

# Justification

of the Resolution of the Federal Joint Committee (G-BA) 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,  $\geq 6$  to  $< 18$  years,  $\geq 15$  kg BW)

of 18 June 2025

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## 1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of all reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to 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. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover threshold according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the G-BA must

be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

## **2. Key points of the resolution**

The active ingredient eliglustat (Cerdelga) was listed for the first time on 1 April 2015 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 6 December 2024, eliglustat received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

Eliglustat for the treatment of Gaucher disease type 1 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.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the approval studies by the G-BA.

On 20 December 2024, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient eliglustat with the new therapeutic indication "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" in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication).

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 1 April 2025 together with the IQWiG assessment on the website of the G-BA ([www.g-ba.de](http://www.g-ba.de)), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA has adopted their resolution on the basis of the dossier of the pharmaceutical company, the dossier evaluation carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G12-01) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA has evaluated the studies relevant for the marketing authorisation with regard to their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7,

sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods <sup>1</sup> was not used in the benefit assessment of eliglustat.

## **2.1 Additional benefit of the medicinal product**

### **2.1.1 Approved therapeutic indication of Eliglustat (Cerdelga) in accordance with the product information**

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 the approved therapeutic indication

### **2.1.2 Extent of the additional benefit and significance of the evidence**

In summary, the additional benefit of eliglustat is assessed as follows:

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)

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

Justification:

For the benefit assessment, the pharmaceutical company submitted the results of the ELIKIDS study. This is a multicentre, open-label, uncontrolled and non-randomised phase III study to investigate the safety, efficacy and pharmacokinetics of eliglustat.

A total of 57 patients aged  $\geq 2$  to  $< 18$  years with a body weight  $> 10$  kg and a clinical diagnosis of Gaucher disease type 1 (GD1) or type 3 (GD3) were enrolled in the study.

The study population was divided into two cohorts: Cohort 1 of the study, relevant for the present benefit assessment, enrolled 51 patients (46 with GD1 and 5 with GD3) who had been receiving enzyme replacement therapy (ERT) for at least 24 months and had no severe clinical GD-related manifestations (defined according to specific criteria based on haemoglobin level, platelet count, spleen and liver volume and the absence of GD-related lung and bone disease). According to the approved therapeutic indication, eliglustat should be used in patients with GD1 who are stable on ERT. However, the product information does not contain any specific requirements regarding a definition of the stable course on ERT required according to the marketing authorisation.

The results of the total population of cohort 1 are used here since only a small percentage of the patients included in cohort 1 deviated from the target population of the approved therapeutic indication in terms of age  $< 6$  years (3 patients corresponding to 6 per cent) or in terms of GD type 3 (5 patients corresponding to 10 per cent). It should also be mentioned that

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<sup>1</sup> General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

only one CYP2D6 PM or IM patient was enrolled in the ELIKIDS study, which means that only a few results are available for this sub-population covered by the approved therapeutic indication.

Cohort 2 enrolled 6 patients who had pre-specified severe clinical GD-related manifestations despite treatment with ERT for at least 36 months. These patients received eliglustat in combination with imiglucerase during the study. In accordance with the pharmaceutical company's estimate in the dossier, only the results for cohort 1 are considered relevant for the present benefit assessment, as cohort 2 is not considered "stable" due to the presence of severe disease manifestations on ERT, thus not corresponding to the target population covered by the approved therapeutic indication.

Screening was followed by the main treatment phase (MTP) up to week 52 and a subsequent long-term treatment phase (LTP) up to week 104 with an optional transition to an extension phase up to week 364 at the latest. During MTP and LTP, patients in cohort 1 received eliglustat.

In the event of clinical deterioration according to pre-specified criteria, a switch to rescue therapy with imiglucerase was possible, whereby study participation and continued observation were to be continued even after the switch to rescue therapy. Overall, rescue therapy was given to 3 patients as part of MTP and 3 patients as part of LTP respectively. Concomitant medications, e.g. analgesics were also used in the study.

The primary analysis was planned for week 52 after the end of the MTP. In the dossier, the data cut-off from 21 June 2023 was presented. At this point in time, 48 patients had completed MTP and 3 patients had prematurely discontinued MTP; 38 patients had completed LTP and one patient had prematurely discontinued LTP. In view of the incomplete data maturity achieved at week 104, the results at week 52 are used here; the results at week 104 are presented additionally. However, the return rates for the endpoints of quality of life and fatigue using the Paediatric Quality of Life Inventory (PedsQL) and PedsQL Fatigue were only 60.8 per cent of the total study population at week 104, meaning that the corresponding results are not presented.

