are no assessable data.
Morbidity	↑	Advantage in the endpoint "change in tumour volume" (compared to baseline).
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
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 ∅: No data available. n.a.: not assessable		

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

Data cut-off: 31 March 2021

Mortality

No deaths occurred in the study.

Morbidity

Endpoint	Selumetinib	
	N	Patients with event n (%)
Objective response rate (presented additionally)		
NCI POB	50	34 (68)
Progression-free survival (PFS) (presented additionally)[a]		
NCI POB	50	10 (20)

[1] Data from the dossier of the pharmaceutical company, unless otherwise indicated.

Endpoint Study	Selumetinib		
	N[b]	Volume at the start of the study in ml MV (SD)	Percentage change at the time of the greatest volume reduction achieved MV (SD)
Change in volume of the target lesion: greatest volume reduction achieved			
SPRINT	48	837 (925)	-26.5 (13.6)

Endpoint	Selumetinib	
	N[b]	Patients with event n (%)
Global assessment of clinical change using GIC, age 8 - 18 years, prior to cycle 13[c] **(presented additionally)**		
Tumour pain	29	15 (44.1)
Total pain	29	12 (35.3)
Tumour-associated morbidity	29	17 (50.0)

Endpoint	Selumetinib	
	N[b]	Patients with n (%)
Global assessment of clinical change using GIC, age 5 - 7 years, prior to cycle 25[c] **(presented additionally)**		
Tumour pain	13	8 (57.1)
Total pain	13	6 (42.9)
Tumour-associated morbidity	13	9 (64.3)

Endpoint	Selumetinib	
	N[a]	Patients with event n (%)[d]
Worst pain patient-determined PN (NRS-11)[e] (presented additionally)		
Baseline MV (SD)	33	3.4 (3.2)
Prior to cycle 13 Improvement by ≥ 2 points[f] Deterioration by ≥ 2 points[g]	29	 17 (50.0) 0 (0)

Endpoint	N[b]	Selumetinib		
		Time [seconds] Median (min; max)	Z-score for time[h] 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)
Prior to 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)
Prior to 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)
Prior to 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)
Prior to cycle 13	16	-3.6 (-111.0; 202.4)	-0.47 (-12.2; 19.5)	0 (-3; 6)
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)
Prior to 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)
Prior to cycle 13	6	5.67 (-12.9; 134.8)	0.92 (-1.2; 10.1)	1 (-1; 5)

Endpoint	Selumetinib N = 33			
	Baseline		Prior to cycle 13	
	N[b]	MV (SD)	N[b]	LSM [95% CI]; p value
PROMIS, age: 8 - 18 years, patient-reported **(presented additionally)**				
"Mobility" scale	23	46.57 (6.54)	20	1.51 [-1.54; 4.57]; 0.327
"Upper extremities" scale	22	45.95 (12.91)	19	1.70 [-1.15; 4.54]; 0.238

Endpoint	Selumetinib N = 9			
	Baseline		Prior to cycle 13	
	N[b]	MV (SD)	N[b]	MV (SD)
PROMIS, age: 5 - 7 years, parent-reported **(presented additionally)**				
"Mobility" scale	8	35.23 (12.90)	7	3.96 (4.02)
"Upper extremities" scale	8	36.15 (5.87)	7	1.67 (4.11)

Endpoint	Eye affected by PN HOTV (logMAR) N = 10		Eye not affected by PN HOTV (logMAR) N = 10	
	N	Patients with event n (%)[i]	N	Patients with event n (%)[i]
Visual acuity (presented additionally)				
Baseline MV (SD) [logMAR]	5	0.54 (0.38)	7	0.01 (0.11)
Prior to cycle 37 Improvement by ≥ 0.2 logMAR Deterioration by ≥ 0.2 logMAR	4	 0 (0) 1 (20)	5	 0 (0) 0 (0)

Endpoint	Selumetinib	
	N[j]	Patients with event n (%) [95% CI]
Exophthalmus (presented additionally)[k]		
Right eye	7	2 (28.6) [3.7; 71.0]
Left eye	7	5 (71.4) [29.0; 96.3]
Eye impaired by PN	7	4 (57.1) [18.4; 90.1]
Eye not impaired by PN	7	3 (42.9) [9.9; 81.6]

Endpoint	Selumetinib	
	N[b]	Patients with event n (%)
Symptom checklist (presented additionally)[l,m]		
Tiredness/ fatigue Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 14 (28.0) 8 (16.0)
Sleep disorders Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 17 (34.0) 2 (4.0)
Reduced appetite Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 9 (18.0) 4 (8.0)
Difficulty swallowing Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 4 (18.0) 0 (0.0)
Snoring Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 13 (26.0) 3 (6.0)
Waking up frequently at night Improvement on visit prior to cycle 25	35	 16 (32.0)

