

# 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  
Marstacimab (severe haemophilia A,  $\geq 12$  years, without factor  
VIII inhibitors)

of 17 July 2025

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## **1. Legal basis**

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) 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 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 relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient marstacimab on 1 February 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 31 January 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 May 2025 on the G-BA website ([www.g-ba.de](http://www.g-ba.de)), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of marstacimab 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. 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 <sup>1</sup> was not used in the benefit assessment of marstacimab.

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

Hypmavzi is indicated for routine prophylaxis of bleeding episodes in patients 12 years of age and older, weighing at least 35 kg, with:

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

#### **Therapeutic indication of the resolution (resolution of 17 July 2025):**

Hypmavzi is indicated for routine prophylaxis of bleeding episodes in patients 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors.

### **2.1.2 Appropriate comparator therapy**

The appropriate comparator therapy was determined as follows:

Adults and adolescents 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors for routine prophylaxis

#### **Appropriate comparator therapy:**

- Routine prophylaxis with human plasma-derived and recombinant coagulation factor VIII products or 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.

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

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 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.

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

On 1. Medicinal products with the following active ingredients are currently approved for the treatment of haemophilia A:

- Recombinant factor VIII products contain the genetically engineered human factor VIII glycoprotein. The factor VIII glycoproteins differ, among other things, in the length of their side chains.
- Octocog alfa contains the natural human factor VIII glycoprotein with the complete amino acid sequence. Rurioctocog alfa pegol and damoctocog alfa pegol are both pegylated, recombinant coagulation factor VIII octocog alfa.

- Moroctocog alfa has a truncated side chain compared to the natural factor VIII glycoprotein.
- Turoctocog alfa has a truncated side chain compared to the natural factor VIII glycoprotein. Turoctocog alfa pegol is the pegylated, recombinant coagulation factor VIII turoctocog alfa.
- Simoctocog alfa is composed of the active domains (domains A and C) of human factor VIII, domains A2 and A3 are linked by a linker sequence.
- Efmoroctocog alfa has a truncated side chain compared to the natural factor VIII glycoprotein, covalently bound to the Fc domain of human immunoglobulin G1.
- Lonoctocog alfa is a single-chain polypeptide with a truncated B-domain that allows for a covalent bridge to link the factor VIII heavy and light chains.
- Efanesoctocog alfa is designed in such a way that it does not bind the endogenous von Willebrand factor (VWF). The Fc domain of human immunoglobulin G1 binds to the neonatal Fc receptor, which delays the lysosomal degradation of immunoglobulins and prolongs the half-life of the fusion protein.

All products are approved for the treatment and prophylaxis of haemophilia A. The pegylated factor VIII products ruriotocog alfa pegol, damoctocog alfa pegol and turoctocog alfa pegol are only approved for patients 12 years of age and older with haemophilia A.

- Human plasma factor VIII products contain the human-identical factor VIII glycoprotein obtained from cryoprecipitates: They are obtained from large human plasma pools and are approved for the treatment and prevention of haemophilia A.
- A human plasma fraction enriched with factor VIII inhibitor bypassing activity is approved for the treatment and prevention of bleeding in haemophilia A patients with factor VIII inhibitors.
- A recombinant coagulation factor VIIa product (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 coagulation factor VIII inhibitors. It is not approved for the permanent treatment of haemophilia A requiring replacement.
- Emicizumab is a bispecific antibody that combines activated factors IX and X to replace the function of the missing activated factor VIII. Emicizumab is approved for the routine prophylaxis of patients with haemophilia A and existing factor VIII inhibitors on the one hand and for the routine prophylaxis of bleeding in severe haemophilia A or moderately severe disease with severe bleeding phenotype without existing factor VIII inhibitors on the other.
- The gene therapy valoctocogene roxaparvovec is approved for the treatment of severe haemophilia A (congenital factor VIII deficiency) in adult patients without a history of factor VIII inhibitors and without detectable antibodies to adeno-associated virus serotype 5 (AAV5).