Parameters of pharmacokinetics and adverse events were collected as the primary endpoints.

#### *On the dosage regimen in the ELIKIDS study*

The initially planned dosage regimen for EMs and IMs with a body weight of 15 to < 25 kg and 25 to < 50 kg was assessed during the study as being unsuitable for achieving the target exposure of eliglustat. Since the dosage regimen for the total of 22 patients in the concerned study sub-population was subsequently adjusted by increasing the dose during the study and no further information is available on the number and timing of dose adjustments during the study, it is unclear over what period of time the concerned patients were treated with a dose of eliglustat in compliance with the marketing authorisation as part of the study. A further deviation from the marketing authorisation results from the use of an oral suspension solution (instead of hard capsules) in 4 patients (corresponding to 8% of the total study population) as part of the study.

#### Results of the ELIKIDS study at week 52

##### Mortality

Deaths were collected as part of the safety assessment. No deaths occurred up to the data cut-off from 21 June 2023.

The single-arm study design does not allow a comparative assessment of the data; no statement can be made on the extent of the additional benefit based on the endpoint of mortality.

## Morbidity

### *Bone pain*

The endpoint of bone pain was assessed in the ELIKIDS study using a patient-reported question about the intensity of bone pain in the last 4 weeks with 6 predefined response options.

At the start of the study, 96% of patients had no pain and 4% had very mild pain. After 52 weeks, 90% of patients were still pain-free, while 4% reported very mild and 6% mild pain.

During the study, both analgesics and topical products were used for joint and muscle pain in 45% of patients, which may lead to bias of the results of the endpoint.

The single-arm study design does not allow a comparative assessment of the data; no statement can be made on the extent of the additional benefit based on the endpoint of bone pain.

### *Fatigue using the Paediatric Quality of Life Inventory Multidimensional Fatigue scale (PedsQL Fatigue)*

PedsQL Fatigue is an additional module to PedsQL for assessing fatigue, for which different versions exist depending on age and the presence of a child or parent report. Values from 0 to 100 can be achieved; higher values indicate lower stress due to fatigue.

For the benefit assessment, the evaluations based on self-reports that are available for patients 5 years and older are used. In contrast to 51 patients in the total population, 47 patients were surveyed for the PedsQL Fatigue and Generic Core Scales and 49 patients for the PedsQL Paediatric Pain (see below). Information on the reasons for the incomplete survey cannot be found in the dossier. Overall, results on PedsQL Fatigue are available for a total of 46 patients.

The mean value was 76.6 points at baseline and 75.4 points at week 52. There were therefore no pronounced numerical changes in the course of the study.

With regard to the change from baseline, no specific calculation method can be found in the study documents. This also applies to all endpoints in the categories of morbidity and quality of life presented below.

The single-arm study design does not allow a comparative assessment of the data; no statement can be made on the extent of the additional benefit based on the endpoint of fatigue.

### *Pain using the Paediatric Quality of Life Inventory (PedsQL) Paediatric Pain Questionnaire*

The PedsQL Paediatric Pain surveys the extent of the current pain ("acute pain") and the worst pain in the last 7 days as well as the localisation of the pain. The first two items are assessed using a visual analogue scale (VAS) from 0 (not painful/ no pain) to 100 (very painful/ severe pain).

Similar to the PedsQL Fatigue, the evaluations based on self-reports are used for the endpoints "acute pain" and "worst pain in the last 7 days"; results are available for 49 patients in each case.

The mean value for the current pain was 9.1 points at baseline and 10.0 points at week 52. The mean values for the worst pain in the last 7 days were 13.2 points at baseline and 14.7 points at week 52. There were therefore no pronounced numerical changes in the course of the study.

The single-arm study design does not allow a comparative assessment of the data; no statement can be made on the extent of the additional benefit based on the endpoints of "acute pain" and "worst pain in the last 7 days".

### *Spleen volume*

In the ELIKIDS study, spleen volume was assessed using abdominal magnetic resonance imaging (MRI). The spleen volume was evaluated by calculating the "multiple of normal" (MN), which takes into account the individual body weight.

Evaluations are available for 46 patients. The average value in MN was 3.35 at baseline and 3.25 at week 52. Overall, the spleen volume thus remained largely stable over the course of the study.

A long-lasting reduction of the pathologically elevated spleen volume combined with a noticeable decrease of impairing disease symptoms and improvement in the quality of life for the patient is considered to be patient-relevant. A prolonged reduction of the pathologically increased spleen volume is patient-relevant in the present therapeutic indication due to the risk of splenectomy and the risk of splenic rupture.

