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 Nirogacestat (progressing desmoid tumour)

of 2 April 2026

At their session on 2 April 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, information on the active ingredient Nirogacestat shall be added in alphabetical order as follows:

Nirogacestat

Resolution of: 2 April 2026
Entry into force on: 2 April 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 14 August 2025):

Ogsiveo as monotherapy is indicated for the treatment of adult patients with progressing desmoid tumours who require systemic treatment.

Therapeutic indication of the resolution (resolution of 2 April 2026):

See therapeutic indication according to marketing authorisation.

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

Nirogacestat 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 SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The G-BA determine 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 Ordinance on the Benefit Assessment of Pharmaceuticals (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).

<u>Adults with progressing desmoid tumours who require systemic treatment</u>

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

Hint for a minor additional benefit

Study results according to endpoints:[1]

Adults with progressing desmoid tumours who require systemic treatment

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 of physical functioning, sleep, pain interference, constipation, and in the DTSS total score, the PGIC and the PGIS. Disadvantages in appetite loss, nausea and vomiting and diarrhoea.
Health-related quality of life	↑	Advantage in physical functioning.
Side effects	↓	Disadvantages in severe AEs and therapy discontinuation.
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		

DeFi study: RCT of phase III, nirogacestat **vs** placebo

Mortality

Endpoint	Nirogacestat		Placebo		Nirogacestat vs placebo
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	Hazard ratio[a] [95% CI] p value[b] Absolute difference (AD)[c]
Overall survival					
	70	n.a. [n.a.; n.a.] *0 (0)*	72	n.a. [n.a.; n.a.] *1 (1)*	n.a.

[1] Data from the dossier assessment of the G-BA (published on 15 January 2026), and from the amendment to the dossier assessment from 13 March 2026, unless otherwise indicated.

Morbidity

Progression-free survival (PFS)[d]					
Qualified clinical or radiographic progression or death	70	n.a. [n.a.; n.a.] *12 (17)*	72	n.a. [n.a.; n.a.] *37 (51)*	0.29 [0.15; 0.55]; < 0.0001
Radiographic progression or death	70	n.a. [n.a.; n.a.] *11 (16)*	72	n.a. [n.a.; n.a.] *31 (43)*	0.31 [0.15; 0.62]; 0.0002
Qualified clinical progression or death	70	n.a. [n.a.; n.a.] *1 (1)*	72	n.a. [n.a.; n.a.] *7 (10)*	0.14 [0.02; 1.10]; 0.014
GODDESS-DTSS (time to first deterioration by ≥ 15% of the scale range)					
Weighted DTSS total score[e]	70	n.a. [10.9; n.a.] *26 (37)*	72	4.4 [2.37; n.a.] *40 (56)*	0.50 [0.30; 0.84]; 0.004
Intra-abdominal symptoms[f]	70	n.a. [1.64; n.a.] *12 (17)*	72	3.52 [0.76; n.a.] *15 (21)*	0.95 [0.41; 2.22]; 0.45
GODDESS DTIS (time to first deterioration by ≥ 15% of the scale range)					
Physical functioning	70	n.a. [n.a.; n.a.] *16 (23)*	72	8.54 [6.18; 14.7] *35 (49)*	0.33 [0.18; 0.6]; < 0.0001
Sleep	70	n.a. [8.28; n.a.] *28 (40)*	72	7.36 [3.84; 11.1] *39 (54)*	0.57 [0.34; 0.94]; 0.01
Emotion	70	n.a. [6.44; n.a.] *30 (43)*	72	4.67 [2.83; 17.5] *37 (51)*	0.61 [0.38; 1.01]; 0.03
BPI-SF (time to first deterioration by ≥ 15% of the scale range)					
Pain interference	70	n.a. [n.a.; n.a.] *12 (17)*	72	n.a. [n.a.; n.a.] *22 (31)*	0.47 [0.23; 0.96]; 0.02
Pain intensity	70	n.a. [n.a.; n.a.] *11 (16)*	72	n.a. [n.a.; n.a.] *19 (26)*	0.50 [0.24; 1.06]; 0.03
PGIC (time to first deterioration by ≥ 15% of the scale range)					
	70	22.3 [3.75; n.a.] *32 (46)*	72	4.86 [3.48; 8.28] *47 (65)*	0.53[g] [0.33; 0.86]; 0.004 AD = 17.4 months
PGIS					
Time to first deterioration by ≥ 15% of the scale range					
	70	n.a. [n.a.; n.a.] *20 (29)*	72	11.96 [6.64; n.a.] *29 (40)*	0.58 [0.32; 1.03]; 0.03

Time to first improvement by ≥ 15% of the scale range					
	70	1.84 [0.92; 2.79] *49 (70)*	72	10.12 [2.99; n.a.] *34 (47)*	2.01 [1.24; 3.27]; 0.002 AD = 8.3 months
EORTC QLQ-C30: Symptom scales (time to first deterioration by ≥ 10 points)					
Constipation	70	n.a. [n.a.; n.a.] *16 (23)*	72	n.a. [4.40; n.a.] *27 (38)*	0.49 [0.26; 0.92]; 0.01
Fatigue	70	1.84 [0.95; 4.63] *48 (69)*	72	2.76 [1.84; 5.55] *45 (63)*	1.05 [0.66; 1.65]; 0.42
Nausea and vomiting	70	0.92 [0.92; 2.73] *51 (73)*	72	21.0 [9.20; n.a.] *28 (39)*	3.00[g] [1.80; 5.00]; < 0.0001 AD = 20.1 months
Pain	70	n.a. [7.49; n.a.] *28 (40)*	72	6.44 [3.48; n.a.] *36 (50)*	0.62 [0.37; 1.05]; 0.04
Dyspnoea	70	19.3 [7.33; n.a.] *31 (44)*	72	11.0 [6.57; n.a.] *27 (38)*	1.07 [0.63; 1.82]; 0.40
Insomnia	70	23.0 [6.44; n.a.] *28 (40)*	72	18.4 [6.44; n.a.] *28 (39)*	0.88 [0.52; 1.52]; 0.33
Appetite loss	70	6.44 [1.84; n.a.] *37 (53)*	72	n.a. [8.54; n.a.] *23 (32)*	1.96 [1.13; 3.41]; 0.01
Diarrhoea	70	0.92 [0.92; 1.84] *55 (79)*	72	9.23 [5.72; n.a.] *32 (44)*	3.58 [2.20; 5.84]; < 0.0001 AD = 8.3 months

Endpoint	**Nirogacestat**		**Placebo**		**Nirogacestat vs placebo**
	N	Mean value (SD) *n (%)*	N	Mean value (SD) *n (%)*	Difference LSM [95% CI] p value[b]
Tumour volume (change at cycle 7), presented additionally					
Tumour volume at baseline (ml)	70	302.3 (423.1) *55 (78.6)*	72	308.6 (340.1) *55 (76.4)*	-
Changes from baseline (%) LS mean [95% CI]		-108.4 [-176.4; -40.3]		-28.2 [-96.5; 40.2]	-80.2 [-170.9; 10.5]; 0.04

Health-related quality of life

Endpoint	Nirogacestat		Placebo		Nirogacestat vs placebo
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	Hazard ratio[a] [95% CI] p value[b] Absolute difference (AD)[c]
EORTC QLQ-C30: Functional scales and global health status (time to first deterioration by ≥ 10 points)					
General health status / quality of life	70	6.21 [2.83; 18.9] *41 (59)*	72	6.47 [3.71; 11.0] *40 (56)*	0.95 [0.60; 1.50]; 0.41
Cognitive functioning	70	4.86 [2.79; 17.5] *40 (57)*	72	12.0 [5.42; 16.6] *32 (44)*	1.35 [0.83; 2.19]; 0.11
Emotional functioning	70	13.8 [6.44; n.a.] *34 (49)*	72	8.28 [3.90; 16.5] *36 (50)*	0.77 [0.48; 1.25]; 0.15
Physical functioning	70	n.a. [n.a.; n.a.] *16 (23)*	72	8.38 [7.39; 18.8] *33 (46)*	0.38 [0.21; 0.70]; 0.001
Role functioning	70	19.3 [4.67; n.a.] *32 (46)*	72	7.56 [4.67; 20.3] *37 (51)*	0.75 [0.46; 1.23]; 0.12
Social functioning	70	6.44 [3.45; n.a.] *38 (54)*	72	5.55 [3.52; 8.54] *39 (54)*	0.87 [0.54; 1.40]; 0.28

