Gemeinsamer Bundesausschuss

Justification

to 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
Concizumab (new therapeutic indication: haemophilia B, ≥ 12 years, without factor IX inhibitors)

From 19 March 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all 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 studies the pharmaceutical company have 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,
7. number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

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 decide 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 concizumab (Alhemo) was listed for the first time on 1 May 2025 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 22 August 2025, concizumab 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 from 12.12.2008, sentence 7).

On 18 September 2025, i.e. at the latest within four weeks of informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company

submitted a dossier in due time 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 concerning the active ingredient concizumab with the new therapeutic indication "Concizumab is indicated for routine prophylaxis of bleeding in patients 12 years of age or more with moderate/severe haemophilia B (congenital factor IX deficiency; FIX ≤ 2%) without FIX inhibitors.".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 January 2026 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

Based on 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, the G-BA decided on the question on whether an additional benefit of risankizumab compared with the appropriate comparator therapy could be determined – Annex XII - Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of concizumab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made 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 Concizumab (Alhemo) in accordance with the product information

Concizumab (Alhemo) is indicated for routine prophylaxis of bleeding in patients 12 years of age or more with:

- severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors.
- moderate/severe haemophilia B (congenital factor IX deficiency, FIX ≤ 2%) without FIX inhibitors.

Therapeutic indication of the resolution (resolution of 19.03.2026):

Concizumab is indicated for routine prophylaxis of bleeding in patients 12 years of age or more with moderate/severe haemophilia B (congenital factor IX deficiency, FIX ≤ 2%) without FIX inhibitors.

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis

Appropriate comparator therapy for concizumab:

- Routine prophylaxis with recombinant or human plasma-derived coagulation factor IX products

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to 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.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1. In addition to concizumab, the following active ingredients are approved for the therapeutic indication of haemophilia B:

- Recombinant factor IX products: Albutrepenonacog alfa, eftrenonacog alfa, nonacog alfa, nonacog beta pegol and nonacog gamma;
- human plasma factor IX products;
- factor VIII inhibitor bypassing activity enriched human plasma fraction;
- Recombinant coagulation factor VIIa product: eptacog alfa;
- gene therapy: etranacogene dezaparvovec;
- monoclonal antibodies: marstacimab.

The recombinant and human plasma-derived factor IX products and factor VIII inhibitor bypassing activity enriched human plasma fraction are approved for long-term routine prophylaxis.

On 2. Non-medicinal treatment is not considered an appropriate comparator therapy in the present therapeutic indication.

On 3. The following G-BA resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V in the therapeutic indication "Haemophilia B" are available:

- Albutrepenonacog alfa from 1 December 2016 (repealed) and from 7 April 2022,
- eftrenonacog alfa from 15 December 2016 (repealed) and from 1 February 2024,
- nonacog beta pegol from 19 April 2018 and from 15 February 2024,
- etranacogene dezaparvovec from 19 October 2023,
- marstacimab from 17 July 2025,
- concizumab from 16 October 2025.

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 indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V". 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.

According to the statements made by clinical experts in the written statement procedure, the significance of human plasma-derived factor products has clearly declined in recent years.

In the overall assessment of the available aggregated evidence, the human plasma-derived and recombinant coagulation factor IX products are however to be regarded as equivalent. 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 human plasma-derived and recombinant coagulation factor IX products in the treatment and prevention of bleeding in patients with haemophilia B.

From the available G-BA resolutions on the benefit assessment of the recombinant factor IX products with prolonged half-life (active ingredients nonacog beta pegol, albutrepenonacog alfa and eftrenonacog alfa), it is not possible to derive any comparative statements on the efficacy, safety and side effect profile compared to other plasma-derived and recombinant coagulation 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.

The gene therapeutic etranacogene dezaparvovec is another treatment option in the present therapeutic indication, the therapeutic significance of which cannot yet be conclusively assessed. Based on the generally recognised state of medical knowledge, etranacogene dezaparvovec is not determined to be an appropriate comparator therapy for the present resolution.

The antibody marstacimab is a new therapy option for the treatment of severe haemophilia B in patients without inhibitors. For marstacimab, it was determined by the G-BA's resolution of 17 July 2025 that an additional benefit is not proven, as no data were available to enable an assessment of the additional benefit. According to the generally recognised state of medical knowledge, marstacimab is not determined to be an appropriate comparator therapy for the present resolution.

In summary, the G-BA determined the appropriate comparator therapy to be routine prophylaxis with recombinant or human plasma-derived coagulation factor IX products for adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis.