However, a comparative assessment of the data is not possible in this case due to the single-arm study design. No statement can be made on the extent of the additional benefit on the basis of the endpoint of spleen volume.

### *Body weight and body height*

Anthropometric parameters are assessed as patient-relevant morbidity parameters, especially in children with characteristic, disease-related growth failures. Data adjusted for age and sex are preferred to absolute values.

For the endpoint of body weight, only results in kg which were not adjusted for age and sex are available.

Separate evaluations by sex are available for body height, which were standardised according to the information provided by the pharmaceutical company in the written statement procedure using reference data from the World Health Organisation (WHO). However, an unusually high maximum z score is given for both sexes at baseline and at week 52, which could indicate a calculation error. As already explained, a specific calculation method for the change from baseline cannot be obtained from the study documents.

In addition, the information submitted by the pharmaceutical company show uncertainties with regard to operationalisation. The dossier does not contain any specific information on the collection of body measurements as part of the study. For example, it remains unclear whether only one measurement was taken per survey time point or whether several measurements were taken and then averaged.

In view of the limitations described above, the data on body weight and body height are not used here.

### *Mobility*

The endpoint of mobility is generally considered patient-relevant in the present therapeutic indication.

However, based on the dossier and taking into account the written statement procedure, there are some contradictory information on the operationalisation of the endpoint. It is not possible to conclusively determine whether the mobility status survey was based on a self-assessment by the patients or on an external assessment by a principal investigator and whether a standardised research question was used. The reference period is also not clearly evident due to the inadequately specified information. Overall, unrestricted comparability of the individual surveys cannot be assumed with certainty. The validity can also not be assessed due to the lack of clarity regarding the operationalisation.

Against the background of the limitations mentioned, the evaluations of the mobility endpoint are not used here.

### Quality of life

Health-related quality of life was assessed using the Paediatric Quality of Life Inventory (PedsQL).

The Generic Core Scales module surveys physical, emotional and social aspects and is considered suitable for the quality of life category. There are different versions of the questionnaire depending on age and the presence of a child or parent report. Values from 0 to 100 can be achieved; higher values indicate a higher quality of life.

In contrast, the Family Impact module assesses the effects of chronic illnesses on relatives and is not taken into account due to the lack of patient relevance.

As with PedsQL Fatigue and Paediatric Pain, the evaluations based on self-reports are used here; results are available for 46 patients.

The mean value was 80.3 points at baseline and 79.5 points at week 52. There were therefore no pronounced numerical changes in the course of the study.

The single-arm study design does not allow a comparative assessment of the data; no statement can be made on the extent of the additional benefit for the quality of life category.

### Side effects

In addition to parameters of pharmacokinetics, side effects were assessed as primary endpoints of the ELIKIDS study. The present evaluations only include adverse events (AEs) that occurred during treatment with eliglustat as part of the study. 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.

A severe AE occurred in 4 patients (8%); 5 patients (10%) suffered a serious adverse event (SAE) and 7 patients (14%) suffered an AE that led to discontinuation of the study medication.

The single-arm study design does not allow a comparative assessment of the data; no statement can be made on the extent of the additional benefit for the side effects category.

### Overall assessment

The benefit assessment of eliglustat for the treatment of 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) is based on the results of the single-arm ELIKIDS study.

Results on mortality, health status, health-related quality of life and side effects are available. Due to the single-arm study design, no comparative statements can be made, which is why it is not possible to quantify the extent of the additional benefit on the basis of the data presented.

In the overall assessment of the available results, the G-BA classified the extent of the additional benefit of eliglustat for the treatment of 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) as non-quantifiable since the scientific data does not allow quantification.

### Significance of the evidence

The present benefit assessment is based on single-arm data. The risk of bias is estimated to be high in view of the lack of comparison at study and endpoint level. In addition, the study shows further limitations, in particular due to deviations from the marketing authorisation with regard to the study population and the dosage of eliglustat used in the study in terms of the adjustment of the dosage regimen of a study sub-population over the course of the study.

The significance of the evidence is classified as a "hint" overall.

### **2.1.3 Summary of the assessment**

This is the benefit assessment of a new therapeutic indication for the active ingredient eliglustat. The medicinal product Cerdelga was approved as an orphan drug. The present therapeutic indication assessed is as follows: "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."

For the benefit assessment, the pharmaceutical company presented the results of the multicentre, single-arm, open-label phase III ELIKIDS study to investigate the safety, pharmacokinetics and efficacy of eliglustat in children and adolescents with Gaucher disease type 1.

