Gemeinsamer Bundesausschuss

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 Albutrepenonacog alfa (exceeding € 50 million turnover limit: haemophilia B, congenital factor IX deficiency)

of 7 April 2022

Contents

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 reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment 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 albutrepenonacog alfa (Idelvion) was listed for the first time on 1 June 2016 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. Idelvion® indicated for the treatment of haemophilia B is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

In its session on 1 December 2016, the G-BA decided on the benefit assessment of albutrepenonacog alfa in the therapeutic indication "Treatment and prevention of bleeding in patients with haemophilia B (congenital factor IX deficiency)" in accordance with Section 35a SGB V.

If the sales of the orphan drug through the statutory health insurance at pharmacy sales prices and outside the scope of SHI-accredited medical care, including value-added tax, exceed an amount of € 50 million in the last twelve calendar months, the pharmaceutical company must

submit evidence in accordance with Section 5, paragraphs 1 to 6 within three months of being requested to do so by the Federal Joint Committee, and in this evidence must demonstrate the additional benefit compared to the appropriate comparator therapy.

By letter dated 12 July 2021, the pharmaceutical company was requested to submit a dossier for the benefit assessment according to Section 35a SGB V by 15 October 2021, due to exceeding the € 50 million turnover limit within the period from May 2020 to April 2021. The pharmaceutical company has submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, number 1 VerfO on 15 October 2021.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de) on 17 January 2022, thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of albutrepenonacog alfa compared to the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. order to determine the extent of the additional benefit, the G-BA assessed the data justifying the finding of an additional benefit in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO on the basis of their therapeutic relevance (qualitative). The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of albutrepenonacog alfa.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

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

2.1.1 Approved therapeutic indication of Albutrepenonacog alfa (Idelvion) according to the product information

Treatment and prophylaxis of bleeding in patients with haemophilia B (congenital factor IX deficiency).

Idelvion can be used for all age groups.

Therapeutic indication of the resolution (resolution of 7 April 2022):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Patients of all age groups with haemophilia B (congenital factor IX deficiency)

appropriate comparator therapy for albutrepenonacog alfa:

recombinant or human plasma-derived coagulation factor IX preparations

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. Currently, various plasma-derived and recombinant coagulation factor IX products are approved for the treatment of haemophilia B.

- Recombinant factor IX products contain the genetically engineered human factor IX glycoprotein:
  - Nonacog alfa and nonacog gamma differ in glycosylation, but both contain the natural human factor IX glycoprotein with the complete amino acid sequence
  - Albutrepenonacog alfa is a recombinant fusion protein of the human factor IX glycoprotein and albumin
  - Nonacog beta pegol is a recombinant human factor IX with a polyethylene glycol (PEG)
  - Eftrenonacog alfa is a recombinant fusion protein of the human factor IX glycoprotein and the Fc domain of human IgG1
- Human plasma factor IX preparations[2] contain the human-identical factor IX glycoprotein obtained from cryoprecipitates. They are obtained from large human plasma pools and are approved for the treatment and prevention of haemophilia B.
- Combination preparations of coagulation factors II, VII, IX and X[3] are approved for the treatment of bleeding and for perioperative prevention in cases of hereditary deficiency of one of the vitamin K-dependent coagulation factors if no purified specific coagulation product is available.
- A human plasma fraction enriched with factor VIII inhibitor bypassing activity is approved for the treatment and prevention of bleeding in haemophilia B patients with FIX inhibitor.

[2] Various proprietary medicinal products are available.
[3] Various proprietary medicinal products are available.

- A recombinant blood coagulation factor VIIa preparation (active ingredient: Eptacog alfa) is approved for the treatment of bleeding and prevention of bleeding associated with surgical or invasive procedures in, among others, patients with congenital haemophilia with inhibitors of coagulation factor IX. It is not approved for the permanent treatment of haemophilia B requiring replacement.

on 2. A non-medicinal treatment cannot be considered as an appropriate comparator therapy in this therapeutic indication.

on 3. There are three resolutions of the G-BA in the therapeutic indication "haemophilia B", for albutrepenonacog alfa dated 1 December 2016, for eftrenonacog alfa dated 15 December 2016 and for nonacog beta pegol dated 19 April 2018.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present therapeutic indication. The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a paragraph 7 SGB V.

