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
Omaveloxolone (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit (Friedreich's ataxia, ≥ 16 years)

of 18 December 2025

At their session on 18 December 2025, 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 is amended as follows:

1. **The information on Omaveloxolone in the version of the resolution of 19 September 2024 (BAnz AT 27.11.2024 B2) is repealed.**
2. **Annex XII shall be amended in alphabetical order to include the active ingredient Omaveloxolone as follows:**

Omaveloxolone

Resolution of: 18 December 2025
Entry into force on: 18 December 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 9 February 2024):

Skyclarys is indicated for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older.

Therapeutic indication of the resolution (resolution of 18 December 2025):

See therapeutic indication according to marketing authorisation.

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

Adults and adolescents aged 16 years and older with Friedreich's ataxia

Appropriate comparator therapy:

Best supportive care

Extent and probability of the additional benefit of omaveloxolone compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults and adolescents aged 16 years and older with Friedreich's ataxia

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A25-86) unless otherwise indicated.

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	↔	No relevant differences for the benefit assessment.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↔	No relevant differences for the benefit assessment; in detail disadvantage in the specific AE "Gastrointestinal disorders".
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		

MOXIe study (part 2):

- randomised, controlled, double-blind, phase II study
- Omaveloxolone versus placebo (1:1); comparator treatment phase of 48 weeks

Mortality

Endpoint	Omaveloxolone		Placebo		Omaveloxolone vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Overall mortality[a]					
	51	0 (0)	52	0 (0)	–

Morbidity

Endpoint	Omaveloxolone			Placebo			Omaveloxolone vs placebo
	N	Values at the start of the study MV (SD)	Mean change at week 48 MV [95% CI]	N	Values at the start of the study MV (SD)	Mean change at week 48 MV [95%-CI];	MD [95% CI]; p value
Physical functioning using the modified Friedreich Ataxia Rating Scale (mFARS)[b]							
Total score	50	40.67	50	52	37.81	52	-1.82 [-3.59; -0.06]; 0.043 Hedges' g: -0.42 [-0.84; -0.01]
Bulbar function	50	0.73 (0.50)	−0.08 [−0.18; 0.03]	52	0.63 (0.63)	−0.03 [−0.13; 0.07]	-0.05 [-0.19; 0.10]; –
Coordination of the upper extremities	50	10.75 (3.71)	−0.72 [−1.51; 0.07]	52	9.90 (3.53)	0.11 [-0.62; 0.84]	-0.83 [-1.91; 0.25]; –
Coordination of the lower extremities	50	6.29 (2.58)	−0.13 [−0.73; 0.48]	52	6.25 (2.29)	−0.30 [−0.86; 0.26]	0.17 [-0.66; 1.00]; –
Upright stability	50	22.89 (6.53)	−0.11 [−0.88; 0.67]	52	21.02 (7.13)	0.94 [0.22; 1.67]	-1.05 [-2.12; 0.02]; –
Activities of daily living using Friedreich Ataxia-Activities of Daily Living (FA-ADL)[c]							
	45	11.03 (4.49)	0.28 [-0.56; 1.12]	51	9.85 (4.72)	1.05 [0.27; 1.84]	-0.78 [-1.93; 0.38] 0.187
Endpoint	**Omaveloxolone**			**Placebo**			**Omaveloxolone vs placebo**
	N	Adjusted incidence rate [95% CI]; n_E/N (SD)		N	Adjusted incidence rate [95% CI]; n_E/N (SD)		Rate ratio [95% CI]; p value
Frequency of falls							
	51	0.04 [0.03; 0.05]; 11.24 (18.98)		52	0.05 [0.03; 0.06]; 15.00 (23.67)		0.82 [0.50; 1.34]; 0.425

Endpoint	Omaveloxolone		Placebo		Omaveloxolone vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
General health status using Patient Global Impression of Change (PGI-C)[d]					
Improvement[e]	44	19 (43.2)	51	13 (25.5)	1.69 [0.95; 3.01]; 0.075
Deterioration[f]	44	13 (29.5)	51	23 (45.1)	0.66 [0.38; 1.14]; 0.134

Health-related quality of life

Endpoint	Omaveloxolone		Placebo		Omaveloxolone vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[g]
Short Form (36)-health survey (SF-36)					
Physical Component Summary (PCS)					
Deterioration[h]	44	3 (7)	51	4 (8)	0.89 [0.21; 3.71]; 0.880
Mental Component Summary (MCS)					
Deterioration[i]	44	3 (7)	51	3 (6)	1.16 [0.25; 5.42]; 0.914

Side effects

Endpoint	Omaveloxolone		Placebo		Omaveloxolone vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[g]
Total adverse events (AE) (presented additionally)					
	51	51 (100)	52	52 (100)	–
Serious adverse events (SAE)					
	51	5 (10)	52	3 (6)	1.70 [0.43; 6.74]; 0.531
Therapy discontinuation due to adverse events					
	51	4 (8)	52	2 (4)	2.04 [0.39; 10.65]; 0.530
Specific adverse events					

Gastrointestinal disorders (SOC, AE)	51	34 (67)	52	21 (40)	1.65 [1.13; 2.42]; 0.010

a. The results on overall mortality are based on the data on fatal AEs.
b. Physical functioning was assessed using the mFARS in the version with a total score of 93 points (scale range for the total score: 0 to 93 points). Lower values mean better symptomatology; negative effects mean an advantage for the intervention.
c. Lower values mean better symptomatology; negative effects mean an advantage for the intervention (scale range: 0 to 36).
d. Data according to dossier and resolution on the benefit assessment of omaveloxolone from 19.09.2024.
e. Improvement is defined as < 4 points (any improvement) in the PGI-C at week 48.
f. Deterioration is defined as > 4 points (any deterioration) in the PGI-C at week 48.
g. p value: IQWiG's own calculation
h. A decrease in score by ≥ 9.4 points at week 48 compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100).
i. A decrease in score by ≥ 9.6 points at week 48 compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100).

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; FA-ADL = Friedreich Ataxia-Activities of Daily Living; CI = confidence interval; mFARS = modified Friedreich Ataxia Rating Scale; MV = mean value; N = number of patients evaluated; n_E = number of events (total number of events across all patients); n = number of patients with (at least one) event; PGI-C = Patient Global Impression of Change; RR = relative risk; SD = standard deviation; SE = standard error; SF-36 = Short Form (36) Health Questionnaire; SOC = system organ class; SAE = serious adverse event; AE = adverse event; vs = versus

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

Adults and adolescents aged 16 years and older with Friedreich's ataxia

Approximately 990 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 Skyclarys (active ingredient: omaveloxolone) at the following publicly accessible link (last access: 15 October 2025):

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

Treatment with omaveloxolone should only be initiated and monitored by specialists experienced in treating patients with Friedreich's ataxia.

4. Treatment costs

Annual treatment costs:

Adults and adolescents aged 16 years and older with Friedreich's ataxia

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Omaveloxolone	€ 277,509.74
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: 15 October 2025)

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 and adolescents aged 16 years and older with Friedreich's ataxia

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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 website of the G-BA on 18 December 2025.

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

Berlin, 18 December 2025

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

Prof. Hecken