Endpoint	Selumetinib	
	N[b]	Patients with event n (%)
Deterioration on visit prior to cycle 25		3 (6.0)
Cough Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 12 (24.0) 7 (14.0)
Nausea Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 2 (4.0) 7 (14.0)
Weakness Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 11 (22.0) 1 (2.0)
Muscle pain Improvement on visit prior to cycle 25 Deterioration on visit prior to cycle 25	35	 12 (24.0) 1 (2.0)

Health-related quality of life

Endpoint	Selumetinib	
	N[b]	Effect estimator
Changes in PedsQL total value, age 8 - 18 years, N = 34 (presented additionally)		
Baseline MV (SD)	33	73.9 (20.7)
Improvement by ≥ 15 points, prior to cycle 13 (n (%))[n]	29	7 (24.1)
Changes in PedsQL total value, age 3 - 7 years; N = 16 (presented additionally)		
Baseline	16	61.0 (18.2)
Improvement by ≥ 15 points, prior to cycle 25 (n (%))[n]	13	6 (37.5)

Side effects

Endpoint	Selumetinib	
	N	Patients with event n (%)
Total adverse events (presented additionally)		
	50	49 (98)
Serious adverse events (SAEs)		
	50	15 (30)
Severe adverse events (CTCAE grade ≥ 3)		
	50	34 (68)

Therapy discontinuation due to adverse events[o]		
	50	6 (12)
SAE with incidence ≥ 10%		
Infections and infestations	50	6 (12)
AE CTCAE grade 3 or higher with incidence ≥ 10% **SOC** PT		
Gastrointestinal disorders	50	**13 (26)**
Diarrhoea	50	8 (16)
Investigations	50	**12 (24)**
Infections and infestations	50	**10 (20)**
Skin and subcutaneous tissue disorders	50	**6 (12)**

[a] Progression according to REiNS criteria.
[b] Number of subjects with available data.
[c] Improvement defined as achieving the response categories "very much better" or "much better".
[d] Percentage based on all subjects who responded.
[e] Scale range from 0 "no pain" to 10 for "worst pain imaginable".
[f] At baseline, 11 study participants (33.3%) had a score < 2 and, therefore, could not improve by 2 points.
[g] At baseline, 4 study participants (12.1%) had a score > 8 and, therefore, could not deteriorate by 2 points.
[h] Age (and sex)-standardised z-score.
[i] Percentage of subjects in relation to the FAS sub-population "subjects with an orbital PN" and available data at baseline.
[j] Patients with PN of the eye socket
[k] Data from the selumetinib Module 4A dossier.
[l] Presentation of the results up to the survey period prior to cycle 25, as the return rate prior to cycle 37 is below 70%.
[m] Change defined as improvement or deterioration by one response category.
[n] Presentation of the results up to the survey period prior to cycle 13 or 25, as the return rate was below 70% thereafter. In addition to the responder analyses of an improvement by ≥ 15 points for the dossier (Module 4), post-hoc responder analyses of a deterioration by ≥ 15 points were submitted.
[o] Study participants received the study medication until occurrence of disease progression, unacceptable AE, withdrawal of informed consent or the decision of the medical investigators, whichever occurred first.

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 = Pediatric 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; SOC = system organ class; SAE: serious adverse event; AE: adverse event

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

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

Approx. 515 – 920 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 March 2026):

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 or specialists in paediatrics and adolescent medicine specialising in neuropaediatrics, paediatric haematology and oncology, all of whom are experienced in the treatment of patients with NF1-related tumours.

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The EMA will assess new information on this medicinal product at least annually and update the product information as necessary.

4. Treatment costs

Annual treatment costs:

Paediatric patients aged 3 years and older 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	€ 97,390.21 - € 292,013.02[2]
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 March 2026)

Costs for additionally required SHI services: not applicable

[2] The lowest annual treatment costs are incurred for 3-year-olds who are administered the hard capsules at the appropriate treatment dose, whilst the highest annual treatment costs are incurred for 17-year-olds. The annual treatment costs incurred for 3-year-olds who are administered the granules in capsule form amount to € 97,443.08, which is within the range.

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

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

– No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient approved in monotherapy.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

II. The resolution will enter into force on the day of its publication on the G-BA website on 7 May 2026.

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

Berlin, 7 May 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken