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 (new therapeutic indication: neurofibromatosis type 1 (≥ 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 following information shall be added after No. 5 to the information on the benefit assessment of Selumetinib in accordance with the resolution of 7 May 2026 on the therapeutic indication "Neurofibromatosis type 1 (≥ 3 to < 18 years)":

Selumetinib

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

New 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 adults with neurofibromatosis type 1 (NF1).

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

Adults with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Appropriate comparator therapy:

- Best supportive care

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

Indication of a minor additional benefit

Study results according to endpoints:[1]

Adults 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	↔	No relevant difference for the benefit assessment.
Morbidity	↑↑	Advantages in the endpoints "change in volume of the target lesion", "chronic pain" (using NRS, PGIS, PGIC-1 and PGIC-2) and "pain peaks" (using NRS, PGIS, PGIC-1 and PGIC-2)
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↓↓	Disadvantage in the endpoint of severe 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
∅: No data available.
n.a.: not assessable

COMET study:

- Ongoing, multicentre, randomised, double-blind phase III study
- Adult patients with neurofibromatosis type 1 and symptomatic, inoperable plexiform neurofibromas
- Selumetinib + Best Supportive Care (BSC) **vs** placebo + BSC

[1] Data from the dossier assessment of the IQWiG (A25-147) and from the addendum (A26-33), unless otherwise indicated.

Mortality

Endpoint	Selumetinib (+BSC)		Placebo (+BSC)		Selumetinib (+BSC) vs Placebo (+BSC)
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	RR [95% CI][a] p value[b] Absolute difference (AD)[c]
Overall survival[d]					
	71	0 (0)	74	0 (0)	-

Morbidity

Endpoint	Selumetinib (+BSC)		Placebo (+BSC)		Selumetinib (+BSC) vs Placebo (+BSC)
	N (%)	Change from baseline LS mean (SE)	N (%)	Change from baseline LS mean (SE)	LS mean difference [95% CI]; p value SMD (Hedges' g) [95% CI]; Absolute difference (AD)[c]
Change in volume of the target lesion[e]					
Best percentage change in volume of the target lesion achieved	65 (91.6)	-15.3 (1.81)	71 (96.0)	-4.18 (1.71)	-11.1 [-15.5; -6.79]; < 0.001 -0.76 [-1.12; -0.41] AD = -11,1 %

Endpoint	Selumetinib (+BSC)		Placebo (+BSC)		Selumetinib (+BSC) vs Placebo (+BSC)
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value[b]
Chronic pain - Improvement at week 48					
NRS[f]	57	25 (43.9)	62	16 (25.8)	1.70 [1.02; 2.84]; 0.042
PGIS[g]	56	20 (51.8)	56	15 (26.8)	1.93 [1.17; 3.19]; 0.007
PGIC 1[h]	57	25 (43.9)	58	12 (20.7)	2.12 [1.18; 3.80]; 0.009
PGIC 2[i]	57	35 (61.4)	58	17 (29.3)	2.09 [1.34; 3.28]; < 0.001
Pain peaks - Improvement at week 48					
NRS[f]	58	39 (67.2)	64	25 (39.1)	1.72 [1.21; 2.45]; 0.002
PGIS[g]	56	37 (66.1)	56	24 (42.9)	1.54 [1.08; 2.20]; 0.015
PGIC 1[h]	57	23 (40.4)	58	11 (19.0)	2.13 [1.15; 3.95]; 0.015
PGIC 2[i]	57	34 (59.7)	58	18 (31.0)	1.92 [1.24; 2.98]; 0.002
Impairment due to pain - Improvement at week 48					
PII-pNF[j]	57	27 (47.4)	59	18 (30.5)	1.55 [0.97; 2.49]; 0.067
Psychosocial morbidity - Improvement at week 48					
PlexiQoL[k]	57	17 (29.8)	59	19 (32.2)	0.93 [0.54; 1.60]; 0.828
Physical functioning					
	No suitable data				
Health status - Improvement at week 48					
EQ-5D VAS[l]	57	18 (31.6)	59	13 (22.0)	1.43 [0.78; 2.65]; 0.260

