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
Sebetralstat (hereditary angioedema, acute treatment, ≥ 12 years)

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 Sebetralstat shall be added in alphabetical order as follows:

Sebetralstat

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 17 September 2025):

Ekterly is indicated for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults and adolescents aged 12 years and older.

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

Sebetralstat 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 and adolescents aged 12 years and older with an acute attack of hereditary angioedema</u>

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

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

Study results according to endpoints:[1]

Adults and adolescents aged 12 years and older with an acute attack of hereditary angioedema

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 of symptom improvement (PGI-C) and reduction in attack severity (PGI-S) within 4 hours.
Health-related quality of life	∅	No data available.
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		

KONFIDENT study: RCT with a 3x3 crossover design (treatment of 3 HAE attacks, each with 3 different study medications over 3 observation periods per subject). Only the HAE attacks in subjects who were treated with both the on-label dosage of 300 mg sebetralstat and placebo are relevant for the benefit assessment (2x2 crossover design with paired samples). The evaluations relate to the treated HAE attacks. Comparison of sebetralstat versus placebo over 2 observation periods at the survey time point within 4 hours of taking the study medication is shown.

Mortality

Endpoint	Sebetralstat N[1] = 87		Placebo N[1] = 84		Sebetralstat vs placebo
	N[2]	Subjects with event n (%)	N[2]	Subjects with event n (%)	Effect estimator
Deaths	86	0	83	0	–

[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

Endpoint	Sebetralstat N[1] = 87		Placebo N[1] = 84		Sebetralstat vs placebo
PGI-C: Number of qualifying HAE attacks[3] with confirmed symptom improvement, defined as at least *"slightly better"* at two consecutive time points					
	N[4]	N[5] (%)	N[4]	n[5] (%)	RR [95% CI]; p value
	61	44 (72.1)	61	28 (45.9)	1.57 [1.15; 2.16] 0.0047
PGI-S: Reduction in the severity of qualifying HAE attacks[3] by at least one point or more					
	N[4]	n[5] (%)	N[4]	n[5] (%)	RR [95% CI]; p value
	62	24 (38.7)	62	14 (22.6)	1.71 [1.02; 2.89] 0.0412
HAE symptoms using a visual analogue scale					
Improvement in abdominal pain on VAS by ≥ 15%					
	N[4]	n[5] (%)	N[4]	n[5] (%)	RR [95% CI]; p value
	61	15 (24.6)	61	10 (16.4)	1.5 [0.78; 2.90] 0.225
Improvement in skin pain on VAS by ≥ 15%					
	N[4]	n[5] (%)	N[4]	n[5] (%)	RR [95% CI]; p value
	61	15 (24.6)	61	8 (13.1)	1.88 [0.94; 3.75] 0.07
Improvement in skin swelling on VAS by ≥ 15%					
	N[4]	n[5] (%)	N[4]	n[5] (%)	RR [95% CI]; p value
	61	16 (26.2)	61	16 (26.2)	1.00 [0.59; 1.68] 1.0

Health-related quality of life

No data available.

Side effects

Endpoint **MedDRA system organ classes/ preferred terms/ AEs of special interest**	**Sebetralstat N[1] = 87**		**Placebo N[1] = 84**		**Sebetralstat vs placebo**
	N[2]	n (%)	N[2]	n (%)	Effect estimator
Adverse events in total (presented additionally)	86	17 (19.8)	83	17 (20.5)	–
Serious adverse events (SAEs)	86	1 (5.8)	83	0	n.d.
Severe adverse events (presented additionally)	86	1 (5.8)	83	0	n.d.
Study discontinuation due to adverse events	86	0	83	0	n.d.
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)					
No severe AEs ≥ 5%					
SAEs according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
No SAEs ≥ 5%					
Adverse events of special interest (with statistically significant difference between the treatment arms)					
No AEs of special interest were collected.					

1. The analysis population for the efficacy endpoints comprises all 110 randomised subjects who received an intervention as the study medication for at least one "qualifying" HAE attack. The attacks treated with 300 mg sebetralstat or placebo were collected as the unit of analysis; 87 HAE attacks were treated with sebetralstat and 84 HAE attacks with placebo.
2. The safety population refers to the HAE attack level and describes the adverse events that occurred during a subsequently observed HAE attack over a follow-up period of 48 hours.
3. HAE attacks with an event occurring within 4 hours. The KONFIDENT study included "eligible" HAE attacks. "Qualifying HAE attacks" were relevant for the analysis.
4. Analysis population taking into account the 2x2 crossover design with paired samples. This corresponds to subjects who have completed a treatment phase with the on-label dosage of 300 mg sebetralstat as well as a placebo.
5. HAE attacks with an event occurring within 4 hours.

Abbreviations used:
GA-NRS: General Anxiety Numerical Rating Scale; HAE: hereditary angioedema; n.d.: no data available; CI: confidence interval; N: number of HAE attacks that occurred, unless otherwise stated; n: number of HAE attacks with (at least one) event, unless otherwise stated; n.a.: not assessable; PGI-C: Patient Global Impression of Change; PGI-S: Patient Global Impression of Severity; RR: relative risk; (S)AE: (serious) adverse event; VAS: visual analogue scale

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

Adults and adolescents aged 12 years and older with an acute attack of hereditary angioedema

Approx. 1,000 to 1,100 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 Ekterly (active ingredient: sebetralstat) at the following publicly accessible link (last access: 4 February 2026):

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

Treatment with sebetralstat should only be initiated and monitored by specialists who are experienced in the treatment of patients with hereditary angioedema.

According to the product information, therapy discontinuation should be considered in patients with normal C1-INH (nC1-INH) if no clinical response is observed.

4. Treatment costs

Annual treatment costs:

Adults and adolescents aged 12 years and older with an acute attack of hereditary angioedema

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Sebetralstat[2]	€ 48,424.11 – € 289,988.08

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 and adolescents aged 12 years and older with an acute attack of hereditary angioedema

- No medicinal product with new active ingredients for use in combination therapy in compliance with 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 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 Ekterly 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.

[2] The annual treatment costs are **different from patient to patient** depending on the frequency of attacks. For the sake of comparability, the costs are indicated for a representative range from a lower limit of 1 attack every 3 weeks to an upper limit of 1 attack every week.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore conducted to a relevant extent 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