Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Faricimab (new therapeutic indication: macular oedema secondary to retinal vein occlusion)

of 20 February 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of 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 trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

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

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

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

2. Key points of the resolution

The active ingredient faricimab (Vabysmo) was listed for the first time on 15 October 2022 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 26 July 2024, faricimab received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 21 August 2024, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient faricimab with the new therapeutic indication

"Faricimab is indicated for the treatment of adult patients with visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)."

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The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 December 2024 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 faricimab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA has 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 faricimab.

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

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

2.1.1 Approved therapeutic indication of Faricimab (Vabysmo) in accordance with the product information

Vabysmo is indicated for the treatment of adult patients with visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).

Therapeutic indication of the resolution (resolution of 20.02.2025):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)

Appropriate comparator therapy for faricimab:

- Aflibercept or ranibizumab

b) Adults with visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)

Appropriate comparator therapy for faricimab:

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

– Aflibercept or ranibizumab

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

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

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

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
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. In addition to faricimab, the glucocorticoid dexamethasone (as an intravitreal implant) and the VEGF inhibitors aflibercept and ranibizumab are approved for the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (BRVO or CRVO).

on 2. Photocoagulation using laser is generally considered as non-medicinal treatment in the present therapeutic indication.

on 3. A resolution on the early benefit assessment according to Section 35a SGB V of 20 March 2014 (macular oedema secondary to central retinal vein occlusion) and of 3 September 2015 (macular oedema secondary to branch retinal vein occlusion) is available for the active ingredient aflibercept.

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".

This therapeutic indication includes visual impairment due to macular oedema secondary to both BRVO and CRVO. Although both entities of retinal vein occlusion are based on the same pathophysiological processes, the affected patients differ in terms of the severity of symptoms, clinical course and prognosis. The G-BA therefore considers it appropriate to determine two sub-populations in the therapeutic indication. Patient population a comprises patients with visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO). Patient population b comprises patients with visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO). Patients with visual impairment due to macular oedema secondary to hemiretinal vein occlusion (HRVO) are assigned to patient population b.

In this therapeutic indication, there is evidence from numerous systematic reviews that analyse the efficacy and safety of the individual therapy options (dexamethasone, VEGF inhibitors, laser coagulation). In addition, a guideline from the American Academy of Ophthalmology from 2020 was taken into account to determine the appropriate comparator therapy. In principle, medicinal therapies appear to be superior to laser therapy in terms of various efficacy endpoints. This is also reflected in the above-mentioned guideline with the highest level of recommendation for VEGF inhibitors and glucocorticoids. However, dexamethasone is associated with increased safety concerns (e.g. cataract risk, increase in intraocular pressure). Accordingly, glucocorticoids are regarded as subordinate to VEGF inhibitors in the German healthcare context.

A superiority or inferiority of the active ingredients within the product class of VEGF inhibitors cannot be inferred on the basis of the available evidence. Different treatment recommendations based on the presence of BRVO or CRVO were also not identified.

In the overall assessment, a therapy with aflibercept or ranibizumab is therefore determined as an appropriate comparator therapy for both patient population a (adults with visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)) and patient population b (adults with visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)). Observe the dosage information in the product information for aflibercept and ranibizumab.

The appropriate comparator therapy determined here includes several therapy options. These therapeutic alternatives are equally appropriate for the comparator therapy.

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

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

2.1.3 Extent and probability of the additional benefit

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

For adults with visual impairment due to macular oedema secondary to retinal vein occlusion (branch retinal vein occlusion [BRVO] or central retinal vein occlusion [CRVO]), the additional benefit of faricimab is not proven.

Justification:

No assessable data are available for the assessment of the additional benefit of faricimab compared with the appropriate comparator therapy.

The pharmaceutical company identifies the two randomised controlled trials (RCT) BALATON and COMINO in the present therapeutic indication. Both studies are double-blind, multicentre RCTs comparing faricimab with aflibercept. Adult patients with visual impairment due to macular oedema secondary to BRVO were enrolled in the BALATON study and those with visual impairment due to macular oedema secondary to CRVO or hemiretinal vein occlusion were enrolled in the COMINO study.

Both studies were divided into two treatment phases. In the first treatment phase, patients received monthly intravitreal injections of faricimab or aflibercept up to and including week 20 (6 injections in total). The primary analysis of treatment phase 1 took place at week 24. This was followed by a non-actively controlled treatment phase 2, in which all patients received faricimab until week 68 and - to blind the treatment intervals - sham injections at different patient-individual intervals. In the absence of an active comparison, treatment phase 2 did not yield any relevant data for the benefit assessment.

