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 (haemophilia A, ≥ 12 years, with factor VIII inhibitors)

of 16 October 2025

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 relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient concizumab on 1 May 2025 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company 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, paragraph 1, number 1 VerfO on 28 April 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 August 2025 on the G-BA website (www.g-ba.de), 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 concizumab compared with 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, as well of the addendum drawn up by the IQWiG on the benefit assessment. 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 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 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:

- haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors.
- haemophilia B (congenital factor IX deficiency) with FIX inhibitors.

Therapeutic indication of the resolution (resolution of 16.10.2025):

Concizumab is indicated for routine prophylaxis of bleeding in patients 12 years of age or more with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults and adolescents 12 years of age or more with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors with an indication for routine prophylaxis

Appropriate comparator therapy:

- Emicizumab

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 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.

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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 it determines 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.

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

On 1. In the therapeutic indication of haemophilia A, the following active ingredients are approved:

- Recombinant factor VIII products: damoctocog alfa pegol, efanesoctocog alfa, efmoroctocog alfa, lonoctocog alfa, moroctocog alfa, octocog alfa, rurioctocog alfa pegol, simoctocog alfa, turoctocog alfa and turoctocog alfa pegol;
- human plasma factor VIII products;
- monoclonal antibodies: emicizumab, marstacimab;
- factor VIII inhibitor bypassing activity enriched human plasma fraction;
- recombinant blood coagulation factor VIIa product: eptacog alfa;
- gene therapy: valoctocogene roxaparvovec.

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

Emicizumab and the factor VIII inhibitor bypassing activity-enriched human plasma fraction in particular are approved for patients with factor VIII inhibitors.

On 2. Non-medicinal treatments are not considered for the therapeutic indication.

On 3. In the therapeutic indication "haemophilia A", the following resolutions from the G-BA on the benefit assessment of medicinal products according to Section 35a SGB V are available:

- Turoctocog alfa from 3 July 2014
- Simoctocog alfa from 7 May 2015
- Efmoroctocog alfa from 16 June 2016
- Lonoctocog alfa from 20 July 2017
- Emicizumab from 20 September 2018, 5 September 2019 and 17 August 2023
- Rurioctocog alfa pegol from 23 October 2018
- Damoctocog alfa pegol from 20 June 2019
- Turoctocog alfa pegol from 6 February 2020
- Valoctocogene roxaparvovec from 16 March 2023
- Marstacimab from 17 July 2025

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as 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.

It is assumed that the patient population in the present indication concerns patients requiring factor VIII replacement.

The aggregated evidence results in a recommendation of emicizumab treatment for patients with haemophilia A and with factor VIII inhibitors. This is also accordingly supported by the scientific-medical societies. Bypassing agents are only recommended for the treatment of acute bleeding complications or operations.

On the basis of the data submitted, no additional benefit of emicizumab over the appropriate comparator therapy could be derived for patients with haemophilia A with factor VIII inhibitors in the benefit assessment procedure according to §35a SGB V on emicizumab.

In the overall assessment of the aggregated evidence, emicizumab is therefore determined as the appropriate comparator therapy for the prevention of bleeding in patients with haemophilia A with factor VIII inhibitors.

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 marketing authorisation and the dosage information in the product information of the active ingredients must be taken into account.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

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 haemophilia A (congenital factor VIII deficiency) with factor VIII 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, multi-centre, partially randomised, open-label Explorer7 study with a comparison between routine prophylaxis with concizumab and treatment on demand with bypassing agents; male patients 12 years of age or more with congenital haemophilia A or B of any disease severity with 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 haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors with an indication for routine prophylaxis.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Alhemo with the active ingredient concizumab.

The therapeutic indication assessed here is as follows: "Routine prophylaxis of bleeding in patients 12 years of age or more with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors."

The G-BA determined the active ingredient emicizumab 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, multi-centre, partially randomised, open-label Explorer7 study with a comparison between routine prophylaxis with concizumab and treatment on demand with bypassing agents; male patients 12 years of age or more with congenital haemophilia A or B of any disease severity with 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 haemophilia A (congenital factor VIII deficiency) with factor VIII 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, which are generally considered plausible. There are uncertainties regarding the transfer of the prevalence rate of male children and adolescents with haemophilia A with factor VIII 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 October 2025):

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 contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 August 2025). 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 co-morbidities) 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.

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	1.0	365.0
Appropriate comparator therapy				
Emicizumab				
Emicizumab	Continuously, 1 x every 7 days, every 14 days or every 28 days	52.1; 26.1 or 13.0	1.0	52.1; 26.1 or 13.0

Consumption:

The theoretical annual consumption of concizumab and the active ingredient of the appropriate comparator therapy required for the prevention of bleeding in patients with major haemophilia A with factor VIII inhibitors are 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 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.

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"[2] as well as "Microcensus 2021 – body measurements of the population"[3] 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 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.

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

[2] Federal Health Reporting. Average body measurements of the population (2017, both sexes, 1 year and older), www.gbe-bund.de

[3] 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
Medicinal product to be assessed					
Concizumab	0.15 mg/kg – 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					
Emicizumab					
Emicizumab	1.5 mg/kg 1 x every 7 days – 6 mg/kg 1 x every 28 days	Adults			
		128.7 mg – 514.8 mg	1 x 105 mg + 1 x 30 mg – 3 x 150 mg + 1 x 60 mg + 1 x 12 mg	52.1 – 13.0	52.1 x 105 mg + 52.1 x 30 mg – 39.0 x 150 mg + 13.0 x 60 mg + 13.0 x 12 mg
		12 to < 18 years			
		71.4 mg – 447.6 mg	1 x 60 mg + 1 x 30 mg – 3 x 150 mg	52.1 – 13.0	52.1 x 60 mg + 52.1 x 30 mg – 39.0 x 150 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.

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 300 mg	1 SFI	€ 35,681.15	€ 1.77	€ 2,034.47	€ 33,644.91
Concizumab 150 mg	1 SFI	€ 17,869.40	€ 1.77	€ 1,017.23	€ 16,850.40
Appropriate comparator therapy					
Emicizumab 150 mg	1 SFI	€ 7,365.89	€ 1.77	€ 417.38	€ 6,946.74
Emicizumab 105 mg	1 SFI	€ 5,173.42	€ 1.77	€ 292.16	€ 4,879.49
Emicizumab 60 mg	1 SFI	€ 2,980.95	€ 1.77	€ 166.95	€ 2,812.23
Emicizumab 30 mg	1 SFI	€ 1,519.00	€ 1.77	€ 83.48	€ 1,433.75
Emicizumab 12 mg	1 SFI	€ 614.40	€ 1.77	€ 33.39	€ 579.24
Abbreviations: SFI = solution for injection					

LAUER-TAXE® last revised: 15 August 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.

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 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 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 haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors with an indication for routine prophylaxis

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils 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 the authorisation dossier for the

assessment of the clinical efficacy and safety of the medicinal product in the therapeutic indication to be assessed.

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.

In the dossier, the pharmaceutical company took the data from the NN7415-3813 (explorer1), NN7415-3981, NN7415-3986 (explorer2), NN7415-4159 (explorer3), NN7415-4255 (explorer5), NN7415-4310 (explorer4), NN7415-4311 (explorer7) and NN7415-4307 (explorer8) studies as the basis. In addition, the pharmaceutical company subsequently submitted information on the calculation of study participants in the written statement procedure. However, this information does not clearly point out the number of participants at German study sites who have already taken part in a previous study.

Taking into account the information in the statement including the subsequently submitted information, a recalculation by IQWiG (G25-27) results in a number of 18 out of 403 study participants at German study sites for each therapeutic indication, and thus a percentage of study participants at German study sites of 4.47% in each case.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant extent 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

At their session on 7 February 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 28 April 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 29 April 2025 in conjunction with the resolution of the G-BA 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 July 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 August 2025. The deadline for submitting statements was 22 August 2025.

The oral hearing was held on 9 September 2025.

By letter dated 9 September 2025, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 26 September 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 7 October 2025, and the proposed draft resolution was approved.

At their session on 16 October 2025, 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
Working group Section 35a	2 September 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	9 September 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	16 September 2025 30 September 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	7 October 2025	Concluding discussion of the draft resolution
Plenum	16 October 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 16 October 2025

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

Prof. Hecken