It is assumed that the patient population in the present indication is haemophilia patients requiring factor IX replacement.

In summary, there is little evidence for the treatment of haemophilia B. No evidence-based data were found on the therapeutic efficacy or on the side-effect profile or safety risk that would lead to a preference for therapy with recombinant or factor IX preparations obtained from human plasma in the prevention of bleeding or treatment of haemophilia B. Direct comparator studies of plasma-derived and recombinant factor IX products are not available.

From the available G-BA resolutions on the benefit assessment of the two low-frequency recombinant factor IX preparations (active ingredients eftrenonacog alfa, nonacog beta pegol), it is also not possible to derive any statements on the comparative efficacy, safety and comparative side effect profile compared to other recombinant or plasma-derived factor IX products, as no comparator studies were available. A human plasma fraction enriched with factor VIII inhibitor bypassing activity is only approved for patients with existing factor IX inhibitors and is therefore not considered as an appropriate comparator therapy for the present therapeutic indication.

In the overall view of the body of evidence, the recombinant and human plasma-derived factor IX preparations are to be regarded as equivalent and are therefore equally eligible as appropriate comparator therapy.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

2.1.3 Extent and probability of the additional benefit

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

For patients of all age groups with haemophilia B (congenital factor IX deficiency), an additional benefit of albutrepenonacog alfa compared to the appropriate comparator therapy has not been proven.

Justification:

For the assessment of the additional benefit of albutrepenonacog alfa for the treatment of patients of all age groups with haemophilia B (congenital factor IX deficiency), the pharmaceutical company did not submit a direct comparator study regarding the appropriate comparator therapy, but descriptive comparisons of the results of individual arms of different studies as well as supplementary matching-adjusted indirect comparisons (MAIC) of individual endpoints. These indirect (adjusted) comparisons are not suitable for deriving an additional benefit of albutrepenonacog alfa compared with the appropriate comparator therapy.

The pharmaceutical company descriptively compares the results of the open-label, non-controlled, multicentre CSL654_2004, CSL654_3001, CSL654_3002, CSL654_3003 and CSL654_5005 studies on albutrepenonacog alfa with the results from the open-label, non-controlled, multicentre studies on eftrenonacog alfa (B-LONG, Kids B-LONG, B-YOND). These are results from the endpoint categories of mortality, morbidity, health-related quality of life and side effects.

The purely descriptive comparison of the results of individual arms of different studies is not suitable for deriving the additional benefit. Furthermore, the pharmaceutical company does not examine the similarity of the studies for intervention and comparison.

In addition, MAIC analyses for the endpoints of annualised bleeding rate and factor consumption in prevention were submitted by the pharmaceutical company. Individual patient data (CSL654_3001) were used for albutrepenonacog alfa and aggregated data for the study on eftrenonacog alfa (B-LONG).

MAIC analyses without a bridge comparator are generally not an adequate way to adjust for confounders. In the case of non-randomised comparisons without a bridge comparator, only those procedures that are carried out using individual patient data, in contrast to MAIC analysis, are generally useful for confounder adjustment. In contrast, the MAIC analysis accounts for confounding based on aggregate data. Thus, the comparisons based on MAIC analyses submitted by the pharmaceutical company are not suitable for the assessment of the additional benefit of albutrepenonacog alfa.

Intravenous injection every 2 to 3 days, given the severity of the disease, may potentially be a limitation in quality of life in certain patient groups, particularly children. However, the data presented showed no evidence of a clinically relevant improvement in quality of life due to the reduction in the required injection frequency, as the data as a whole could not be used to assess an additional benefit.

2.1.4 Summary of the assessment

The present assessment is a new benefit assessment of the active ingredient albutrepenonacog alfa due to the exceeding of the € 50 million turnover limit.

Idelvion (active ingredient albutrepenonacog alfa) has been approved as an orphan drug and is used for the treatment and prevention of bleeding in patients of all age groups with haemophilia B (congenital Factor IX deficiency).

