

# 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 and  
Annex XIIa – Combinations of medicinal products with new  
active ingredients according to Section 35a SGB V  
Givinostat (Duchenne muscular dystrophy,  $\geq 6$  years,  
combination with a corticosteroid)

of 22 January 2026

At their session on 22 January 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. Annex XII shall be amended in alphabetical order to include the active ingredient Givinostat as follows:**

## **Givinostat**

Resolution of: 22 January 2026  
Entry into force on: 22 January 2026  
Federal Gazette, BAnz AT DD. MM YYYY Bx

### **Therapeutic indication (according to the marketing authorisation of 6 June 2025):**

Duvyzat is indicated for the treatment of Duchenne muscular dystrophy (DMD) in ambulant patients, aged 6 years and older, and with concomitant corticosteroid treatment.

### **Therapeutic indication of the resolution (resolution of 22 January 2026):**

See therapeutic indication according to marketing authorisation.

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

Givinostat is approved as a medicinal product for the treatment of rare diseases in accordance with 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).

### Ambulant patients aged 6 years and older with Duchenne muscular dystrophy (DMD)

#### **Extent of the additional benefit and significance of the evidence of givinostat with concomitant corticosteroid treatment:**

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

#### **Study results according to endpoints:<sup>1</sup>**

### Ambulant patients aged 6 years and older with Duchenne muscular dystrophy (DMD)

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<sup>1</sup> Data from the dossier assessment of the G-BA (published on 15. October 2025), and from the amendment to the dossier assessment from 12 December 2025, unless otherwise indicated.

## Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↔	No relevant differences for the benefit assessment.
Health-related quality of life	∅	No data available.
Side effects	↔	No relevant differences for the benefit assessment.
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		

EPIDYS study: Phase III RCT, givinostat vs placebo, treatment duration 18 months

### Mortality

Endpoint	Givinostat		Placebo		Givinostat vs placebo
	N <sup>1</sup>	Patients with event n (%)	N <sup>1</sup>	Patients with event n (%)	RR [95% CI] <sup>2</sup> p value <sup>2</sup>
<b>Deaths</b>					
	118	0	61	0	-

## Morbidity

Endpoint	Givinostat			Placebo			Givinostat vs placebo
	N <sup>3</sup>	Baseline MV (SD)	Change at week 72/ EOS <sup>4</sup> LS mean [95% CI] <sup>5</sup>	N <sup>3</sup>	Baseline MV (SD)	Change at week 72/ EOS <sup>4</sup> LS mean [95% CI] <sup>5</sup>	LS mean difference [95% CI] <sup>5</sup> ; p value <sup>4)</sup>
<b>4-stair climb (4SC) - Time in seconds</b>							
	104	3.58 (1.26)	1.40 [1.07; 1.73]	53	3.60 (1.27)	2.13 [1.66; 2.59]	-0.73 [-1.30; -0.15] 0.013
<b>Rise from the floor (RFTF) - Time in seconds</b>							
	85	5.98 (2.42)	2.28 [1.70; 2.87]	44	5.88 (2.25)	3.45 [2.64; 4.27]	-1.17 [-2.18; -0.16] 0.023
<b>10-metre walk/run test (10-MWT) - Time in seconds</b>							
	104	5.54 (1.33)	1.08 [0.81; 1.35]	55	5.30 (1.03)	1.63 [1.26; 2.00]	-0.55 [-1.01; -0.10] 0.018
<b>6-minute walk test (6-MWT) - Distance in metres</b>							
	101	398.9 (70.9)	-47.8 [-56.8; -38.9]	54	393.7 (61.4)	-62.4 [-74.7; -50.0]	14.5 [-0.82; 29.9] 0.064
<b>Functional performance (NSAA total score<sup>6</sup>) - presented additionally</b>							
	103	23.9 (5.34)	-3.35 [-4.01; -2.70]	56	24.1 (4.85)	-5.06 [-5.96; -4.16]	1.71 [0.59; 2.83] 0.003

Endpoint	Givinostat			Placebo			Givinostat vs placebo
	N	Events (%) <sup>7</sup>	Median time to event, months [95% CI]	N	Events (%) <sup>7</sup>	Median time to event, months [95% CI]	Hazard ratio [95% CI] <sup>8</sup> p value <sup>8)</sup>
<b>Time to a confirmed loss of the ability to rise from the floor<sup>9</sup> - presented additionally</b>							
	118	1 (0.9)	n.a.	61	2 (3.3)	n.a.	0.14 [0.01; 2.26] 0.17

Endpoint	Givinostat		Placebo		Givinostat vs placebo
	N	Events, n (%)	N	Events, n (%)	RR [95% CI] <sup>10</sup> p value <sup>10</sup>
<b>Loss of walking ability without aids<sup>11</sup> - presented additionally</b>					
	117	1 (0.8)	59	2 (3.3)	0.26 [0.02; 2.79]; 0.27

### Health-related quality of life

No data on quality of life were assessed.

### Side effects

Endpoint MedDRA system organ classes/ preferred terms/ AEs of special interest	Givinostat		Placebo		Givinostat vs placebo
	N <sup>1</sup>	Patients with event n (%)	N <sup>1</sup>	Patients with event n (%)	RR [95% CI] <sup>2</sup> ; p value <sup>2</sup>
<b>Total adverse events</b> (presented additionally)	118	112 (94.9)	61	57 (93.4)	-
<b>Serious adverse events (SAE)</b>	118	8 (6.8)	61	2 (3.3)	2.07 [0.45; 9.44]; 0.35
<b>Severe adverse events (CTCAE grade 3 or 4)</b>	118	5 (4.2)	61	1 (1.6)	2.58 [0.31; 21.6]; 0.39
<b>Therapy discontinuation due to adverse events</b>	118	4 (3.4)	61	0 (0)	4.69 [0.26; 85.7]; 0.30
<b>Severe adverse events according to MedDRA</b> (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
No severe AEs ≥ 5%					
<b>SAEs according to MedDRA</b> (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
No SAEs ≥ 5%					
<b>Adverse events of special interest</b> (with statistically significant difference between the treatment arms)					
No AEs of special interest were collected.					
Endpoint	Givinostat		Placebo		Givinostat vs placebo

	N	Baseline MV (SD)	Change at week 72/ EOS <sup>3</sup> LS mean [95% CI] <sup>4</sup>	N	Baseline MV (SD)	Change at week 72/ EOS <sup>3</sup> LS mean [95% CI] <sup>4</sup>	LS mean difference [95% CI] <sup>4</sup> ; p value <sup>4</sup>
<b>Body height (z score)</b>	109	-1.84 (1.08)	0.63 [0.56; 0.70]	58	-1.78 (1.19)	0.71 [0.62; 0.81]	-0.08 [-0.20; 0.04] 0.19
<b>Body weight (z scores)</b>	111	-0.37 (1.27)	0.49 [0.43; 0.55]	58	-0.32 (1.50)	0.73 [0.64; 0.81]	-0.24 [-0.34; -0.14] < 0.0001

1. The number corresponds to those subjects who were used to calculate the respective statistics.
2. RR with associated 95%-CI and p value based on logistic regressions adjusted for glucocorticoid treatment regimen and age at baseline. If the model does not converge, the Wald method was used.
3. Number of available values for the analysis (at week 72), a maximum of 2 subjects were missing in the givinostat and control arms at baseline.
4. The analyses also included subjects who made the visit after the extended visit time window (+/- 7 days plus 2 months). The percentage of subjects who made the study visit outside the ±7-day analysis time window was 24% in the givinostat arm and 33% in the control arm. These patients made the study visit in the median of approx. 14.5 or 15 days later.
5. MMRM without imputation under MAR assumption, adjusted for baseline values of 4SC, RFTF, 10-MWT and 6-MWT, treatment group, visit, treatment\*visit, patient age at the start of the study and the stratification factor glucocorticoid treatment regimen ("deflazacort daily"; "deflazacort intermittent"; "other corticosteroids daily"; "other corticosteroids intermittent").
6. The NSAA total score (0-34 points) consists of 17 items (0-2 points) that measure functional performance in DMD. Higher values indicate better functional performance.
7. Analysis based on imputed data.
8. Cox proportional hazards adjusted for baseline values of the 4SC, RFTF, 10-MWT, 6-MWT, treatment group, age and the stratification factor glucocorticoid treatment regimen.
9. Loss of ability to rise from the floor was defined as RFTF grade 1 ("unable to rise from the floor, even with the aid of a chair") and NSAA score 0b ("unable to perform the test") and was to be confirmed on 2 consecutive visits.
10. RR with associated 95%-CI and p value based on logistic regressions adjusted for "age at baseline" and "treatment group" as well as the stratification factor "glucocorticoid treatment regimen". If the model does not converge, the Wald method was used.
11. Loss of walking ability without aids was present if the following criteria were met at a visit at any time before or at the end of the study (last study visit at week 72/ EOS visit): Patient was unable to perform the 6-MWT and complete the 10-MWT in ≤ 30 seconds (10-MWT ≤ grade 2) without support or aids due to physical limitations. The criteria had to be met at all subsequent visits until the end of the study at week 72/ EOS visit.

Abbreviations used:

4SC = 4-stair climb; 6-MWT = 6-minute walk test; 10-MWT = 10-metre walk/run test; CTCAE = Common Terminology Criteria for Adverse Events; DMD = Duchenne Muscular Dystrophy; EOS = end of study; CI = confidence interval; LS = least squares; MMRM = mixed model for repeated measures; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; RFTF = rise from the floor; RR = relative risk; (S)AE = (serious) adverse event; vs = versus

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

### Ambulant patients aged 6 years and older with Duchenne muscular dystrophy (DMD)

approx. 270 – 400 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 Duvyzat (active ingredient: givinostat) at the following publicly accessible link (last access: 22 September 2025):

[https://www.ema.europa.eu/en/documents/product-information/duvyzat-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/duvyzat-epar-product-information_en.pdf)

Treatment with givinostat should only be initiated and monitored by specialists experienced in treating patients with Duchenne muscular dystrophy.

This medicinal product received a conditional marketing authorisation. 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:

Ambulant patients aged 6 years and older with Duchenne muscular dystrophy (DMD)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Givinostat	€ 242,589.82 - € 582,215.57
Additionally required SHI services	1st year: € 3.75
	Subsequent years: € 1.50
<i>Corticosteroid treatment</i>	
Vamorolone	€ 55,593.24 - € 92,655.40

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 November 2025)

### 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:

Ambulant patients aged 6 years and older with Duchenne muscular dystrophy (DMD)

The following medicinal products with new active ingredients that can be used in a combination therapy with givinostat in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active

ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

- Vamorolone (Agamree)

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.

#### **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 Duvyzat 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% (3.9%) 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 extent within the scope of SGB V.

#### **II. In Annex XIIa of the Pharmaceuticals Directive, the following information shall be added in alphabetical order:**

"Active ingredient of the assessed medicinal product

Givinostat

Resolution according to Section 35a paragraph 3 SGB V from

22 January 2026

Therapeutic indication of the resolution

Duvyzat is indicated for the treatment of Duchenne muscular dystrophy (DMD) in ambulant patients, aged 6 years and older, and with concomitant corticosteroid treatment.

Patient group

Ambulant patients aged 6 years and older with Duchenne muscular dystrophy (DMD)

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names<sup>2</sup>)

Vamorolone (Agamree)

Period of validity of the designation (since... or from... to)

Since 22 January 2026

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.

### **III. Entry into force**

- 1. The resolution will enter into force on the day of its publication on the website of the G-BA on 22 January 2026.**
- 2. The period of validity of the resolution is limited to 1 February 2034.**

The justification to this resolution will be published on the website of the G-BA at [www.g-ba.de](http://www.g-ba.de).

Berlin, 22 January 2026

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

Prof. Hecken