No statements on the extent of the additional benefit can be derived on the basis of the results presented due to the single-arm study design of the ELIKIDS study. In addition, the study has further limitations, in particular due to deviations from the marketing authorisation with regard to the study population and the dosage of eliglustat used in the study.

In the overall assessment, a hint for a non-quantifiable additional benefit of eliglustat for the treatment of 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) was identified, since the scientific data does not allow quantification.

## **2.2 Number of patients or demarcation of patient groups eligible for treatment**

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The resolution is based on the information on patient numbers from the dossier of the pharmaceutical company. These are based on a determination of the number of paediatric patients with Gaucher disease type 1 (GD1) in Germany using, among others, the results of a survey conducted in Gaucher study sites in 2021 (lower limit) and a survey conducted by the European Gaucher Alliance (now the International Gaucher Alliance) between 2012 and 2013 (upper limit). In further steps, the percentages of patients aged 6 to 17 years and those who are CYP2D6 PMs, IMs or EMs are determined.

Limitations of this approach arise due to uncertainties with regard to the data basis used to determine the number of patients with GD1. Overall, the data on the number of patients is subject to uncertainties.

## **2.3 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](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 metabolism status. Eliglustat should not be used in patients who are ultra-rapid metabolisers (URMs) with regard to CYP2D6 or in patients with an unclear metabolism 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.

## 2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 June 2025).

### Treatment period:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Eliglustat	Continuously, 1 - 2 x daily	365.0	1	365.0

### Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
<i>Children and adolescents 6 years and older with a body weight <math>\geq 25</math> kg; EMs and IMs</i>					
Eliglustat	84 mg	168 mg	2 x 84 mg	365.0	730 x 84 mg
<i>Children and adolescents 6 years and older with a body weight <math>\geq 50</math> kg; PMs</i>					
Eliglustat	84 mg	84 mg	1 x 84 mg	365.0	365 x 84 mg
<i>Children and adolescents 6 years and older with a body weight <math>\geq 25</math> to <math>&lt; 50</math> kg; PMs</i>					
Eliglustat	42 mg	42 mg	2 x 21 mg	365.0	730 x 21 mg
<i>Children and adolescents 6 years and older with a body weight <math>\geq 15</math> to <math>&lt; 25</math> kg; EMs and IMs</i>					
Eliglustat	42 mg	84 mg	4 x 21 mg	365.0	1,460 x 21 mg
<i>Children and adolescents 6 years and older with a body weight <math>\geq 15</math> to <math>&lt; 25</math> kg; PMs</i>					
Eliglustat	21 mg	21 mg	1 x 21 mg	365.0	365 x 21 mg

### Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates

in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Since the medicinal product Cerdelga® with the active ingredient eliglustat is currently not available in Germany in a potency of 21 mg, the costs for this cannot be quantified.

### Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Eliglustat 84 mg	196 HC	€ 88,912.50	€ 1.77	€ 0.00	€ 88,910.73
Eliglustat 21 mg	Not calculable				
<u>Abbreviations:</u> HC = hard capsules					

LAUER-TAXE® last revised: 1 June 2025

### Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

According to the product information for Cerdelga®, all patients must undergo CYP2D6 genotyping to determine their metabolisation status prior to treatment with eliglustat. This is accordingly considered as an additionally required SHI service for the cost representation.

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient
Medicinal product to be assessed				
Eliglustat	Genotyping to determine the CYP2D6 metabolisation status			
	GOP 32865	1	€ 308.50	€ 308.50

## 2.5 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

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed

medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

### Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

### Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

### Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

### Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

### Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

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.

### Justification for the findings on designation in the present resolution:

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)

- 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.

#### References:

Product information for eliglustat (Cerdelga); Cerdelga ® 21 mg/84 mg; last revised: December 2024

### 3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

### 4. Process sequence

On 20 December 2024, the pharmaceutical company submitted a dossier for the benefit assessment of eliglustat to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 1 April 2025 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA ([www.g-ba.de](http://www.g-ba.de)), thus initiating the written statement procedure. The deadline for submitting statements was 22 April 2025.

The oral hearing was held on 5 May 2025.

An amendment to the benefit assessment with a supplementary assessment was submitted on 30 May 2025.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 11 June 2025, and the draft resolution was approved.

At their session on 18 June 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

### Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	25 March 2025	Information of the benefit assessment of the G-BA
Working group Section 35a	30 April 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	5 May 2025	Conduct of the oral hearing
Working group Section 35a	14 May 2025 4 June 2025	Consultation on the dossier evaluation by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and

		the evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 June 2025	Concluding discussion of the draft resolution
Plenum	18 June 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 18 June 2025

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

Prof. Hecken