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
Eliglustat (new therapeutic indication: Gaucher disease type 1, ≥ 6 to < 18 years, ≥ 15 kg BW)

of 18 June 2025

At their session on 18 June 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. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Eliglustat in accordance with the resolution of 1 October 2015:

Eliglustat

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

New therapeutic indication (according to the marketing authorisation of 6 December 2024):

Cerdelga is indicated for paediatric patients with GD1 who are 6 years and older with a minimum body weight of 15 kg, who are stable on enzyme replacement therapy (ERT), and who are CYP2D6 PMs, IMs or EMs.

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

See new therapeutic indication according to marketing authorisation.

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

Eliglustat 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 determines 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).

> Children and adolescents who are 6 years and older with a minimum body weight of 15 kg with Gaucher disease type 1 (GD1) who are stable on enzyme replacement therapy (ERT) and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs)
>
> **Extent of the additional benefit and significance of the evidence of eliglustat:**
>
> Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Children and adolescents who are 6 years and older with a minimum body weight of 15 kg with Gaucher disease type 1 (GD1) who are stable on enzyme replacement therapy (ERT) and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	The data are not assessable.
Morbidity	n.a.	The data are not assessable.
Health-related quality of life	n.a.	The data are not assessable.
Side effects	n.a.	The data are not assessable.
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		

ELIKIDS study: single-arm open-label phase III study on eliglustat; data presented at week 52 (end of main treatment phase); long-term treatment phase not completed until week 104

Mortality

Endpoint	Eliglustat N = 51
	Patients with event n (%)
Overall mortality	
No deaths occurred.[a]	

Morbidity

Endpoint	Eliglustat N = 51	
	N	Patients with event n (%)
Bone pain		
Baseline		
No pain	51	49 (96.1)
Very mild pain	51	2 (3.9)

1 Data from the dossier assessment of the G-BA (published on 1. April 2025), and from the amendment to the dossier assessment from 30 May 2025, unless otherwise indicated.

Mild pain	51	0
Moderate pain	51	0
Severe pain	51	0
Very severe pain	51	0
Week 52[b]		
No pain	51	46 (90.2)
Very mild pain	51	2 (3.9)
Mild pain	51	3 (5.9)
Moderate pain	51	0
Severe pain	51	0
Very severe pain	51	0
Week 104[c] ***(presented additionally)***		
No pain	*36*	*33 (64.7)*
Very mild pain	*36*	*1 (2.0)*
Mild pain	*36*	*1 (2.0)*
Moderate pain	*36*	*1 (2.0)*
Severe pain	*36*	*0*
Very severe pain	*36*	*0*
Endpoint	**Eliglustat N = 51**	
	N	**MV (SD)**
Fatigue using the Paediatric Quality of Life Inventory Multidimensional Fatigue scale (PedsQL Fatigue)[d]		
Baseline	46	76.6 (17.7)
Week 52[b]	46	75.4 (20.1)
Change from baseline[e]	45	-1.2 (13.0)
Acute pain using the Paediatric Quality of Life Inventory (PedsQL) Paediatric Pain Questionnaire[f]		
Baseline	49	9.1 (20.1)
Week 52[b]	49	10.0 (19.5)
Change from baseline[e]	49	0.9 (21.5)
Week 104[c] *(presented additionally)*	*36*	*11.5 (22.0)*
Change from baseline[e]	*36*	*1.3 (21.0)*

Worst pain in the last 7 days using the Paediatric Quality of Life Inventory (PedsQL) Paediatric Pain Questionnaire[f]		
Baseline	49	13.2 (22.1)
Week 52[b]	49	14.7 (24.4)
Change from baseline[e]	49	1.4 (23.9)
Week 104[c] (presented additionally)	*36*	*24.6 (31.8)*
Change from baseline[e]	*36*	*11.0 (33.7)*
Spleen volume in multiples of normal[a]		
Baseline	46	3.35 (1.42)
Week 52[b]	46	3.25 (1.33)
Change from baseline[e]	46	-0.09 (0.84)
Week 104[c] (presented additionally)	*36*	*3.09 (1.40)*
Change from baseline[e]	*36*	*-0.29 (0.81)*

Quality of life

Endpoint	**Eliglustat N = 51**	
	N	**MV (SD)**
Quality of life using the Paediatric Quality of Life Inventory (PedsQL)[h]		
Baseline	45	80.3 (16.8)
Week 52[b]	46	79.5 (19.2)
Change from baseline[e]	44	-1.0 (10.6)

Side effects[i, j]

Endpoint MedDRA system organ classes/ AEs of special interest	**Eliglustat N = 51**	
	N	**Patients with event n (%)**
Total adverse events (presented additionally)	51	48 (94.1)
Serious adverse events (SAE)	51	5 (9.8)
Severe adverse events (CTCAE grade 3 or 4)[k]	51	4 (7.8)
Therapy discontinuation due to adverse events	51	7 (13.7)
Severe adverse events according to MedDRA system organ class (with an incidence ≥ 10%)		
No severe AEs with an incidence ≥ 10%		
SAEs according to MedDRA system organ class (with an incidence ≥ 10%)		
No SAE with an incidence ≥ 10%		
AEs of special interest[l] (with an incidence ≥ 10%)		
No AEs of special interest with an incidence ≥ 10%		

Endpoint MedDRA system organ classes/ AEs of special interest	**Eliglustat** **N = 51**	
	N	**Patients with event** **n (%)**
a. The result relates to the survey period up to the data cut-off from 21 June 2023. At this point in time, 48 patients had completed the main treatment phase and 38 patients had completed the long-term treatment phase. b. In the case of missing values at week 52 or study discontinuation or switch to rescue therapy before week 52, the last available values of eliglustat monotherapy were used for the analysis. c. Only those patients who did not have missing values at week 104 were included in the analyses. d. Scale from 0 to 100; higher values indicate lower stress due to fatigue. e. According to the protocol, the descriptive results for the change from baseline were calculated using parametric and non-parametric methods depending on the distributions of the observed values. A specific calculation method for determining the change from baseline could not be found in the study documents. f. Item range from 0 to 100 in each case. A total score was not calculated, the presentation is per item. Higher values reflect greater pain intensity. g. Spleen MN = volume (cm^3) / 2 x weight (kg) h. Scale from 0 to 100; higher values mean higher quality of life. i. The safety endpoints were the primary endpoint of the ELIKIDS study. j. Only AEs that occurred during primary eliglustat monotherapy are shown here. AEs after the switch to rescue therapy are not included in the presentation. The results relate to the survey period up to the data cut-off from 21 June 2023. k. In Module 4, the presentation is based on CTCAE, although it remains unclear whether this assignment was made post hoc. l. Results for the AE of special interest "Peripheral neuropathy" could not be obtained from the study documents.		
Abbreviations used: CTCAE = Common Terminology Criteria for Adverse Events; MN = multiples of normal; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; PedsQL = Paediatric Quality of Life Inventory; SD = standard deviation; SAE = serious adverse event; AE = adverse event; vs = versus		

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

Children and adolescents who are 6 years and older with a minimum body weight of 15 kg with Gaucher disease type 1 (GD1) who are stable on enzyme replacement therapy (ERT) and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs)

Approx. 10 – 30 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 Cerdelga (active ingredient: eliglustat) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 15 May 2025):

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

Treatment with eliglustat should only be initiated and monitored by specialists who are experienced in the treatment of patients with Gaucher disease.

Prior to treatment with eliglustat, patients must undergo CYP2D6 genotyping to determine their CYP2D6 metabolisation status. Eliglustat should not be used in patients who are ultra-rapid metabolisers (URMs) with regard to CYP2D6 or in patients with an unclear metabolisation type.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients including a therapy pass.

4. Treatment costs

Annual treatment costs:

Children and adolescents who are 6 years and older with a minimum body weight of 15 kg with Gaucher disease type 1 (GD1) who are stable on enzyme replacement therapy (ERT) and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Eliglustat[2]	€ 165,573.55[3] - € 331,147.11[4]
Additionally required SHI services:	€ 308.50
Total:	€ 165,882.05[3] - € 331,455.61[4]

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 June 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:

Children and adolescents who are 6 years and older with a minimum body weight of 15 kg with Gaucher disease type 1 (GD1) who are stable on enzyme replacement therapy (ERT) and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs)

2 As Cerdelga® is not yet available in Germany at the potency of 21 mg, the annual treatment costs for children and adolescents with a body weight ≥ 15 to < 25 kg (regardless of metabolisation status) or those with a body weight ≥ 25 to < 50 kg who are CYP2D6 poor metabolisers (PMs) cannot be calculated here.
3 The lowest annual treatment costs presented here are for children and adolescents 6 years and older with a body weight ≥ 50 kg, who are CYP2D6 poor metabolisers (PMs).
4 The highest annual treatment costs presented here are for children and adolescents 6 years and older with a body weight ≥ 25 kg who are CYP2D6 intermediate metabolisers (IMs) or CYP2D6 extensive metabolisers (EMs).

- No medicinal product with new active ingredients that can be used in a combination therapy and 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 June 2025.

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

Berlin, 18 June 2025

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

Prof. Hecken