The G-BA determined recombinant or human plasma-derived blood coagulation factor IX preparations to be the appropriate comparator therapy.

For the assessment of the additional benefit of albutrepenonacog alfa for the treatment of patients of all age groups with haemophilia B (congenital factor IX deficiency), the pharmaceutical company did not submit any direct comparator study compared to the appropriate comparator therapy. The analyses presented are unsuitable for deriving an additional benefit of albutrepenonacog alfa compared to the appropriate comparator therapy.

In the overall assessment, an additional benefit of albutrepenonacog alfa for this patient population compared to the appropriate comparator therapy is not proven.

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 G-BA's resolution is based on the patient numbers stated in the pharmaceutical company's dossier. These are updated figures compared to the initial assessment from 2016, taking into account more recent data on prevalence and incidence.

The figures are within a plausible upper limit range. The lower limit is underestimated.

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 Idelvion (active ingredient: albutrepenonacog alfa) at the following publicly accessible link (last access: 19 January 2022):

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

Treatment with albutrepenonacog alfa should only be initiated and monitored by doctors experienced in treating patients with haemophilia B.

The safety and efficacy of Idelvion in previously untreated patients has not yet been established.

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: 15 March 2022). The costs of treatment on demand for haemophilia B patients vary from person to person and are not shown. Only the costs of prevention therapy are presented.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient /year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Albutrepenonacog alfa	Continuously, 1 x every 7 days or every 10 to 14 days	52.1 or 26.1 – 36.5	1	52.1 or 26.1 – 36.5
Appropriate comparator therapy				
Recombinant blood coagulation factor IX				
Nonacog alfa	Continuously, every 3 - 4 days or every 3 to 7 days	91.3 – 121.7 or 52.1 – 121.7	1	91.3 – 121.7 or 52.1 – 121.7
Nonacog beta pegol	Continuously, every 7 days	52.1	1	52.1
Nonacog gamma	Continuously, every 3 - 4 days	91.3 – 121.7	1	91.3 – 121.7
Eftrenonacog alfa	Continuously, every 7 - 10 days	36.5 – 52.1	1	36.5 – 52.1
Blood coagulation factor IX derived from human blood plasma				
Human plasma-derived preparations[4]	Continuously, every 3 - 4 days	91.3 – 121.7	1	91.3 – 121.7

Consumption:

The consumption of factor IX preparations in patients with haemophilia B is patient-individual and depends on the respective demand. For this reason, the consumption of the patient-individual therapy on demand cannot be determined.

The theoretical annual consumption of albutrepenonacog alfa and the active ingredients (factor IX preparations) of the appropriate comparator therapy required for the prevention of

[4] Cost representation based on the information in the Haemonine® product information. Other proprietary medicinal products are available.

bleeding in patients with haemophilia B is presented. Consumption is calculated per injection for the relevant age groups (children aged below 6 years, children aged 6 to below 12 years, adolescents aged 12 to below 18 years and adults) according to the respective product information. For the calculation of the consumption of medicinal products to be dosed according to weight, the G-BA generally uses non-indication-specific average weights as a basis. Therefore, an adult male's average weight of 85 kg[5] is assumed for the body weight, according to the official representative statistics "Microcensus 2017 – Body measurements of the population". For the underlying average weight (kg) in the respective male age group below 18 years, the mean value of the age group was used: 12 to below 18 years: 61.8 kg; 6 to below 12 years: 32.7 kg; below 6 years: 15.1 kg.

Albutrepenonacog alfa is administered at doses of 35 to 50 IU per kg body weight once a week and well-set patients can be treated with up to 75 IU per kg body weight at intervals of 10 or 14 days. For the cost representation, only the maximum dose of 75 IU was considered for the second dosing scheme. According to the product information, nonacog alfa is administered in patients 6 years and older at the dosage of 40 IU per kg body weight every 3 to 4 days. In children aged below 6 years, nonacog alfa is given at a dose of 63.7 IU per kg body weight every 3 to 7 days. For nonacog beta pegol, the dosing scheme for adults and children aged 12 years and older is 40 IU per kg body weight (once a week) according to product information. For nonacog gamma, the dosing scheme for adults and children aged 12 years and older is 40 to 60 IU per kg body weight every 3 to 4 days. In children aged below 12 years, a dosage of 40 to 80 IU per kg body weight is administered every 3 to 4 days. The treatment regimen of eftrenonacog alfa according to the product information in patients aged 12 years and older is 50 IU per kg body weight once weekly or 100 IU per kg body weight once every 10 days. For children aged below 12 years, the recommended starting dose is 50-60 IU per kg BW every 7 days.

Shorter dosing intervals or higher doses may be required in some cases, especially in younger patients.

Since factor IX preparations are only stable for a maximum of 8 hours after reconstitution and therefore cannot be stored, discarding must be taken into account, consequently the consumption per injection is presented.

The consumption of vials was divided into optimum packaging sizes on the basis of the weight-adjusted requirement of IU factor IX/ injection. For example, for an adult requiring 2,975 IU/ injection, this was composed of two vials of 2,000 IU and 1,000 IU factor IX each.

[5] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

Designation of the therapy	Dosage (IU per kg BW)	Dose/ patient/ treatment day (IU)	Consumption by potency (IU) per treatment day	Treatment days/ patient/ year	Average annual consumption by potency (VIA)[6]
Medicinal product to be assessed					
Albutrepenonacog alfa	35 – 50	Adults			
		2,975 – 4,250	1 x 2,000 1 x 1,000 to 1 x 3,500 1 x 250 1 x 500	52.1	52.1 x 2,000 52.1 x 1,000 to 52.1 x 3,500 52.1 x 250 52.1 x 500
		12 - < 18 years			
		2,163 – 3,090	1 x 2,000 1 x 250 to 1 x 2,000 1 x 1,000 1 x 250	52.1	52.1 x 2,000 52.1 x 250 to 52.1 x 2,000 52.1 x 1,000 52.1 x 250
		6 - < 12 years			
		1,144.5 – 1,635	1 x 1,000 1 x 250 to 1 x 1,000 1 x 500 1 x 250	52.1	52.1 x 1,000 52.1 x 250 to 52.1 x 1,000 52.1 x 500 52.1 x 250
		< 6 years 528.5 - 755	1 x 500 1 x 250 to 1 x 1,000	52.1	52.1 x 500 52.1 x 250 to 52.1 x 1,000
	75	Adults			
		6,375	1 x 3,500 1 x 2,000 1 x 1,000	26.1 – 36.5	26.1 x 3,500 26.1 x 2,000 26.1 x 1,000 to 36.5 x 3,500 36.5 x 2,000 36.5 x 1,000
		12 - < 18 years			
		4,635	1 x 3,500 1 x 1,000 1 x 250	26.1 – 36.5	26.1 x 3,500 26.1 x 1,000 26.1 x 250 to 36.5 x 3,500 36.5 x 1,000 36.5 x 250

[6] The annual average consumption of vials was based on the most economical splitting of IU required per injection.

Designation of the therapy	Dosage (IU per kg BW)	Dose/ patient/ treatment day (IU)	Consumption by potency (IU) per treatment day	Treatment days/ patient/ year	Average annual consumption by potency (VIA)[6]
Appropriate comparator therapy					
Recombinant blood coagulation factor IX					
Nonacog alfa	40	Adults			
		3,400	1 x 3,000 1 x 500	91.3 – 121.7	91.3 x 3,000 91.3 x 500 to 121.7 x 3,000 121.7 x 500
		12 - < 18 years			
		2,472	1 x 2,000 1 x 500	91.3 – 121.7	91.3 x 2,000 91.3 x 500 to 121.7 x 2,000 121.7 x 500
		6 - < 12 years			
		1,308	1 x 1,000 1 x 500	91.3 – 121.7	91.3 x 1,000 91.3 x 500 to 121.7 x 1,000 121.7 x 500
	63.7	< 6 years			
		961.9	1 x 1,000	52.1 – 121.7	52.1 x 1,000 to 121.7 x 1,000
Nonacog beta pegol	40	Adults			
		3,400	1 x 2,000 1 x 1,000 1 x 500	52.1	52.1 x 2,000 52.1 x 1,000 52.1 x 500
		12 - < 18 years			
		2,472	1 x 2,000 1 x 500	52.1	52.1 x 2,000 52.1 x 500
Nonacog gamma	40 – 60	Adults			
		3,400 – 5,100	1 x 3,000 1 x 500 to 1 x 3,000 1 x 2,000 1 x 250	91.3 – 121.7	91.3 x 3,000 91.3 x 500 to 121.7 x 3,000 121.7 x 2,000 121.7 x 250
		12 - < 18 years			
		2,472 – 3,708	1 x 2,000 1 x 500 to	91.3 – 121.7	91.3 x 2,000 91.3 x 500 to

Designation of the therapy	Dosage (IU per kg BW)	Dose/ patient/ treatment day (IU)	Consumption by potency (IU) per treatment day	Treatment days/ patient/ year	Average annual consumption by potency (VIA)[6]
			1 x 3,000 1 x 500 1 x 250		121.7 x 3,000 121.7 x 500 121.7 x 250
	40 – 80	<u>6 - < 12 years</u>			
		1,308 – 2,616	1 x 1,000 1 x 500 to 1 x 2,000 1 x 500 1 x 250	91.3 – 121.7	91.3 x 1,000 91.3 x 500 to 121.7 x 2,000 121.7 x 500 121.7 x 250
		<u>< 6 years</u>			
		604 - 1208	1 x 500 1 x 250 to 1 x 1,000 1 x 250	91.3 – 121.7	91.3 x 500 91.3 x 250 to 121.7 x 1,000 121.7 x 250
Eftrenonacog alfa	50 – 100	<u>Adults</u>			
		4,250 – 8,500	2 x 3,000 1 x 2,000 1 x 500 to 1 x 3,000 1 x 1,000 1 x 250	36.5 - 52.1	73 x 3,000 36.5 x 2,000 36.5 x 500 to 52.1 x 3,000 52.1 x 1,000 52.1 x 250
		<u>12 - < 18 years</u>			
		3,090 – 6,180	1 x 3,000 1 x 250 to 2 x 3,000 1 x 250	36.5 - 52.1	52.1 x 3,000 52.1 x 250 to 73 x 3,000 36.5 x 250
	50 – 60	<u>6 - < 12 years</u>			
		1,635 – 1,962	1 x 1,000 1 x 500 1 x 250 to 1 x 2,000	52.1	52.1 x 1,000 52.1 x 500 52.1 x 250 to 52.1 x 2,000
		<u>< 6 years</u>			
		755 – 906	1 x 1,000	52.1	52.1 x 1,000
Blood coagulation factor IX derived from human blood plasma					
	20 – 40	<u>Adults</u>			
		1,700 – 3,400	2 x 1,000 to	91.3 – 121.7	182.6 x 1,000 to

Designation of the therapy	Dosage (IU per kg BW)	Dose/ patient/ treatment day (IU)	Consumption by potency (IU) per treatment day	Treatment days/ patient/ year	Average annual consumption by potency (VIA)[6]
Human plasma-derived preparations			3 x 1,000 1 x 500		368.1 x 1,000 121.7 x 500
		12 - < 18 years			
		1,236 – 2,472	1 x 1,000 1 x 500 to 2 x 1,000 1 x 500	91.3 – 121.7	91.3 x 1,000 91.3 x 500 to 245.4 x 1,000 121.7 x 500
		6 - < 12 years			
		654 – 1,308	1 x 1,000 to 1 x 1,000 1 x 500	91.3 – 121.7	91.3 x 1,000 to 121.7 x 1,000 121.7 x 500
VIA = vials					

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.

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					
Albutrepenonacog alfa 250 IU	1 PSI	€ 633.95	€ 1.77	€ 34.48	€ 597.70
Albutrepenonacog alfa 500 IU	1 PSI	€ 1,256.63	€ 1.77	€ 68.95	€ 1,185.91
Albutrepenonacog alfa 1,000 IU	1 PSI	€ 2,472.25	€ 1.77	€ 137.90	€ 2,332.58
Albutrepenonacog alfa 2,000 IU	1 PSI	€ 4,886.88	€ 1.77	€ 275.80	€ 4,609.31
Albutrepenonacog alfa 3,500 IU	1 PSI	€ 8,508.82	€ 1.77	€ 482.65	€ 8,024.40
Appropriate comparator therapy					
Recombinant blood coagulation factor IX					
Nonacog alfa 250 IU	1 PSI	€ 287.27	€ 1.77	€ 15.28	€ 270.22
Nonacog alfa 500 IU	1 PSI	€ 563.22	€ 1.77	€ 30.56	€ 530.89

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
Nonacog alfa 1,000 IU	1 PSI	€ 1,115.15	€ 1.77	€ 61.12	€ 1,052.26
Nonacog alfa 2,000 IU	1 PSI	€ 2,197.93	€ 1.77	€ 122.23	€ 2,073.93
Nonacog alfa 3,000 IU	1 PSI	€ 3,268.09	€ 1.77	€ 183.35	€ 3,082.97
Nonacog beta pegol 500 IU	1 PSI	€ 958.33	€ 1.77	€ 52.43	€ 904.13
Nonacog beta pegol 1,000 IU	1 PSI	€ 1,893.87	€ 1.77	€ 104.87	€ 1,787.23
Nonacog beta pegol 2,000 IU	1 PSI	€ 3,730.11	€ 1.77	€ 209.74	€ 3,518.60
Nonacog gamma 250 IU	1 PSI	€ 255.33	€ 1.77	€ 13.51	€ 240.05
Nonacog gamma 500 IU	1 PSI	€ 499.38	€ 1.77	€ 27.02	€ 470.59
Nonacog gamma 1,000 IU	1 PSI	€ 987.49	€ 1.77	€ 54.05	€ 931.67
Nonacog gamma 2,000 IU	1 PSI	€ 1,950.41	€ 1.77	€ 108.10	€ 1,840.54
Nonacog gamma 3,000 IU	1 PSI	€ 2,896.81	€ 1.77	€ 162.15	€ 2,732.89
Eftrenonacog alfa 250 IU	1 PSI	€ 474.33	€ 1.77	€ 0.00	€ 472.56
Eftrenonacog alfa 500 IU	1 PSI	€ 937.39	€ 1.77	€ 0.00	€ 935.62
Eftrenonacog alfa 1,000 IU	1 PSI	€ 1,853.27	€ 1.77	€ 0.00	€ 1,851.50
Eftrenonacog alfa 2,000 IU	1 PSI	€ 3,648.92	€ 1.77	€ 0.00	€ 3,647.15
Eftrenonacog alfa 3,000 IU	1 PSI	€ 5,444.57	€ 1.77	€ 0.00	€ 5,442.80
Blood coagulation factor IX derived from human blood plasma					
Haemonine 500 IU	1 PSI	€ 472.12	€ 1.77	€ 25.52	€ 444.83
Haemonine 1,000 IU	1 PSI	€ 932.96	€ 1.77	€ 51.03	€ 880.16
Abbreviations: PSI = powder and solvent for solution for injection					

LAUER-TAXE® last revised: 15 March 2022

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.

Because there are no 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, no costs for additionally required SHI services had to be taken into account.

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

At its session on 8 December 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 15 October 2021 the pharmaceutical company submitted a dossier for the benefit assessment of albutrepenonacog alfa to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 6 VerfO.

By letter dated 15 October 2021 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient albutrepenonacog alfa.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 January 2022, and the written statement procedure was initiated with publication on the website of the G-BA on 17 January 2022. The deadline for submitting written statements was 7 February 2022.

The oral hearing was held on 21 February 2022.

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 29 March 2022, and the proposed resolution was approved.

At its session on 7 April 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	8 December 2020	Determination of the appropriate comparator therapy
Working group Section 35a	15 February 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	21 February 2022	Conduct of the oral hearing
Working group Section 35a	1 March 2022 15 March 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	29 March 2022	Concluding discussion of the draft resolution
Plenum	7 April 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 7 April 2022

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

Prof. Hecken