On 2. A non-medicinal treatment option is not an appropriate comparator therapy for the therapeutic indication in question.

On 3. In the present therapeutic indication for the treatment of haemophilia A, the following resolutions of the G-BA on – Annex XII Pharmaceuticals Directive – the benefit assessment 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,
- rurioctocog alfa pegol from 23 October 2018,
- damoctocog alfa pegol from 20 June 2019,
- emicizumab from 20 September 2018 and 5 September 2019,
- turoctocog alfa pegol from 6 February 2020,
- valoctocogene roxaparvovec from 16 March 2023,
- emicizumab from 17 August 2023.

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.

The available body of evidence includes two Cochrane reviews (2021 and 2024) and two systematic reviews. In addition, two guidelines were identified that do not fully meet the methodological requirements, but were additionally included due to a lack of higher-quality evidence.

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

In the overall assessment of the aggregated evidence, the recombinant and human plasma-derived factor VIII products are to be regarded as equivalent and are therefore equally eligible as the appropriate comparator therapy. No evidence-based data have been found on therapeutic efficacy, side-effect profile (e.g. development of inhibitory haemophilia) or safety risk (e.g. risk of infection) that would lead to recombinant or human plasma-derived factor VIII products being regularly preferred in the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). This also applies to recombinant factor VIII products with prolonged half-life, which are equally covered by the appropriate comparator therapy.

A human plasma fraction enriched with factor VIII inhibitor bypassing activity is only approved for patients with existing factor VIII inhibitors and is therefore not considered as an appropriate comparator therapy for this patient population.

In addition to the factor VIII products, the bifunctional antibody emicizumab is another approved medicinal product in the present therapeutic indication. In addition to routine prophylaxis of bleeding in patients with existing factor VIII inhibitors, the marketing authorisation also covers routine prophylaxis of bleeding in severe haemophilia A and moderately severe haemophilia A with severe bleeding phenotype without existing factor VIII inhibitors. In the benefit assessment procedures for emicizumab according to Section 35a SGB V, no additional benefit of emicizumab over the appropriate comparator therapy could be derived for patients with haemophilia A

without factor VIII inhibitors on the basis of the data submitted, as no comparator studies were available.

Nevertheless, emicizumab is now an established alternative to therapy with factor VIII products in medical treatment practice. Taking into account in particular the existing therapy recommendations and the statements of the scientific-medical societies, emicizumab is therefore considered equally appropriate in the present patient population.

The gene therapeutic valoctocogene roxaparvovec is another new treatment option approved for the haemophilia A patient population without factor VIII inhibitors, but its therapeutic significance cannot yet be conclusively assessed. Based on the generally accepted state of medical knowledge, valoctocogene roxaparvovec is therefore not determined to be an appropriate comparator therapy for this patient population.

In summary, the G-BA determined routine prophylaxis with recombinant or human plasma-derived coagulation factor VIII products or emicizumab as the appropriate comparator therapy for patients with haemophilia A without factor VIII inhibitors with an indication for routine prophylaxis.

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

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

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 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.

#### Change of the appropriate comparator therapy

Initially, a therapy according to doctor's instructions with the selection of routine prophylaxis with recombinant or human plasma-derived coagulation factor VIII products and emicizumab was determined for adults and adolescents 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors.

Based on the equivalent recommendations as part of the available evidence and the increasing relevance of the use of the bifunctional antibody emicizumab in the German healthcare context, both routine prophylaxis with recombinant or human plasma-derived coagulation factor VIII products and routine prophylaxis with emicizumab are considered equally appropriate therapy options for patients with severe haemophilia A.



### 2.1.3 Extent and probability of the additional benefit

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

Adults and adolescents 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors for routine prophylaxis

An additional benefit is not proven.

Justification:

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

In addition, the pharmaceutical company presented the label-enabling, open-label, single-arm phase III BASIS study (B7841005) with an intra-individual before-after comparison, in which male patients aged 12 to 74 years with severe haemophilia A (factor VIII activity < 1%) or moderate-to-severe haemophilia B (factor IX activity ≤ 2%) and a body weight of at least 35 kg were enrolled. The single-arm study presented is unsuitable for the assessment of an additional benefit due to the lack of comparison with the appropriate comparator therapy.

Overall, on the basis of the presented study, no additional benefit of marstacimab over the appropriate comparator therapy can be derived for adults and adolescents 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors 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 marstacimab (invented name: Hympavzi).

The therapeutic indication assessed here is as follows: "Routine prophylaxis of bleeding episodes in patients 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors."

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

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

In addition, the pharmaceutical company presented the label-enabling, open-label, single-arm phase III BASIS study (B7841005) with an intra-individual before-after comparison, in which male patients aged 12 to 74 years with severe haemophilia A (factor VIII activity < 1%) or moderate-to-severe haemophilia B (factor IX activity ≤ 2%) and a body weight of at least 35 kg were enrolled.

In the overall assessment, the additional benefit of marstacimab over the appropriate comparator therapy is not proven for adults and adolescents 12 years of age and older, weighing at least 35 kg, with severe haemophilia A without factor VIII inhibitors 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. However, the figures are subject to uncertainty due to uncertainties regarding the WFH report, which is based on a voluntary survey of member organisations, and due to the calculated percentage of patients with severe haemophilia.

## 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 Hymravzi (active ingredient: marstacimab) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 8 July 2025):

[https://www.ema.europa.eu/en/documents/product-information/hympavzi-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/hympavzi-epar-product-information_en.pdf)

Treatment with marstacimab should only be initiated and monitored by specialists experienced in treating patients with haemophilia A.

## 2.4 Treatment costs

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

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.

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				
Marstacimab	Continuously, 1 x every 7 days	52.1	1	52.1

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Appropriate comparator therapy				
Plasma-derived and recombinant coagulation factor VIII products used for routine prophylaxis				
recombinant blood coagulation factor VIII products				
Damoctocog alfa pegol	Continuously, 1 x every 5 days or every 7 days or 2 x weekly	73.0; 52.1 or 104.3	1	73.0; 52.1 or 104.3
Efmoroctocog alfa	Continuously, 1 x every 3 to 5 days	73.0 – 121.7	1	73.0 – 121.7
Lonoctocog alfa	Continuously, 2 to 3 x weekly	104.3 – 156.4	1	104.3 – 156.4
Moroctocog alfa	Continuously, every 2 to 3 days	121.7 – 182.5	1	121.7 – 182.5
Octocog alfa <sup>2</sup>	Continuously, 2 to 3 x weekly or every 2 days	104.3 – 182.5	1	104.3 – 156.4
Rurioctocog alfa pegol	Continuously, 2 x weekly	104.3	1	104.3
Simoctocog alfa <sup>3</sup>	Continuously, every 2 to 3 days	121.7 – 182.5	1	121.7 – 182.5
Turoctocog alfa	Continuously, every 2 to 3 days or 2 to 3 x weekly	104.3 – 156.4	1	104.3 – 156.4
Turoctocog alfa pegol	Continuously, every 4 days	91.3	1	91.3
Human plasma-derived coagulation factor VIII products				
Human plasma-derived products <sup>4</sup>	Continuously, every 2 to 3 days	121.7 – 182.5	1	121.7 – 182.5
IgG antibody				
Emicizumab	Continuously, 1 x every 7, 14 or 28 days	52.1; 26.1 or 13.0	1	52.1; 26.1 or 13.0

<sup>2</sup> Cost representation based on the requirements in the product information for Kovaltry. Other proprietary medicinal products are available.

<sup>3</sup> Cost representation based on the requirements in the product information for Nuwiq. Other proprietary medicinal products are available.

<sup>4</sup> Cost representation based on the requirements in the product information for Faktor VIII SDH Intersero. Other proprietary medicinal products are available.