The appropriate comparator therapy determined here includes several therapeutic alternatives. These therapeutic alternatives are equally appropriate for the comparator therapy. The additional benefit can be demonstrated compared to one of the therapeutic alternatives mentioned.

Treatment on demand alone is not an adequate appropriate comparator therapy in the present indication. An additional treatment on demand must be possible in all study arms, in general.

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

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

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

An additional benefit is not proven for adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis

Justification:

In their dossier for the assessment of the additional benefit of concizumab, the pharmaceutical company did not present any direct comparator studies versus the appropriate comparator therapy.

The pharmaceutical company additionally presented the label-enabling, multicentre, partially randomised, open-label Explorer8 study with a comparison between routine prophylaxis with concizumab and treatment on demand with factor products; male patients 12 years of age or more with congenital severe haemophilia A (FVIII < 1%) or moderate/severe haemophilia B (FIX ≤ 2%) without factor VIII or factor IX inhibitors were enrolled in the study. The study presented is unsuitable for the assessment of an additional benefit due to the lack of comparison with the appropriate comparator therapy.

Overall, no additional benefit of concizumab over the appropriate comparator therapy can be derived on the basis of the presented study for adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient concizumab (invented name: Alhemo).

The therapeutic indication assessed here is as follows: "Routine prophylaxis of bleeding in patients 12 years of age or more with moderate/severe haemophilia B (congenital factor IX deficiency, FIX ≤ 2%) without FIX inhibitors.

The G-BA determined routine prophylaxis with recombinant or human plasma-derived coagulation factor IX products as the appropriate comparator therapy.

The pharmaceutical company did not submit a direct comparator study for concizumab versus the appropriate comparator therapy.

The pharmaceutical company additionally presented the label-enabling Explorer8 study with a comparison between routine prophylaxis with concizumab and treatment on demand with factor products; male patients 12 years of age or more with congenital severe haemophilia A (FVIII < 1%) or moderate/severe haemophilia B (FIX ≤ 2%) without factor VIII or factor IX inhibitors were enrolled in the study. The study presented is unsuitable for the assessment of an additional benefit due to the lack of comparison with the appropriate comparator therapy.

In the overall assessment, the additional benefit of concizumab over the appropriate comparator therapy is not proven for adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis.

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 based the present resolution on the patient numbers derived by the pharmaceutical company. The stated number of patients in the SHI target population is subject to uncertainty due to the lack of data on the distribution of residual factor activity in the sample sizes, which is why the lower limit is likely to be underestimated and the upper limit overestimated. There are uncertainties regarding the transfer of the prevalence rate of male children and adolescents with haemophilia B without factor IX inhibitors to the number of adolescents.

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 Alhemo (active ingredient: concizumab) at the following publicly accessible link (last access: 7 January 2026):

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

Treatment with concizumab should only be initiated and monitored by specialists who are experienced in the treatment of patients with haemophilia and/or other blood coagulation disorders.

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 and caregivers (including patient identification card). In particular, the training material contains information and warnings on dealing with thromboembolic events and the use of bypassing agents.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 January 2026). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

Adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis

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				
Concizumab	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Recombinant blood coagulation factor IX products				
Albutrepenonacog alfa	Continuously, 1 x every 7 or 1 x every 10 to 14 days	52.1 or 26.1 – 36.5	1	52.1 or 26.1 – 36.5
Eftrenonacog alfa	Continuously, 1 x every 7 or 1 x every 10 days	52.1 – 36.5	1	52.1 – 36.5
Nonacog alfa	Continuously, 1 x every 3 to 4 days	91.3 – 121.7	1	91.3 – 121.7
Nonacog beta pegol	Continuously, 1 x every 7 days	52.1	1	52.1
Nonacog gamma	Continuously, 1 x every 3 to 4 days	91.3 – 121.7	1	91.3 – 121.7
Human plasma-derived coagulation factor IX products				
Human plasma-derived products[2]	Continuously, every 3 to 4 days	91.3 – 121.7	1	91.3 – 121.7

Consumption:

The theoretical annual consumption of concizumab and the factor IX products of the appropriate comparator therapy required for the prevention of bleeding in patients 12 years of age or more with moderate and severe haemophilia B is presented.

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 is different 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.

Consumption is calculated per injection for the relevant age groups (adolescents aged 12 to below 18 years and adults) according to the respective product information.