The requirements in the product information for both faricimab and aflibercept states that treatment can be individually adjusted depending on the disease activity after 3 initial monthly injections of faricimab or aflibercept ("*treat and extend*"). In the BALATON and COMINO studies, a flexibilisation of the treatment regimen was only possible in the second, non-comparative study phase design.

In the BALATON study, the percentage of patients whose visual acuity had improved by ≥ 15 letters in the best corrected visual acuity (BCVA) analysis at week 24 was 53% in the faricimab arm and 55% in the aflibercept arm. In the COMINO study, 54% with faricimab and 55% with aflibercept achieved an improvement in visual acuity by ≥ 15 letters at week 24. Approximately 50% (BALATON study) and 53% (COMINO study) of patients achieved this improvement as early as week 12. The analyses of the average improvement in visual acuity and central subfield thickness of all patients show a plateau formation between weeks 8 and 12. It can therefore be assumed that in the BALATON and COMINO studies, a stabilisation of the disease occurred after just 8 to 12 weeks in a relevant percentage of patients and that an individual

flexibilisation of the treatment regimen would have been indicated in accordance with the product information.

Since flexibilisation, which would have been indicated in a relevant percentage of patients in accordance with the product information for both faricimab and aflibercept, was not planned in either study, both studies were not considered for the present benefit assessment in accordance with the pharmaceutical company's approach in the dossier.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient faricimab.

The therapeutic indication assessed here is as follows: "Vabysmo is indicated for the treatment of adult patients with visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)."

In the therapeutic indication under consideration, two patient groups were differentiated by the presence of BRVO or CRVO.

a) Adults with visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)

   The G-BA determined a therapy with aflibercept or ranibizumab as the appropriate comparator therapy.

   For this patient group, the pharmaceutical company presented the BALATON RCT, which compared faricimab with aflibercept. In the BALATON study, all patients in both arms received 6 monthly intravitreal injections. Flexibilisation of the treatment regimen was not planned in the comparative study phase. Based on the data on best-corrected visual acuity and central visual field thickness, it can be seen that the disease stabilised in a relevant percentage of patients after just 8 to 12 weeks. Since flexibilisation, which would have been indicated in a relevant percentage of patients in accordance with the product information for both faricimab and aflibercept, was not planned, the BALATON study was not considered for the present benefit assessment in accordance with the pharmaceutical company's approach in the dossier.

   An additional benefit of faricimab compared to the appropriate comparator therapy is therefore not proven.

b) Adults with visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)

   The G-BA determined a therapy with aflibercept or ranibizumab as the appropriate comparator therapy.

   For this patient group, the pharmaceutical company presented the COMINO RCT, which compared faricimab with aflibercept. In the COMINO study, all patients in both arms received 6 monthly intravitreal injections. Flexibilisation of the treatment regimen was not planned in the comparative study phase. Based on the data on best-corrected visual acuity and central visual field thickness, it can be seen that the disease stabilised in a relevant percentage of patients after just 8 to 12 weeks. Since flexibilisation, which would have been indicated in a relevant percentage of patients in accordance with the product information for both faricimab and aflibercept, was not planned, the COMINO study was not considered for the present benefit assessment in accordance with the pharmaceutical company's approach in the dossier.

An additional benefit of faricimab compared to the appropriate comparator therapy is therefore 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 patient numbers submitted by the pharmaceutical company with the dossier are underestimated due to the exclusion of patients aged 75 years and older in the lower limit and due to insufficient consideration of mild impairment of visual acuity (≥ 0.5 logMAR) in both limits. The resolution is therefore not based on the figures presented in the dossier, but on the subsequently submitted information from the written statement procedure and the addendum from IQWiG.

The derivation subsequently submitted by the pharmaceutical company is more adequate than the original derivation in view of the missing age cohorts. However, IQWiG's recalculation, which takes into account a higher percentage of patients with impairment of visual acuity (≥ 0.3 logMAR) is used for the upper limit of the range. Uncertainties arise from the prevalence value transferred to the age group 75 years and older and the lack of information on the percentage of patients with a logMAR value of 0.2 to < 0.3.

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 Vabysmo (active ingredient: faricimab) at the following publicly accessible link (last access: 11 November 2024):

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

Treatment with faricimab should only be initiated and monitored by doctors experienced in the therapy of macular oedema secondary to retinal vein occlusion.

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 patients. In particular, the training material contains information and warnings about infective endophthalmitis and intraocular inflammation.

2.4 Treatment costs

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

In the present case, the treatment duration, consumption and costs shown refer to the first year of treatment on the one hand and to the subsequent years on the other; whole injection solutions consumed within the first year were rounded up for the first year of treatment.

In the present case, the treatment duration, consumption and costs shown refer to the first year of treatment on the one hand and to the subsequent years on the other.

Due to the patient-individual approach regarding the adjustment of the treatment intervals according to the product information, the possible upper and lower limits of the costs for faricimab are presented in the present resolution for the following years.

Patient-individual dose adjustments, e.g. because of side effects or comorbidities, are not taken into account when calculating the annual treatment costs.

On faricimab: According to the requirements in the product information, the treatment is initiated with 3 or more injections at an interval of 4 weeks. Subsequently, the treatment is individually adapted depending on the disease activity ("treat and extend"). Based on the physician's assessment of the anatomical and/or visual findings, the dosing interval may be extended in increments of up to 4 weeks. Treatment intervals longer than 4 months were not investigated. This has no change for the cost calculation, as prolongation of the dosing interval beyond 4 months is still possible according to the product information. Taking into account the acute nature of the retinal vein occlusion and based on the statements of the clinical experts during the oral hearing, it is assumed that it is possible to terminate the therapy after the initial 3 injections. A lower limit of 3 injections is therefore assumed in the 1st year of treatment.

On ranibizumab: Treatment starts with one injection per month until maximum visual acuity is achieved and/or there are no more signs of disease activity. Initially, three or more injections may be necessary. Finally, patients can be treated according to a "treat & extend" regimen, whereby the treatment interval can be extended incrementally. However, there is too little data available in this indication to be able to draw conclusions about the length of these intervals. Taking into account the acute nature of the retinal vein occlusion and based on the statements of the clinical experts during the oral hearing, it is assumed that it is possible to terminate the therapy after the initial 3 injections. A lower limit of 3 injections is therefore assumed in the 1st year of treatment.

On aflibercept: Treatment starts with one injection per month until maximum visual acuity is achieved and/or there are no more signs of disease activity. Initially, three or more injections may be necessary. Finally, patients can be treated according to a "treat & extend" regimen, whereby the treatment interval can be extended incrementally. However, there is too little data available in this indication to be able to draw conclusions about the length of these intervals. Taking into account the acute nature of the retinal vein occlusion and based on the statements of the clinical experts during the oral hearing, it is assumed that it is possible to terminate the therapy after the initial 3 injections. A lower limit of 3 injections is therefore assumed in the 1st year of treatment.

The information on treatment costs refers to the application on one eye. Treatment of the second eye is possible.

a) <u>Adults with visual impairment due to macular oedema macular oedema secondary to branch retinal vein occlusion (BRVO)</u>

and

b) <u>Adults with visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)</u>

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 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 the maximum treatment duration, if specified in the product information.

The necessary injections are calculated on the basis of the time unit "days". Any treatment intervals specified in other time units in the respective product information are converted to "days". A year corresponds to 365 days, a month corresponds to 30.4 days and a week corresponds to 7 days.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Faricimab 1st year	1 x every 28 days for 3 applications	3	1	3 – 14
	Then 1 x every 28 days until treat & extend[2]	11 – 0		
Faricimab Subsequent years	1 x every 28 days until treat & extend[2]	13.0 – 0	1	0 – 13.0
Appropriate comparator therapy				
Aflibercept or ranibizumab				
Aflibercept 1st year	1 x monthly[3] for 3 applications	3	1	3 – 12
	Then 1 x monthly[3] until treat & extend[4]	0 – 9		
Aflibercept Subsequent years	1 x monthly[3] until treat & extend[4]	12.0 – 0	1	0 – 12.0
Ranibizumab 1st year	1 x monthly[3] for 3 applications	3	1	3 – 12
	Then 1 x monthly[3] until treat & extend[4]	0 – 9		
Ranibizumab Subsequent years	1 x monthly[3] until treat & extend[4]	12.0 – 0	1	0 – 12.0

[2] To calculate the lower limit: The treatment interval is prolonged by 28 days for each treatment.
[3] One month corresponds to 30.4 days.
[4] The treatment intervals are incrementally adjusted based on the disease activity. The product information does not state how long the treatment interval should be extended in increments.

Consumption:

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					
Faricimab 1st year	6 mg	6 mg	1 x 6 mg	3 – 14	3 x 6 mg – 14 x 6 mg
Faricimab Subsequent years	6 mg	6 mg	1 x 6 mg	0 – 13.0	0 x 6 mg – 13.0 x 6 mg
Appropriate comparator therapy					
Ranibizumab or aflibercept					
Aflibercept 1st year	2 mg	2 mg	1 x 2 mg	3 – 12	3 x 2 mg – 12 x 2 mg
Aflibercept Subsequent years	2 mg	2 mg	1 x 2 mg	0 – 12.0	0 x 2 mg – 12.0 x 2 mg
Ranibizumab 1st year	0.5 mg	0.5 mg	1 x 0.5 mg	3 – 12	3 x 0.5 mg – 12 x 0.5 mg
Ranibizumab Subsequent years	0.5 mg	0.5 mg	1 x 0.5 mg	0 – 12.0	0 x 0.5 mg – 12.0 x 0.5 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 Sections 130 and 130 a 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					
Faricimab 21 mg	1 SFI	€ 963.98	€ 1.77	€ 52.75	€ 909.46
Appropriate comparator therapy					
Aflibercept 3.6 mg	1 SFI	€ 1,099.42	€ 1.77	€ 60.24	€ 1,037.41