### Consumption:

The theoretical annual consumption of marstacimab and the active ingredients of the appropriate comparator therapy required for the prevention of bleeding in patients with severe haemophilia A 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 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"<sup>5</sup> as well as "Microcensus 2021 – body measurements of the population"<sup>6</sup> 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:

For the upper limit of the cost range, the highest dosage with the most frequent application and the highest body weight of the respective age group is calculated. For the calculation of the lower cost limit, the lowest dosage with the largest interval and the lowest body weight of the respective age range is used.

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

Since factor VIII products can be stored only for a maximum of 24 hours after reconstitution, discarding must be taken into account, consequently the consumption per injection is presented.

The consumption of vials and pre-filled syringes was optimised according to the packaging size on the basis of the weight-adjusted demand for factor VIII I.U./ injection. For example, for an adult requiring 1716 I.U./ injection, this was composed of three vials each of 1000 I.U., 500 I.U. and 250 I.U. of factor VIII.

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					
Marstacimab	150 – 300 mg	<b>Adults and adolescents 12 years of age and older</b>			

<sup>5</sup> Federal Health Reporting. Average body measurements of the population (2017, both sexes, 1 year and older), [www.gbe-bund.de](http://www.gbe-bund.de)

<sup>6</sup> Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), [www.gbe-bund.de](http://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
		≥ 35 kg			
		150 mg	1 x 150 mg	52.1	52.1 x 150 mg
		≥ 50 kg			
		150 mg	1 x 150 mg	52.1	52.1 x 150 mg
		– 300 mg	– 2 x 150 mg		– 104.2 x 150 mg
Appropriate comparator therapy					
recombinant blood coagulation factor VIII products					
Damoctocog alfa pegol	60 I.U./kg	Adults			
		5,148 I.U.	1 x 3,000 I.U. + 1 x 2,000 I.U. + 1 x 250 I.U.	52.1 - 73.0	52.1 x 3,000 I.U. + 52.1 x 2,000 I.U. + 52.1 x 250 I.U. - 73.0 x 3,000 I.U. + 73.0 x 2,000 I.U. + 73.0 x 250 I.U.
		12 to < 18 years			
		4,476 I.U.	1 x 3,000 I.U. + 1 x 1,000 I.U. + 1 x 500 I.U.	73.0	73.0 x 3,000 I.U. + 73.0 x 1,000 I.U. + 73.0 x 500 I.U.
		2856 I.U.	1 x 3,000 I.U.	52.1	52.1 x 3,000 I.U.
Efmoctocog alfa	50 I.U./kg	Adults			
		4,290 I.U.	1 x 4,000 I.U. + 1 x 500 I.U.	73.0 – 121.7	73.0 x 4,000 I.U. + 73.0 x 500 I.U. - 121.7 x 4,000 I.U. + 121.7 x 500 I.U.
		12 to < 18 years			
		3,730 I.U.	1 x 3,000 I.U. + 1 x 750 I.U.	121.7	121.7 x 3,000 I.U. + 121.7 x 750 I.U.
		2,380 I.U.	1 x 2,000 I.U. + 1 x 500 I.U.	73.0	73.0 x 2,000 I.U. + 73.0 x 500 I.U.
Lonoctocog alfa	20 – 50 I.U. /kg	Adults			
		4,290 I.U.	2 x 2,000 I.U. + 1 x 500 I.U.	156.4	312.8 x 2,000 I.U. + 156.4 x 500 I.U.
		1,716 I.U.	1 x 1,500 I.U. + 1 x 250 I.U.	104.3	104.3 x 1,500 I.U. + 104.3 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
		3,730 I.U.	1 x 3,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	156.4	156.4 x 3,000 I.U. + 156.4 x 500 I.U. + 156.4 x 250 I.U.
		952 I.U.	1 x 1,000 I.U.	104.3	104.3 x 1,000 I.U.
Moroctocog alfa	20 – 40 I.U. /kg	<b>Adults</b>			
		3,432 I.U.	1 x 3,000 I.U. + 1 x 500 I.U.	182.5	182.5 x 3,000 I.U. + 182.5 x 500 I.U.
		1,716 I.U.	1 x 1,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	121.7	121.7 x 1,000 I.U. + 121.7 x 500 I.U. + 121.7 x 250 I.U.
		<b>12 to &lt; 18 years</b>			
		2,984 I.U.	1 x 3,000 I.U.	182.5	182.5 x 3,000 I.U.
		952 I.U.	1 x 1,000 I.U.	121.7	121.7 x 1,000 I.U.
Octocog alfa	20 – 40 I.U. /kg	<b>Adults</b>			
		3,432 I.U.	1 x 3,000 I.U. + 1 x 500 I.U.	156.4	156.4 x 3,000 I.U. + 156.4 x 500 I.U.
		1,716 I.U.	1 x 1,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	104.3	104.3 x 1,000 I.U. + 104.3 x 500 I.U. + 104.3 x 250 I.U.
		<b>12 to &lt; 18 years</b>			
		2,984 I.U.	1 x 3,000 I.U.	156.4	156.4 x 3,000 I.U.
		952 I.U.	1 x 1,000 I.U.	104.3	104.3 x 1,000 I.U.
Rurioctocog alfa pegol	40 – 50 I.U./kg	<b>Adults</b>			
		4,290 I.U.	2 x 2,000 I.U. + 1 x 500 I.U.	104.3	208.6 x 2,000 I.U. + 104.3 x 500 I.U.
		3,432 I.U.	1 x 3,000 I.U. + 1 x 500 I.U.	104.3	104.3 x 3,000 I.U. + 104.3 x 500 I.U.
		<b>12 to &lt; 18 years</b>			
		3,730 I.U.	1 x 3,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	104.3	104.3 x 3,000 I.U. + 104.3 x 500 I.U. + 104.3 x 250 I.U.
		1904 I.U.	1 x 2,000 I.U.	104.3	104.3 x 2,000 I.U.
Simoctocog alfa	20 – 40 I.U. /kg	<b>Adults</b>			
		3,432 I.U.	1 x 3,000 I.U. + 1 x 500 I.U.	182.5	182.5 x 3,000 I.U. + 182.5 x 500 I.U.
		1,716 I.U.	1 x 1,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	121.7	121.7 x 1,000 I.U. + 121.7 x 500 I.U. + 121.7 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
		<b>12 to &lt; 18 years</b>			
		2,984 I.U.	1 x 3,000 I.U.	182.5	182.5 x 3,000 I.U.
		952 I.U.	1 x 1,000 I.U.	121.7	121.7 x 1,000 I.U.
Turoctocog alfa <sup>7</sup>	20 – 50 I.U. /kg	<b>Adults</b>			
		4,290 I.U.	1 x 3,000 I.U. + 1 x 1,500 I.U.	156.4	156.4 x 3,000 I.U. + 156.4 x 1500 I.U.
		1,716 I.U.	1 x 1,500 I.U. + 1 x 250 I.U.	156.4	156.4 x 1,500 I.U. + 156.4 x 250 I.U.
		<b>12 to &lt; 18 years</b>			
		3,730 I.U.	1 x 3,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	156.4	156.4 x 3,000 I.U. + 156.4 x 500 I.U. + 156.4 x 250 I.U.
		952 I.U.	1 x 1,000 I.U.	156.4	156.4 x 1,000 I.U.
Turoctocog alfa pegol	50 I.U./kg	<b>Adults</b>			
		4,290 I.U.	1 x 3,000 I.U. + 1 x 1,500 I.U.	91.3	91.3 x 3,000 I.U. + 91.3 x 1,500 I.U.
		<b>12 to &lt; 18 years</b>			
		3,730 I.U.	1 x 3,000 I.U. + 1 x 1,000 I.U.	91.3	91.3 x 3,000 I.U. + 91.3 x 1,000 I.U.
		2,380 I.U.	1 x 2,000 I.U. + 1 x 500 I.U.	91.3	91.3 x 2,000 I.U. + 91.3 x 500 I.U.
Human plasma-derived coagulation factor VIII products					
Human plasma-derived products	20 – 40 I.U. /kg	<b>Adults</b>			
		3,432 I.U.	3 x 1,000 I.U. + 1 x 500 I.U.	182.5	547.5 x 1,000 I.U. + 182.5 x 500 I.U.
		1,716 I.U.	1 x 1,000 I.U. + 1 x 500 I.U. + 1 x 250 I.U.	121.7	121.7 x 1,000 I.U. + 121.7 x 500 I.U. + 121.7 x 250 I.U.
		<b>12 to &lt; 18 years</b>			
		2,984 I.U.	3 x 1,000 I.U.	182.5	547.5 x 1,000 I.U.
		952 I.U.	1 x 1,000 I.U.	121.7	121.7 x 1,000 I.U.
IgG antibody					
Emicizumab	1.5 – 6 mg/kg	<b>Adults</b>			
		514.8 mg	3 x 150 mg +	13.0	39.0 x 150 mg +

<sup>7</sup> The product information for turoctocog alfa provides for different therapy regimens. In determining consumption, the dosing schemes with the widest range of consumption (from 12 years: 20 – 50 I.U. per kg body weight three times a week). Consumption using the other dosing schemes is within the calculated consumption range.

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 x 60 mg + 1 x 12 mg		13.0 x 60 mg + 13.0 x 12 mg
		128.7 mg	1 x 105 mg + 1 x 30 mg	52.1	52.1 x 105 mg + 52.1 x 30 mg
		<b>12 to &lt; 18 years</b>			
		447.6 mg	3 x 150 mg	13.0	39.0 x 150 mg
		71.4 mg	1 x 60 mg + 1 x 30 mg	52.1	52.1 x 60 mg + 52.1 x 30 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					
Marstacimab 150 mg	1 SFI	€ 7,531.64	€ 1.77	€ 426.84	€ 7,103.03
Appropriate comparator therapy					
<i>recombinant blood coagulation factor VIII products</i>					
Damoctocog alfa pegol 3,000 I.U. <sup>8</sup>	1 PSI	€ 2,316.68	€ 1.77	€ 0.00	€ 2,314.91
Damoctocog alfa pegol 2,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,568.68	€ 1.77	€ 0.00	€ 1,566.91
Damoctocog alfa pegol 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 795.10	€ 1.77	€ 0.00	€ 793.33
Damoctocog alfa pegol 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 405.44	€ 1.77	€ 0.00	€ 403.67
Damoctocog alfa pegol 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 209.50	€ 1.77	€ 0.00	€ 207.73
Efmoroctocog alfa 4,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 2,503.32	€ 1.77	€ 0.00	€ 2,501.55
Efmoroctocog alfa 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,896.24	€ 1.77	€ 0.00	€ 1,894.47

<sup>8</sup> Fixed reimbursement rate



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
Efmoroctocog alfa 2,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,279.87	€ 1.77	€ 0.00	€ 1,278.10
Efmoroctocog alfa 750 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 503.07	€ 1.77	€ 0.00	€ 501.30
Efmoroctocog alfa 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 356.55	€ 1.77	€ 0.00	€ 354.78
Lonoctocog alfa 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,942.98	€ 1.77	€ 0.00	€ 1,941.21
Lonoctocog alfa 2,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,328.24	€ 1.77	€ 0.00	€ 1,326.47
Lonoctocog alfa 1,500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 989.24	€ 1.77	€ 0.00	€ 987.47
Lonoctocog alfa 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 649.20	€ 1.77	€ 0.00	€ 647.43
Lonoctocog alfa 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 356.55	€ 1.77	€ 0.00	€ 354.78
Lonoctocog alfa 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 160.30	€ 1.77	€ 0.00	€ 158.53
Moroctocog alfa 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PS	€ 1,989.74	€ 1.77	€ 0.00	€ 1,987.97
Moroctocog alfa 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PS	€ 697.88	€ 1.77	€ 0.00	€ 696.11
Moroctocog alfa 500 I.U.Fehler! Textmarke nicht definiert.	1 PS	€ 356.55	€ 1.77	€ 0.00	€ 354.78
Moroctocog alfa 250 I.U.Fehler! Textmarke nicht definiert.	1 PS	€ 160.30	€ 1.77	€ 0.00	€ 158.53
Octocog alfa 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 2,129.91	€ 1.77	€ 0.00	€ 2,128.14
Octocog alfa 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 746.50	€ 1.77	€ 0.00	€ 744.73
Octocog alfa 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 356.55	€ 1.77	€ 0.00	€ 354.78
Octocog alfa 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 209.50	€ 1.77	€ 0.00	€ 207.73
Rurioctocog alfa pegol 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,896.24	€ 1.77	€ 0.00	€ 1,894.47
Rurioctocog alfa pegol 2,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,279.87	€ 1.77	€ 0.00	€ 1,278.10
Rurioctocog alfa pegol 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 356.55	€ 1.77	€ 0.00	€ 354.78
Rurioctocog alfa pegol 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 160.30	€ 1.77	€ 0.00	€ 158.53
Simoctocog alfa 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,989.74	€ 1.77	€ 0.00	€ 1,987.97
Simoctocog alfa 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 697.88	€ 1.77	€ 0.00	€ 696.11
Simoctocog alfa 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 356.55	€ 1.77	€ 0.00	€ 354.78
Simoctocog alfa 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 160.30	€ 1.77	€ 0.00	€ 158.53
Turoctocog alfa 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,615.52	€ 1.77	€ 0.00	€ 1,613.75
Turoctocog alfa 1,500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 795.10	€ 1.77	€ 0.00	€ 793.33

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
Turoctocog alfa 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 551.81	€ 1.77	€ 0.00	€ 550.04
Turoctocog alfa 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 258.59	€ 1.77	€ 0.00	€ 256.82
Turoctocog alfa 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 160.30	€ 1.77	€ 0.00	€ 158.53
Turoctocog alfa pegol 3,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,896.24	€ 1.77	€ 0.00	€ 1,894.47
Turoctocog alfa pegol 2,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 1,279.87	€ 1.77	€ 0.00	€ 1,278.10
Turoctocog alfa pegol 1,500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 989.24	€ 1.77	€ 0.00	€ 987.47
Turoctocog alfa pegol 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 649.20	€ 1.77	€ 0.00	€ 647.43
Turoctocog alfa pegol 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 356.55	€ 1.77	€ 0.00	€ 354.78
<i>Human plasma-derived coagulation factor VIII products</i>					
Coagulation factor VIII 1,000 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 790.30	€ 1.77	€ 0.00	€ 788.53
Coagulation factor VIII 500 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 400.84	€ 1.77	€ 0.00	€ 399.07
Coagulation factor VIII 250 I.U.Fehler! Textmarke nicht definiert.	1 PSI	€ 206.10	€ 1.77	€ 0.00	€ 204.33
<i>IgG antibody</i>					
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: PS = prefilled syringe; SFI = solution for injection; PSI = powder and solvent for solution for injection					

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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 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 and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors for routine prophylaxis

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

#### References:

Product information for marstacimab (Hympavzi); Hympavzi 150 mg solution for injection;  
last revised: April 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 Hymfavzi 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% (0.0%) of the total number of study participants.

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 11 June 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 31 January 2025, the pharmaceutical company submitted a dossier for the benefit assessment of marstacimab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 3 February 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 marstacimab.

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

The oral hearing was held on 10 June 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 08 July 2025, and the proposed draft resolution was approved.

At their session on 17 July 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

### Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 June 2024	Determination of the appropriate comparator therapy
Working group Section 35a	4 June 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 June 2025	Conduct of the oral hearing,
Working group Section 35a	18 June 2025 3 July 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	8 July 2025	Concluding discussion of the draft resolution
Plenum	17 July 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 17 July 2025

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

Prof. Hecken