For dosages depending on body weight, the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population"3 as well

[2] Cost representation based on the requirements in the product information for AlphaNine. Other proprietary medicinal products are available.
[3] Federal Health Reporting. Average body measurements of the population (2017, both sexes, 1 year and older), www.gbe-bund.de

as "Microcensus 2021 – body measurements of the population"4 were applied. For body weight, the average weight of an adult male aged 18 years and over is therefore assumed to be 85.8 kg. For the underlying weight in the respective male age groups, the ranges were determined from 12 to below 18 years (47.6 kg – 74.6 kg).

The following dosage ranges are used for the cost calculation:

The cost representation is by indicating the cheapest and most expensive dosage possible. The dosage range can depend on both the frequency of application and the body weight.

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

Since factor IX products can be stored only for a maximum of 8 hours after reconstitution, discarding must be taken into account, consequently the consumption per injection is presented.

The consumption of vials and prefilled syringes was optimised according to the packaging size on the basis of the weight-adjusted demand for factor IX I.U./ injection. For example, for a 12-year-old child requiring 1,666 I.U./ injection, this was composed of three vials each of 1,000 I.U., 500 I.U. and 250 I.U. of factor IX.

The maintenance dose of concizumab is determined after a 4-week lead-in phase by determining the plasma level of concizumab.

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					
Concizumab	0.15 – 0.25 mg/kg	**Adults**			
		12.9 mg – 21.4 mg	13 mg – 21 mg	365.0	15.8 x 300 mg – 25.6 x 300 mg
		12 to < 18 years			
		7.1 mg – 18.7 mg	7 mg – 19 mg	365.0	17.0 x 150 mg – 23.1 x 300 mg
Appropriate comparator therapy					
Recombinant blood coagulation factor IX products					
Albutrepenonacog alfa	35 – 50 I.U./kg	**Adults**			
		3,003 I.U. – 4,290 I.U.	1 x 2,000 I.U. + 1 x 1,000 I.U. + 1 x 250 I.U. – 2 x 2,000 I.U. + 1 x 500 I.U.	52.1	52.1 x 2,000 I.U. + 52.1 x 1,000 I.U. + 52.1 x 250 I.U. – 104.2 x 2,000 I.U. +

[4] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
					52.1 x 500 I.U.
		12 to < 18 years			
		1,666 I.U. – 3,730 I.U.	1 x 1,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U. – 1 x 3,500 I.U. + 1 x 250 I.U.	52.1	52.1 x 1,000 I.U. + 52.1 x 500 I.U. + 52.1 x 250 I.U. - 52.1 x 3,500 I.U. + 52.1 x 250 I.U.
	75 I.U./kg	**Adults**			
		6,435 I.U.	1 x 3,500 I.U. + 1 x 2,000 I.U. + 1 x 1,000 I.U.	26.1 – 36.5	26.1 x 3,500 I.U. + 26.1 x 2,000 I.U. + 26.1 x 1,000 I.U. – 36.5 x 3,500 I.U. + 36.5 x 2,000 I.U. + 36.5 x 1,000 I.U.
		12 to < 18 years			
		3,570 I.U. – 5,595 I.U.	1 x 3,500 I.U. + 1 x 2,000 I.U. + 1 x 250 I.U.	26.1 – 36.5	26.1 x 3,500 I.U. + 26.1 x 250 I.U. – 36.5 x 3,500 I.U. + 36.5 x 2,000 I.U. + 36.5 x 250 I.U.
Eftrenonacog alfa	50 – 100 I.U./kg	**Adults**			
		4,290 I.U. – 8,580 I.U.	2 x 2,000 I.U. + 1 x 500 I.U. – 2 x 3,000 I.U. + 1 x 2,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	52.1 – 36.5	104.2 x 2,000 I.U. + 52.1 x 500 I.U. – 73 x 3,000 I.U. + 36.5 x 2,000 I.U. + 36.5 x 500 I.U. + 36.5 x 250 I.U.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
		12 to < 18 years			
		2,380 I.U. – 7,460 I.U.	1 x 2,000 I.U. + 1 x 500 I.U. – 2 x 3,000 I.U. + 1 x 1,000 I.U. + 1 x 500 I.U.	52.1 – 36.5	52.1 x 2,000 I.U. + 52.1 x 500 I.U. – 73 x 3,000 I.U. + 36.5 x 1,000 I.U. + 36.5 x 500 I.U.
Nonacog alfa	40 I.U./kg	**Adults**			
		3,432 I.U.	1 x 3,000 I.U. + 1 x 500 I.U.	91.3 – 121.7	91.3 x 3,000 I.U. + 91.3 x 500 I.U. – 121.7 x 3,000 I.U. + 121.7 x 500 I.U.
		12 to < 18 years			
		1,904 I.U. – 2,984 I.U.	1 x 2,000 I.U. – 1 x 3,000 I.U.	91.3 – 121.7	91.3 x 2,000 I.U. – 121.7 x 3,000 I.U.
Nonacog beta pegol	40 I.U./kg	**Adults**			
		3,432 I.U.	1 x 3,000 I.U. + 1 x 500 I.U.	52.1	52.1 x 3,000 I.U. + 52.1 x 500 I.U.
		12 to < 18 years			
		1,904 I.U. – 2,984 I.U.	1 x 2,000 I.U. – 1 x 3,000 I.U.	52.1	52.1 x 2,000 I.U. – 52.1 x 3,000 I.U.
Nonacog gamma	40 – 60 I.U./kg	**Adults**			
		3,432 I.U. – 5,136 I.U.	1 x 3,000 I.U. + 1 x 500 I.U. – 1 x 3,000 I.U. + 1 x 2,000 I.U. + 1 x 250 I.U.	91.3 – 121.7	91.3 x 3,000 I.U. + 91.3 x 500 I.U. – 121.7 x 3,000 I.U. + 121.7 x 2,000 I.U. + 121.7 x 250 I.U.
		12 to < 18 years			