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
Ranibizumab 2.3 mg	1 SFI	€ 1,200.09	€ 1.77	€ 65.82	€ 1,132.50
Abbreviations: SFI = solution for injection					

LAUER-TAXE® last revised: 1 February 2025

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Additionally required SHI services when using the medicinal product to be assessed and the appropriate comparator therapy according to the product information and package information leaflet are given by the treatment costs of the intravitreal injections and the necessary postoperative checks.

All three active ingredients are applied by intravitreal injection. For intravitreal injections, GOPs of the EBM are available [GOP 31371 / 36371 (right eye), GOP 31372 / 36372 (left eye) or GOP 31373 / 36373 (both eyes)]. The information on the costs represented here refers to the application on one eye.

Visual acuity checks are included in the basic specialist flat rate.

The product information for faricimab, aflibercept and ranibizumab recommends setting the treatment interval based on disease activity as determined by morphological parameters and/or visual acuity or functional findings.
The check-up interval should be determined by the attending physician, this can be more frequent than the injection interval.

Costs are incurred for the check-ups carried out for all treatment options. Among others, there are GOPs of the EBM for optical coherence tomography (OCT) for therapy management [GOP 06338 (right eye) or GOP 06339 (left eye)]. The frequency and type of examination used can vary from patient to patient. Due to the individual specification of the control intervals by the attending physician, the costs incurred cannot be quantified.

Type of service	Costs/ service	Number/ year	Costs/ year
Medicinal product to be assessed			
Faricimab			
Intravitreal administration of the medicinal product to the left or right eye (EBM 31372/ 36372 or 31371/ 36371)	€ 96.42 – 206.35	1st year: 3 – 14 Subsequent years: 0 – 13.0	1st year: € 289.26 – € 2,888.90 Subsequent years: € 0 – € 2,682.55

Type of service	Costs/ service	Number/ year	Costs/ year
Postoperative treatment (EBM 31716 or 31717)	€ 20.70 – € 28.88	1st year: 3 – 14 Subsequent years: 0 – 13.0	1st year: € 62.10 – € 404.32 Subsequent years: € 0 – € 375.44
Optical coherence tomography (EBM 06338 or 06339)	€ 50.07	Different from patient to patient	non-quantifiable
Further check-ups	non-quantifiable	Different from patient to patient	non-quantifiable
Appropriate comparator therapy			
Aflibercept, ranibizumab			
Intravitreal administration of the medicinal product to the left or right eye (EBM 31372/ 36372 or 31371/ 36371)	€ 96.42 – 206.35	1st year: 3 – 12 Subsequent years: 0 – 12.0	1st year: € 289.26 – € 2,476.20 Subsequent years: € 0 – € 2,476.20
Postoperative treatment (EBM 31716 or 31717)	€ 20.70 – € 28.88	1st year: 3 – 12 Subsequent years: 0 – 12.0	1st year: € 62.10 – € 346.56 Subsequent years: € 0 – € 346.56
Optical coherence tomography (EBM 06338 or 06339)	€ 50.07	Different from patient to patient	non-quantifiable
Further check-ups	non-quantifiable	Different from patient to patient	non-quantifiable

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 designates 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 has 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 has 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 has 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:

a) Adults with visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)

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 faricimab (Vabysmo); Vabysmo 120 mg/ml solution for injection; last revised: July 2024

b) Adults with visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)

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

References:
Product information for faricimab (Vabysmo); Vabysmo 120 mg/ml solution for injection; last revised: July 2024

3. Bureaucratic costs calculation

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

4. Process sequence

At its session on 27 June 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 21 August 2024, the pharmaceutical company submitted a dossier for the benefit assessment of faricimab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2, sentence 2 VerfO.

By letter dated 27 August 2024 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 faricimab.

The dossier assessment by the IQWiG was submitted to the G-BA on 21 November 2024, and the written statement procedure was initiated with publication on the G-BA website on 2 December 2024. The deadline for submitting statements was 23 December 2024.

The oral hearing was held on 6 January 2025.

By letter dated 7 January 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 30 January 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 11 February 2025, and the proposed draft resolution was approved.

At its session on 20 February 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	27 June 2023	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	6 January 2025 7 January 2025	Information on statements received, conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	15 January 2025 5 February 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 February 2025	Concluding discussion of the draft resolution
Plenum	20 February 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 February 2025

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

Prof. Hecken