Health-related quality of life

No suitable data

Side effects

Endpoint	Selumetinib (+BSC)		Placebo (+BSC)		Selumetinib (+BSC) vs Placebo (+BSC)
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI][a] p value[b]
Total adverse events (presented additionally)					
	71	71 (100)	74	68 (91.9)	-
Serious adverse events (SAEs)					
	71	10 (14.1)	74	9 (12.2)	1.16 [0.50; 2.68]; 0.775
Severe adverse events (AEs)[l]					
	71	23 (32.4)	74	13 (17.6)	1.84 [1.01; 3.35]; 0.043
Therapy discontinuation due to adverse events					
	71	9 (12.7)	74	5 (6.8)	1.88 [0.66; 5.33]; 0.254
Gastrointestinal disorders (SOC, AEs)					
Gastrointestinal disorders (SOC, AEs)	71	53 (74.7)	74	32 (43.2)	1.73 [1.29; 2.32]; < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)					
Skin and subcutaneous tissue disorders (SOC, AEs)	71	64 (90.1)	74	26 (35.1)	2.57 [1.86; 3.53]; < 0.001
Peripheral oedema (PT, AEs)	71	11 (15.5)	74	1 (1.4)	11.46 [1.52; 86.52]; 0.002

Other specific AEs					
Infections and infestations (SOC, severe AEs[m])	71	6 (8.5)	74	1 (1.4)	6.25 [0.77; 50.65]; 0.048
Investigations (SOC, severe AEs[m])	71	10 (14.1)	74	1 (1.4)	10.42 [1.37; 79.33]; 0.005

a. RR [95% CI] unstratified
b. Own calculation, unconditional exact test (CSZ method[2])
c. Indication of absolute difference (AD) only in case of statistically significant difference; own calculation.
d. The results on overall mortality are based on the data on fatal AEs.
e. Information from the dossier of the pharmaceutical company
f. A decrease by ≥ 1.5 points compared to the start of the study is considered as clinically relevant improvement (scale range: 1 to 10).
g. A decrease by ≥ 1 point compared to the start of the study is considered as clinically relevant improvement (scale range: 0 "no pain" to 4 "severe").
h. Defined as "much better", "moderately better" or "minimally better" compared with the last visit is considered as clinically relevant improvement (scale range: 1 "much better" to 7 "much worse").
i. Defined as "much better", "moderately better" or "minimally better" compared with the start of the study medication is considered as clinically relevant improvement (scale range: 1 "much better" to 7 "much worse").
j. A decrease by ≥ 0.9 points compared to the start of the study is considered as clinically relevant improvement (scale range: 0 to 6).
k. A decrease by ≥ 2.7 points compared to the start of the study is considered as clinically relevant improvement (scale range: 1 to 18).
l. An increase by ≥ 15 points compared to the start of the study is considered as clinically relevant improvement (scale range: 0 to 100).
m. Operationalised as CTCAE grade ≥ 3

CTCAE: Common Terminology Criteria for Adverse Events; CI: confidence interval; LS mean: least squares mean; MV: mean value; MD: mean difference; N: number of patients evaluated; n: number of patients with (at least 1) event; NRS: Numerical Rating Scale; PGIC: Patient Global Impression of Change; PGIS: Patient Global Impression of Severity; PT: preferred term; PlexiQoL: Plexiform Neurofibroma Quality of Life Scale; RCT: randomised controlled trial; RR: relative risk; SD: standard deviation; SE: standard error; SE: standard error; SOC: system organ class; SMD: standardised mean difference; SAE: serious adverse event; AE: adverse event; VAS: visual analogue scale

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

Adults with symptomatic, inoperable plexiform neurofibromas (PN) in neurofibromatosis type 1 (NF1)

Approx. 515 – 920 patients

[2] Martín Andrés A, Silva Mato A. Choosing the optimal unconditioned test for comparing two independent proportions. Computat Stat Data Anal 1994; 17(5): 555-574. https://doi.org/10.1016/0167-9473(94)90148-1

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: 28 April 2026):

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

Therapy 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 and other doctors from other specialist groups participating in the Oncology Agreement.

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:

Adults 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	€ 324,318.80
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

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:

Adults 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