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
		1,904 I.U. – 4,476 I.U.	1 x 2,000 I.U. – 1 x 3,000 I.U. + 1 x 1,000 I.U. + 1 x 500 I.U.	91.3 – 121.7	91.3 x 2,000 I.U. – 121.7 x 3,000 I.U. + 121.7 + 1,000 I.U. + 121.7 x 500 I.U.
Human plasma-derived coagulation factor IX products					
Human plasma-derived products[2]	20 – 40 I.U./kg	**Adults**			
		1,716 I.U. – 3,432 I.U.	2 x 1,000 I.U. – 3 x 1,000 I.U. + 1 x 500 I.U.	91.3 – 121.7	182.6 x 1,000 I.U. – 365.1 x 1,000 I.U. + 121.7 x 500 I.U.
		12 to < 18 years			
		952 I.U. – 2,984 I.U.	1 x 1,000 I.U. – 3 x 1,000 I.U.	91.3 – 121.7	91.3 x 1,000 I.U. – 365.1 x 1,000 I.U.

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.

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					
Concizumab 150 mg	1 SFI	€ 17,869.40	€ 1.77	€ 1,017.23	€ 16,850.40
Concizumab 300 mg	1 SFI	€ 35,681.15	€ 1.77	€ 2,034.47	€ 33,644.91
Appropriate comparator therapy					
Recombinant blood coagulation factor IX products					
Albutrepenonacog alfa 250 I.U.	1 PSI	€ 457.97	€ 1.77	€ 24.73	€ 431.47

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
Albutrepenonacog alfa 500 I.U.	1 PSI	€ 904.64	€ 1.77	€ 49.46	€ 853.41
Albutrepenonacog alfa 1,000 I.U.	1 PSI	€ 1,789.72	€ 1.77	€ 98.92	€ 1,689.03
Albutrepenonacog alfa 2,000 I.U.	1 PSI	€ 3,521.78	€ 1.77	€ 197.84	€ 3,322.17
Albutrepenonacog alfa 3,500 I.U.	1 PSI	€ 6,119.88	€ 1.77	€ 346.22	€ 5,771.89
Eftrenonacog alfa 250 I.U.	1 PSI	€ 300.14	€ 1.77	€ 15.99	€ 282.38
Eftrenonacog alfa 500 I.U.	1 PSI	€ 588.95	€ 1.77	€ 31.98	€ 555.20
Eftrenonacog alfa 1,000 I.U.	1 PSI	€ 1,166.58	€ 1.77	€ 63.96	€ 1,100.85
Eftrenonacog alfa 2,000 I.U.	1 PSI	€ 2,297.62	€ 1.77	€ 127.93	€ 2,167.92
Eftrenonacog alfa 3,000 I.U.	1 PSI	€ 3,417.60	€ 1.77	€ 191.89	€ 3,223.94
Nonacog alfa 500 I.U.	1 DSS	€ 563.25	€ 1.77	€ 30.56	€ 530.92
Nonacog alfa 2,000 I.U.	1 DSS	€ 2,197.97	€ 1.77	€ 122.23	€ 2,073.97
Nonacog alfa 3,000 I.U.	1 DSS	€ 3,268.12	€ 1.77	€ 183.35	€ 3,083.00
Nonacog beta pegol 500 I.U.	1 PSI	€ 948.97	€ 1.77	€ 51.91	€ 895.29
Nonacog beta pegol 3,000 I.U.	1 PSI	€ 5,511.71	€ 1.77	€ 311.48	€ 5,198.46
Nonacog gamma 250 I.U.	1 PSI	€ 302.43	€ 1.77	€ 16.12	€ 284.54
Nonacog gamma 500 I.U.	1 PSI	€ 593.54	€ 1.77	€ 32.24	€ 559.53
Nonacog gamma 1,000 I.U.	1 PSI	€ 1,175.79	€ 1.77	€ 64.47	€ 1109.55
Nonacog gamma 2,000 I.U.	1 PSI	€ 2,315.47	€ 1.77	€ 128.94	€ 2,184.76
Nonacog gamma 3,000 I.U.	1 PSI	€ 3,444.37	€ 1.77	€ 193.42	€ 3249.18
Human plasma-derived coagulation factor IX products					
ALPHANINE 500 I.U.	1 DSS	€ 463.30	€ 1.77	€ 25.03	€ 436.50
ALPHANINE 1,000 I.U.	1 DSS	€ 915.30	€ 1.77	€ 50.05	€ 863.48
Abbreviations: PSS = powder and solvent for the preparation of an infusion solution; PSI = powder and solvent for solution for injection; DSS = dry substance with solvent					