Side effects

Endpoint MedDRA system organ classes/ Preferred terms	Nirogacestat		Placebo		Nirogacestat vs placebo
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[b]
Total adverse events (presented additionally)	69	0.10 [0.03; 0.16] *69 (100)*	72	0.26 [0.10; 0.30] *69 (96)*	-
Serious adverse events (SAEs)	69	n.a. [n.a.; n.a.] *14 (20)*	72	n.a. [21.3; n.a.] *8 (11)*	1.77[g] [0.74; 4.26]; 0.10
Severe adverse events (CTCAE grade 3 or 4)	69	17.5 [3.32; 27.6] *38 (55)*	72	n.a. [21.3; n.a.] *12 (17)*	3.80 [1.98; 7.31]; < 0.0001
Therapy discontinuation due to adverse events	69	n.a. [n.a.; n.a.] *16 (23)*	72	n.a. [22.7; n.a.] *2 (3)*	8.26[g] [1.90; 36.0]; 0.0004
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					

Gastrointestinal disorders	69	n.a. [n.a.; n.a.] *16 (23)*	72	n.a. [n.a.; n.a.] *4 (6)*	4.56[g] [1.52; 13.7]; 0.002
Diarrhoea	69	n.a. [n.a.; n.a.] *11 (16)*	72	n.a. [21.3; n.a.] *1 (1)*	11.5[g] [1.48; 89.5]; 0.002

a The HR was estimated using the stratified Cox proportional hazards model. The "Exact method for ties" was used. Stratification is based on tumour localisation.
b The pharmaceutical company shall provide a p value from a one-sided stratified log-rank test ($\alpha = 0.025$). p values below 0.025 are considered statistically significant.
c Indication of absolute difference (AD) only in case of statistically significant difference; own calculation.
d Information from the pharmaceutical company's dossier, Module 4
e The "Weighted DTSS total score" takes into account items 1 to 7, with the mean pain scale (items 1–3) being included in the calculation of the DTSS total score.
f The "Intra-abdominal symptoms" domain score is based on items 9–11 of the GODDESS-DTSS; these items were answered only by subjects who selected the corresponding tumour localisation in item 8.
g There is a statistically significant violation of the proportional hazards assumption.

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; CI = confidence interval; n.d.: no data available; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; n.c. = not calculable; n.r. = not reached; PT = preferred term; SD = standard deviation; SOC = system organ class; SAE = serious adverse event; vs = versus

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

Adults with progressing desmoid tumours who require systemic treatment

Approx. 350 to 630 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 Ogsiveo (active ingredient: nirogacestat) at the following publicly accessible link (last access: 9 January 2026):

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

Therapy with nirogacestat should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with desmoid tumours and other doctors from other specialist groups participating in the Oncology Agreement.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide information material for medical professionals and patients (including patient identification card).

The information material contains, in particular, information and warnings of the potential risk of embryo-foetal toxicity.

4. Treatment costs

Annual treatment costs:

Adults with progressing desmoid tumours who require systemic treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nirogacestat	260,760.82

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 February 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 progressing desmoid tumours who require systemic treatment

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 statutory 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.

6. Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Ogsiveo is a medicinal product placed on the market from 1 January 2025.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5 per cent of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant percentage within the scope of SGB V.

II. The resolution will enter into force on the day of its publication on the G-BA website on 2 April 2026.

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

Berlin, 2 April 2026

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

Prof. Hecken