Gemeinsamer Bundesausschuss

Justification

for 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

Iptacopan (reassessment of orphan drug > 30 million: paroxysmal nocturnal haemoglobinuria)

From 4 June 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical studies the pharmaceutical company have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

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

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

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

2. Key points of the resolution

The active ingredient iptacopan (Fabhalta) was listed for the first time on 1 July 2024 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. Fabhalta for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

At their session on 19 December 2024, the G-BA decided on the benefit assessment of iptacopan in the therapeutic indication "Fabhalta is indicated as monotherapy in the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia" in accordance with Section 35a SGB V.

If the sales of the orphan drug through the statutory health insurance at pharmacy sales prices and outside the scope of SHI-accredited medical care, including value-added tax, exceed an amount of € 30 million in the last twelve calendar months, the pharmaceutical company must

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

By letter dated 9 September 2025, the pharmaceutical company was requested to submit a dossier for the benefit assessment according to Section 35a SGB V by 15 December 2025, due to exceeding the EUR 30 million turnover limit. Pursuant to Section 4, paragraph 3, number 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 6 Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 12 December 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 16 March 2026 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 iptacopan 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, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. 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 iptacopan.

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

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

2.1.1 Approved therapeutic indication of Iptacopan (Fabhalta) in accordance with the product information

Fabhalta is indicated as monotherapy in the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia.

Therapeutic indication of the resolution (resolution of 04.06.2026):

See the approved therapeutic indication.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

Appropriate comparator therapy:

- eculizumab

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

or

- ravulizumab

or

- pegcetacoplan

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated

Appropriate comparator therapy:

- pegcetacoplan

or

- eculizumab + danicopan

or

- ravulizumab + danicopan

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

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

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

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

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

assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

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

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

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

On 1. In addition to iptacopan, medicinal products with the active ingredients eculizumab, ravulizumab, pegcetacoplan, danicopan and crovalimab are approved for the treatment of PNH.

On 2. It is assumed that an allogeneic stem cell transplant is not indicated at the time of therapy with iptacopan. Accordingly, non-medicinal treatment is not considered as the appropriate comparator therapy for iptacopan.

On 3. For the present therapeutic indication, the following resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Crovalimab: resolution of 6 March 2025
- Danicopan: resolution of 22 November 2024
- Pegcetacoplan: resolutions of 15 September 2022 and 22 November 2024
- Ravulizumab: resolution of 6 February 2020

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V. However, no written statements have been received.

Overall, the evidence in the present therapeutic indication is very limited. Only systematic reviews could be identified during the systematic search. Cochrane reviews or methodologically sound guidelines, by contrast, could not be identified.

The systematic review by Lee et al. (2023) described an overall positive effect of complement inhibitors in the treatment of PNH. However, it is pointed out that there are no direct comparisons between the various complement inhibitors.

A comparison between proximal complement inhibitors with terminal complement inhibition in terms of efficacy and safety is made in the systematic review by Sobral et al. (2024). However, several limitations were identified here, meaning that the differences observed between the complement inhibitor groups are subject to uncertainty.

Given that treatment decisions are influenced by disease activity and that there are different therapeutic approaches with regard to complement inhibition, the G-BA consider it appropriate overall to distinguish between the following patient groups when determining the appropriate comparator therapy.

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

The terminal complement inhibitors (C5 inhibitors) eculizumab, ravulizumab and crovalimab are available for the treatment of adults with PNH who have not been pretreated. In addition, the proximal complement inhibitor (C3 inhibitor) pegcetacoplan has been approved.

The systematic review by Zhou et al (2021) discusses the therapeutic significance of eculizumab in the treatment of PNH. The authors conclude that eculizumab can reduce the transfusion rate, but further safety studies are needed.

As part of the written statement procedure for the present benefit assessment procedure, the scientific-medical societies state that the proximal complement inhibitor pegcetacoplan in addition to the terminal complement inhibitors ravulizumab, eculizumab and crovalimab represent the therapy standard for non-pretreated patients with PNH.

In the benefit assessment of ravulizumab for the treatment of adult patients with PNH, the G-BA concluded by resolution of 6 February 2020 that an additional benefit over eculizumab is not proven.

By resolution of 6 March 2025, it was also found that an additional benefit of crovalimab over eculizumab is not proven.

Crovalimab is a relatively new treatment option in the present therapeutic indication. According to the generally recognised state of medical knowledge, crovalimab is not determined to be an appropriate comparator therapy for the present resolution.

A hint for a non-quantifiable additional benefit of pegcetacoplan was found in the benefit assessment thereof in adults who have haemolytic anaemia and have not received prior therapy with a complement inhibitor, since the scientific data did not allow quantification (resolution of 22 November 2024).

In the overall assessment, the G-BA determined the appropriate comparator therapy to be eculizumab or ravulizumab or pegcetacoplan for patient group a).

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated

With regard to patients who have been pretreated with primary terminal complement inhibition and continue to be symptomatic despite treatment with a C5 inhibitor, the continuation of inadequate therapy with existing optimisation options does not represent the appropriate comparator therapy.

The systematic review by Syed et al. (2023) specifically investigated further therapy options in the presence of eculizumab refractoriness. The authors conclude that the development of an individualised treatment plan is recommended.

As part of the written statement procedure for the present benefit assessment procedure, the scientific-medical societies state that pegcetacoplan or danicopan plus eculizumab or ravulizumab represent the therapy standard for pretreated patients.

By resolution of 15 September 2022, the G-BA found a hint for a non-quantifiable additional benefit of pegcetacoplan in adult patients with PNH who remain anaemic for at least 3 months following treatment with a C5 inhibitor, since the scientific data did not allow quantification.

The proximal complement inhibitor danicopan is approved as an add-on therapy to ravulizumab or eculizumab for adults with PNH who have residual haemolytic anaemia. By resolution of 22 November 2024, the G-BA found also a hint for a non-quantifiable additional benefit in this therapeutic indication, since the scientific data did not allow quantification.

The systematic review by Muvaffak et al. (2024) found that the use of danicopan in addition to eculizumab or ravulizumab reduced haemolysis in patients with PNH compared with the use of a placebo.

In the overall assessment, the G-BA determined the appropriate comparator therapy to be pegcetacoplan or the combination therapies comprising eculizumab and danicopan or ravulizumab and danicopan for patient group b).

For both patient groups, the G-BA are of the opinion that supportive measures should be implemented in the intervention and control arms of a clinical study according to the generally recognised state of medical knowledge.

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

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

Change in the appropriate comparator therapy:

Compared to the original determination of the appropriate comparator therapy for patient group a), the present resolution adds the active ingredient pegcetacoplan to the appropriate comparator therapy. This takes particular account of the statements submitted by clinical experts in the present benefit assessment procedure. This does not affect the present assessment of the additional benefit of iptacopan.

2.1.3 Extent and probability of the additional benefit

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

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

An additional benefit is not proven.

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated

An additional benefit is not proven.

Justification:

In the dossier, the pharmaceutical company divided the patients covered by the therapeutic indication into the following sub-populations and comparisons:

- Sub-population a: adults with PNH who have haemolysis accompanied by one or more clinical symptoms (without pretreatment): eculizumab or ravulizumab,
- Sub-population b: adults with PNH who remain anaemic with clinically relevant extravascular haemolysis for at least 3 months following treatment with eculizumab or ravulizumab: pegcetacoplan,
- Sub-population c: adults with PNH who remain anaemic without clinically relevant extravascular haemolysis for at least 3 months following treatment with eculizumab or ravulizumab: eculizumab or ravulizumab.

The pharmaceutical company did not provide any data on sub-populations a and b in the dossier, whereas they drew on data on sub-population c from the APPLY-PNH study.

APPLY-PNH study

The APPLY-PNH study is a completed, multicentre, open-label RCT comparing iptacopan with eculizumab or ravulizumab. Adults with PNH who had received eculizumab or ravulizumab as part of a stable treatment regimen for at least 6 months but still had a mean haemoglobin (Hb) level < 10 g/dl were enrolled in the study. The APPLY-PNH study comprised a 24-week randomised treatment phase followed by a 24-week extension phase, during which patients in both study arms received iptacopan.

A total of 97 patients were randomly assigned in an 8:5 ratio to receive treatment with iptacopan (N = 62) or with eculizumab or ravulizumab (continuation of existing treatment with a C5 inhibitor; [N = 35]). Randomisation was stratified by previous treatment (eculizumab vs ravulizumab) and transfusion history in the last 6 months prior to randomisation (received transfusion vs received no transfusion).

Treatment with Iptacopan was carried out in accordance with the product information. Treatment with eculizumab or ravulizumab largely complied with the requirements in the relevant product information. The study did not provide for any dose adjustments in accordance with the product information, for example, by adjusting the dose interval.

The co-primary endpoints were the increase in Hb level by ≥ 2 g/dl and the increase in Hb level to ≥ 12 g/dl, whilst avoiding red blood cell transfusions in each case. Patient-relevant endpoints were assessed in the categories of morbidity, health-related quality of life and side effects.

In the dossier, the pharmaceutical company provided data on a sub-population of the study as of the final data cut-off from 6 March 2023 (n = 44 in the intervention arm and n = 22 in the comparator arm), which they use for sub-population c.

In this context, the pharmaceutical company applied the following criteria for the operationalisation of clinically relevant extravascular haemolysis:

- Residual anaemia was defined as mean Hb level < 10 g/dl,

- reticulocytosis was defined as reticulocyte count > upper limit of normal (ULN; [123 × 10^9/l]); this corresponds to the threshold value set by the study's central laboratory and
- symptomatology, defined on the basis of PNH symptoms (reddish or cola-coloured urine/ haemoglobinuria, fatigue, dyspnoea, dysphagia, chest pain, abdominal pain and erectile dysfunction) and the manifestations of the symptoms (none, mild, moderate or severe) collected in the study via patient survey conducted by the principal investigator. Clinically relevant symptoms require the presence of at least 1 of the following moderate or severe symptoms: reddish or cola-coloured urine/ haemoglobinuria, fatigue, dysphagia, erectile dysfunction, or at least 1 of the following mild, moderate or severe symptoms: abdominal pain, chest pain, dyspnoea.

In their written statement, the pharmaceutical company presented three further sensitivity analyses of the sub-population c they considered (c1: patients without clinically relevant symptomatology at baseline: those without reticulocytosis were also excluded if they had clinically relevant symptoms and anaemia; c2: patients without any symptoms or without reticulocytosis; c3: patients without any symptoms and without transfusions 7 days prior to baseline).

Assessment

The pharmaceutical company did not provide any data on patient group a) (adults with PNH who have haemolytic anaemia and have not been pretreated). An additional benefit of iptacopan as monotherapy for patient group a) is therefore not proven.

No suitable data on patient group b) (adults with PNH who continue to have haemolytic anaemia and have been pretreated) were available for comparing iptacopan with the appropriate comparator therapy, as the APPLY-PNH study did not involve a therapy switch to pegcetacoplan or danicopan in combination with eculizumab or ravulizumab. Instead, treatment with eculizumab or ravulizumab that had been given prior to randomisation was continued in the comparator arm. The APPLY-PNH study is therefore unsuitable for the benefit assessment.

It is generally assumed that patient group b) continues to predominantly comprise anaemic patients who are indicated for a switch to proximal complement inhibition due to persistent, clinically relevant symptoms.

With regard to the sub-population c under consideration and the sensitivity analyses submitted in this regard, the pharmaceutical company state that the therapeutic indication of iptacopan under assessment is based solely on the presence of haemolytic anaemia and would therefore result in a sub-population of pretreated patients, for whom continuation of the terminal complement inhibition would be an appropriate benchmark, particularly in the absence of clinically relevant extravascular haemolysis.

In this context, clinical experts stated at the oral hearing on the present benefit assessment procedure that a switch of patients from terminal to proximal complement inhibition at a patient-individual level should primarily be based on symptomatology persisting under terminal complement inhibition, particularly in the context of the onset of extravascular haemolysis. According to the experts, the extent to which patients below the threshold for clinically relevant extravascular haemolysis – that is, patients with mild to moderate symptomatology – can switch to proximal complement inhibition or continue with terminal complement inhibition depends on further patient-individual factors, and must be decided on a case-by-case basis within the overall context. Overall, the size of the sub-population of patients for whom a switch to proximal complement inhibition is not yet indicated is unclear.

Regardless of the failure to implement the appropriate comparator therapy in the APPLY-PNH study, it cannot be assumed with the necessary certainty, against this background, that the evaluations or sensitivity analyses presented by the pharmaceutical company would in fact be suitable - with regard to the assumptions made in the definition of the analysis populations - for identifying patients, for whom a switch to proximal complement inhibition is not yet indicated.

Overall, an additional benefit of iptacopan as monotherapy for patient group b) is not proven.

2.1.4 Summary of the assessment

The present assessment is the new benefit assessment of the medicinal product Fabhalta with the active ingredient iptacopan due to exceeding the EUR 30 million turnover limit. Fabhalta was approved as an orphan drug. The therapeutic indication assessed here is as follows:

"Fabhalta is indicated as monotherapy in the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia."

The following patient groups were differentiated in this therapeutic indication:

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

and

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated.

On patient group a)

Eculizumab or ravulizumab or pegcetacoplan were determined as the appropriate comparator therapy.

The pharmaceutical company did not provide any data on patient group a). An additional benefit of iptacopan as monotherapy is therefore not proven.

On patient group b)

The appropriate comparator therapy was determined to be pegcetacoplan or eculizumab + danicopan or ravulizumab + danicopan.

In the dossier, the pharmaceutical company divided the patients included in patient group b) into two sub-populations and presented analyses of a sub-population from the APPLY-PNH study (as well as further sensitivity analyses in the written statement procedure) for the sub-population of patients - considered separately by the pharmaceutical company - who remain anaemic for at least 3 months following treatment with eculizumab or ravulizumab and in whom there is no clinically relevant extravascular haemolysis, and compared iptacopan with eculizumab or ravulizumab.

No suitable data on patient group b) were therefore available for comparing iptacopan with the appropriate comparator therapy, as the APPLY-PNH study presented by the pharmaceutical company did not involve a therapy switch to pegcetacoplan or danicopan in combination with eculizumab or ravulizumab. Instead, treatment with eculizumab or ravulizumab that had been given prior to randomisation was continued in the comparator arm. The APPLY-PNH study is therefore unsuitable for the benefit assessment.

Regardless of the failure to implement the appropriate comparator therapy, it cannot be assumed with sufficient certainty that the analyses presented by the pharmaceutical company would be suitable for identifying patients, for whom a switch to proximal complement inhibition is not yet indicated.

Overall, an additional benefit of iptacopan as monotherapy for patient group b) is not proven.

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

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

The pharmaceutical company's derivation of the patient numbers in the dossier is mathematically comprehensible. The pharmaceutical company determined the number of patients with PNH who have haemolytic anaemia based on the information in the resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V in this therapeutic indication for pegcetacoplan dated 22 November 2024 and 15 September 2022 and for iptacopan dated 19 December 2024, and assumed an extrapolation of the patient numbers at a growth rate of 8.18% or 7% (for 2025). In their written statement, the pharmaceutical company also carried out a further calculation at a constant growth rate of 8.18% per year. This rate refers to the number of patients with PNH identified in an analysis of statutory health insurance claims data from the InGef research database within the general German population.

However, the main uncertainty regarding the patient numbers stated in the above-mentioned resolutions on pegcetacoplan and iptacopan relates to the demarcation of patients with PNH who also meet the additional criterion of haemolytic anaemia. Against this background, it is unclear whether extrapolation of the figures on the basis of the growth rates estimated by the pharmaceutical company would lead to a more accurate estimate than the figures from the earlier resolutions.

In order to enable a consistent analysis of patient numbers in the therapeutic indication under assessment, given these uncertainties, the present resolution continues to be based on data from the resolutions on pegcetacoplan dated 22 November 2024 and 15 September 2022, as well as on iptacopan dated 19 December 2024.

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 Fabhalta (active ingredient: iptacopan) at the following publicly accessible link (last access: 13 April 2026):

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

Treatment with iptacopan should only be initiated and monitored by specialists who are experienced in the treatment of patients with haematological diseases.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (incl. patient card). The training

material contains, in particular, informations and warnings of the increased risk of infection with encapsulated bacteria associated with the use of iptacopan.

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 April 2026).

The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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

Treatment period:

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

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed:				
Iptacopan	Continuously, 2 x daily	365.0	1	365.0
Appropriate comparator therapy				
eculizumab or ravulizumab or pegcetacoplan				
eculizumab	Continuously, 1 x every 12 - 16 days	22.8 – 30.4	1	22.8 – 30.4
ravulizumab	Continuously, 1 x every 56 days	6.5	1	6.5
pegcetacoplan	Continuously, 2 x in 7 days	104.3	1	104.3

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed:				
Iptacopan	Continuously, 2 x daily	365.0	1	365.0
Appropriate comparator therapy				
pegcetacoplan				
pegcetacoplan	Continuously, 2 x in 7 days	104.3	1	104.3
eculizumab + danicopan				
eculizumab	Continuously, 1 x every 12 - 16 days	22.8 – 30.4	1	22.8 – 30.4
danicopan	Continuously, 3 x daily	365.0	1	365.0
ravulizumab + danicopan				
ravulizumab	Continuously, 1 x every 56 days	6.5	1	6.5
danicopan	Continuously, 3 x daily	365.0	1	365.0

Consumption:

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.

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg).[2]

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

[2] Federal Health Reporting. Average body measurements of the population (2021, both sexes, from 15 years: 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
Medicinal product to be assessed:					
Iptacopan	200 mg	400 mg	2 x 200 mg	365.0	730 x 200 mg
Appropriate comparator therapy					
eculizumab or ravulizumab or pegcetacoplan					
eculizumab	900 mg	900 mg	3 x 300 mg	22.8 – 30.4	68.4 x 300 mg – 91.2 x 300 mg
ravulizumab	3,300 mg	3,300 mg	3 x 1,100 mg	6.5	19.5 x 1,100 mg
pegcetacoplan	1,080 mg	1,080 mg	1 x 1,080 mg	104.3	104.3 x 1,080 mg

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated

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:					
Iptacopan	200 mg	400 mg	2 x 200 mg	365.0	730 x 200 mg
Appropriate comparator therapy					
pegcetacoplan					
pegcetacoplan	1,080 mg	1,080 mg	1 x 1,080 mg	104.3	104.3 x 1,080 mg
eculizumab + danicopan					
eculizumab	900 mg	900 mg	3 x 300 mg	22.8 – 30.4	68.4 x 300 mg – 91.2 x 300 mg
danicopan	150 mg – 200 mg	450 mg – 600 mg	3 x 100 mg + 3 x 50 mg – 6 x 100 mg	365.0	1,095 x 100 mg + 1,095 x 50 mg – 2,190 x 100 mg
ravulizumab + danicopan					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
ravulizumab	3,300 mg	3,300 mg	3 x 1,100 mg	6.5	19.5 x 1,100 mg
danicopan	150 mg – 200 mg	450 mg – 600 mg	3 x 100 mg + 3 x 50 mg – 6 x 100 mg	365.0	1,095 x 100 mg + 1,095 x 50 mg – 2,190 x 100 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:					
Iptacopan 200 mg	168 HC	€ 93,519.58	€ 1.77	€ 5,340.33	€ 88,177.48
Appropriate comparator therapy					
Eculizumab 300 mg	1 CIS	€ 5,586.75	€ 1.77	€ 318.47	€ 5,266.51
Danicopan 100 mg | 50 mg[3]	1 CMB	€ 7,520.65	€ 1.77	€ 428.91	€ 7,089.97
Danicopan 200 mg	180 FCT	€ 10,024.04	€ 1.77	€ 571.88	€ 9,450.39
Pegcetacoplan 1,080 mg	8 INF	€ 29,481.74	€ 1.77	€ 1,683.11	€ 27,796.86
Ravulizumab 1,100 mg	1 CIS	€ 16,418.81	€ 1.77	€ 937.09	€ 15,479.95
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; INF = solution for injection; CMB = combo pack					

LAUER-TAXE® last revised: 1 April 2026

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there

[3] The combo pack contains 1 bottle of 90 × 50 mg film-coated tablets and 1 bottle of 90 × 100 mg film-coated tablets.

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.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-apply unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

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

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication)

and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

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

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

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

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

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

Concomitant active ingredient

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

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

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

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

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

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

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

Designation

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

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

Exception to the designation

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

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1

SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

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

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

a) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia and have not been pretreated

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient approved as monotherapy.

b) Adults with paroxysmal nocturnal haemoglobinuria (PNH) who continue to have haemolytic anaemia and have been pretreated

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient approved as monotherapy.

3. Bureaucratic costs calculation

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

4. Process sequence

The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 11 November 2025.

On 12 December 2025, the pharmaceutical company submitted a dossier for the benefit assessment of iptacopan to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 6 VerfO.

By letter dated 15 December 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient iptacopan.

The dossier assessment by the IQWiG was submitted to the G-BA on 12 March 2026, and the written statement procedure was initiated with publication on the G-BA website on 16 March 2026. The deadline for submitting written statements was 7 April 2026.

The oral hearing was held on 27 April 2026.

By letter dated 28 April 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by the IQWiG was submitted to the G-BA on 13 May 2026.

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

The evaluation of the written statements received and the oral hearing were discussed at the Subcommittee's session on 27 May 2026, and deliberation of the draft resolution was concluded.

At their session on 4 June 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 November 2025	Determination of the appropriate comparator therapy
Working group Section 35a	15 April 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	27 April 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	6 May 2026; 20 May 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	27 May 2026	Concluding discussion of the draft resolution
Plenum	4 June 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 4 June 2026

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

Prof. Hecken