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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.

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 designate 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 have 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 have 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 data from the product 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 have 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 statutory 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:

Adults and adolescents 12 years of age or more with moderate/severe haemophilia B (FIX ≤ 2%) without factor IX inhibitors with an indication for routine prophylaxis

No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:

Product information for concizumab (Alhemo); Alhemo; last revised: August 2025

2.6 Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Alhemo is a medicinal product placed on the market from 1 January 2025. In accordance with Section 35a, paragraph 3, sentence 5 SGB V, the G-BA must determine whether a relevant percentage of the clinical studies on the medicinal product were conducted within the scope of SGB V. This is the case if the percentage of study participants who have participated in the clinical studies on the medicinal product to be assessed in the therapeutic indication to be assessed at study sites within the scope of SGB V is at least five per cent of the total number of study participants.

The calculation is based on all studies that were submitted as part of the benefit assessment dossier in the therapeutic indication to be assessed in accordance with Section 35a, paragraph 1, sentence 3 SGB V in conjunction with Section 4, paragraph 6 AM-NutzenV.

Approval studies include all studies submitted to the regulatory authority in section 2.7.3 (Summary of Clinical Efficacy) and 2.7.4 (Summary of Clinical Safety) of the authorisation dossier in the therapeutic indication for which marketing authorisation has been applied for. In addition, studies, which were conducted in whole or in part within the therapeutic indication described in this document, and in which the company was a sponsor or is otherwise financially involved, must also be indicated.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5% (4.5%) of the total number of study participants according to the information provided by the pharmaceutical company.

In the dossier, the pharmaceutical company took the data from the NN7415-3813, NN7415-3981, NN7415-3986, NN7415-4159, NN7415-4255, NN7415-4310, NN7415-4311 and NN7415-4307 studies as the basis.

For the NN7415-4311 study, a minor discrepancy was found between the information provided by the pharmaceutical company in Module 3A/ SAS extracts and the information in the study registry.

Furthermore, the pharmaceutical company classified the NN7415-4616 study, listed in the Common Technical Document (CTD), as ongoing, even though, according to the latest information in the study registry, its status was "active but not recruiting" at the time the dossier was submitted. It is unclear whether the study should be taken into account in the calculation. If the study were taken into account, this would result in a lower percentage, which would still be below 5%.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant percentage within the scope of SGB V.

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

The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 7 February 2023.

A review of the appropriate comparator therapy took place. The Subcommittee on Medicinal Products newly determined the appropriate comparator therapy at their session on 23 September 2025.

On 18 September 2025, the pharmaceutical company submitted a dossier for the benefit assessment of concizumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 22 September 2025 in conjunction with the G-BA resolution of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit 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 concizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 December 2025, and the written statement procedure was initiated with publication on the G-BA website on 2 January 2026. The deadline for submitting statements was 23 January 2026.

The oral hearing took place on 9 February 2026.

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 Subcommittee's session on 10 March 2026, and the draft resolution was approved.

At their session on 19 March 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal products	7 February 2023	Determination of the appropriate comparator therapy
Subcommittee on Medicinal products	23 September 2025	New determination of the appropriate comparator therapy
Working group Section 35a	3 February 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal products	9 February 2026	Conduct of the oral hearing
Working group Section 35a	17 February 2026 3 March 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal products	10 March 2026	Concluding discussion of the draft resolution
Plenum	19 March 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 19 March 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken