Gemeinsamer Bundesausschuss

Justification

to the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Bevacizumab (neovascular (wet) age-related macular degeneration (nAMD))

of 16 October 2025

Contents

1. Legal basis

According to Section 35a paragraph 6 SGB V, the G-BA can initiate a benefit assessment according to paragraph 1 for a medicinal product with an active ingredient that is not a new active ingredient according to Section 35a, paragraph 1, sentence 1 SGB V, if a new marketing authorisation with new dossier protection is granted for the medicinal product. According to Chapter 5 Section 16, paragraph 1, sentence 3 of the Rules of Procedure of the G-BA (VerfO), a benefit assessment according to Section 35a paragraph 6 SGB V can be initiated in particular for medicinal products whose therapeutic indication differs from the therapeutic indication of medicinal products with the same known active ingredients. According to Chapter 5 Section 16, paragraph 1, sentence 4 VerfO, a deviation may result in particular from changes in a therapeutic indication that are attributable to a different therapeutic indication compared to the therapeutic indication of the medicinal product with the same known active ingredient, by the fact that:

– the therapeutic indication relates to a different group of patients or

– the therapeutic area (treatment, diagnosis or prevention) differs.

The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical studies the pharmaceutical company have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application,
7. number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

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

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

2. Key points of the resolution

At their session on 23 April 2024, the Federal Joint Committee (G-BA) decided to initiate a benefit assessment for the active ingredient bevacizumab in the indication of neovascular (wet) age-related macular degeneration according to Section 35a, paragraph 6 SGB V in conjunction with Chapter 5 Section 16, paragraph 1 VerfO.

The medicinal product Lytenava, containing the active ingredient bevacizumab, was first placed on the market on 1 May 2025. Relevant date according to Chapter 5 Section 8, paragraph 1, number 7 VerfO for the start of the assessment procedure for the active ingredient bevacizumab is within three months of the request by the G-BA. If the medicinal product has not yet been placed on the market at that time, the procedure shall start on the date on which it is first placed on the market.

The final dossier was submitted to the G-BA in due time on 29 April 2025. On 1 May 2025, the assessment procedure started.

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

The G-BA came to a resolution on whether an additional benefit of bevacizumab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of bevacizumab.

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 Bevacizumab (Lytenava) in accordance with the product information

Lytenava is indicated in adults for treatment of neovascular (wet) age-related macular degeneration (nAMD).

Therapeutic indication of the resolution (resolution of 16.10.2025):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

Adults with neovascular (wet) age-related macular degeneration (nAMD)

Appropriate comparator therapy for bevacizumab:

- Aflibercept or faricimab 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 the marketing authorisation for bevacizumab, there are also marketing authorisations for aflibercept, brolucizumab, faricimab and ranibizumab in the present therapeutic indication. The active ingredient verteporfin is approved "for the treatment of adults with exudative (wet) age-related macular degeneration (AMD) with predominantly classic subfoveal choroidal neovascularisation". The active ingredient pegaptanib is no longer approved.

On 2. The following non-medicinal treatment options are available in the present therapeutic indication: Photodynamic therapy (PDT), photocoagulation by laser, proton therapy for age-related macular degeneration (resolution of 17 September 2009) and photodynamic therapy (PDT) with verteporfin for age-related wet macular degeneration with classic subfoveal choriodal neovascularisation (resolution of 16 October 2000).

On 3. The following resolutions of the G-BA on the benefit assessment according to Section 35a SGB V are available for the present therapeutic indication:

- Brolucizumab (resolution of 2 May 2024)
- Faricimab (resolution of 6 April 2023)
- Aflibercept (resolution of 6 June 2013)

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

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V.

Based on the aggregated evidence, it can be stated that according to the guideline recommendations, the standard therapy for the targeted treatment setting consists of treatment with a vascular endothelial growth factor (VEGF) inhibitor. Within the group of VEGF inhibitors, no clear superiority could be demonstrated for any of the active ingredients available in Germany (aflibercept, brolucizumab, faricimab and ranibizumab). This applies both to initial therapy in therapy naive patients and to a switch after an inadequate response to a VEGF inhibitor.

In this therapeutic indication, resolutions on the benefit assessment according to Section 35a SGB V have been made for the active ingredients aflibercept, brolucizumab and faricimab. An additional benefit compared to the appropriate comparator therapy has not been proven for any of the active ingredients mentioned.

A Direct Healthcare Professional Communication ("Rote-Hand-Brief") from November 2021 on an increased risk of intraocular inflammation is available for brolucizumab. Against this background, the significance of brolucizumab in healthcare is considered to be secondary to the other VEGF inhibitors.

Based on the aggregated evidence in the indication, the significance of non-medicinal measures is also considered lower than the VEGF inhibitors established in neovascular (wet) AMD.

Based on the available, aggregated evidence, the G-BA therefore determined aflibercept or faricimab or ranibizumab as the appropriate comparator therapy for bevacizumab for the treatment of adults with neovascular (wet) AMD. The active ingredients of the specific appropriate comparator therapy are suitable both for patients who are receiving treatment for their neovascular (wet) AMD for the first time and in the sense of a switch for patients previously treated with VEGF inhibitors after an inadequate response to the existing anti-VEGF therapy.

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

The 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 bevacizumab is assessed as follows:

Adults with neovascular (wet) age-related macular degeneration (nAMD)

An additional benefit is not proven.

Justification:

In their dossier, the pharmaceutical company did not present any relevant study for the assessment of the additional benefit of bevacizumab in comparison with the appropriate comparator therapy. They present the approval studies (NORSE TWO and NORSE ONE) in the dossier. Both studies are double-blind, randomised phase III studies comparing bevacizumab versus ranibizumab in patients aged 50 years and older with neovascular age-related macular degeneration.

According to the product information for bevacizumab and ranibizumab, the treatment intervals should be individually adjusted during therapy. Therapy with bevacizumab should start with one injection per month and continued until maximum visual acuity is achieved and/or there are no more signs of disease activity. Initially, three or more injections may be necessary. The treatment intervals can then be individualised on the basis of the disease activity, although the product information does not contain any specific requirements regarding the length of the treatment intervals in the context of individualisation. Ranibizumab therapy should start 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 by up to two weeks at a time.

In contrast, bevacizumab and ranibizumab were administered in the NORSE TWO and NORSE ONE studies according to a fixed dosage regimen. Bevacizumab was administered monthly over the entire duration of the study, while ranibizumab was only administered on day 150 and day 240 after initiation with 3-monthly injections. The individual adjustments to the treatment interval provided for in the product information were therefore not possible in

either the comparator or the intervention arms of the studies. It remains unclear for how many patients the respective dosage regimen was indicated.

In accordance with the pharmaceutical company's approach in the dossier, these studies are not considered for the present benefit assessment due to the lack of consideration of the individual adjustment to the treatment intervals provided for in the product information for bevacizumab and ranibizumab.

In addition, IQWiG identified five studies comparing bevacizumab with ranibizumab, which were conducted with the proprietary medicinal product Avastin in off-label use. These studies are assessed by IQWiG as potentially relevant for the present procedure. However, the pharmaceutical company did not present the results of these studies either in the dossier or as part of the written statement procedure. One of the reasons given by the pharmaceutical company is the non-availability of patient-individual data from these studies. The suitability of the five identified studies cannot be conclusively assessed. However, the information available gives no reason to assume that the results justify a change in the assessment.

In the overall assessment, an additional benefit of bevacizumab over the appropriate comparator therapy in adults with neovascular (wet) age-related macular degeneration is therefore not proven.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Lytenava with the active ingredient bevacizumab.

Bevacizumab is approved for the treatment of adults with neovascular (wet) age-related macular degeneration (nAMD).

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

For the assessment of the additional benefit, the pharmaceutical company presented the NORSE ONE and NORSE TWO RCTs, each of which compared bevacizumab with ranibizumab.

According to the product information for bevacizumab and ranibizumab, the treatment intervals should be individually adjusted during therapy. In contrast, bevacizumab and ranibizumab were administered in the NORSE TWO and NORSE ONE studies according to a fixed dosage regimen. In accordance with the pharmaceutical company's approach in the dossier, these studies are therefore not considered for the present benefit assessment due to the lack of consideration of the individual adjustment to the treatment intervals provided for in the product information.

An additional benefit of bevacizumab over the appropriate comparator therapy in adults with neovascular (wet) age-related macular degeneration 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 resolution is based on the information presented by the pharmaceutical company in the dossier. These are based on a current routine data analysis for the upper limit of patient numbers and on the patient numbers from the resolution on the benefit assessment of the

active ingredient brolucizumab (resolution of 2 May 2024) in the same therapeutic indication for the lower limit.

The derivation of the patient numbers in the dossier for the active ingredient bevacizumab is basically comprehensible. The specification of a range in the current procedure is generally appropriate for the estimation of the SHI target population, thus taking into account any uncertainties in the course of a routine data analysis. Overall, despite existing uncertainties, the range determined by the pharmaceutical company is preferable to those used in previous procedures.

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 Lytenava (active ingredient: bevacizumab) at the following publicly accessible link (last access: 20 June 2025):

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

Treatment with bevacizumab should only be initiated and monitored by specialists experienced in the administration of intravitreal injections.

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. The training material contains, in particular, information and warnings about infective endophthalmitis.

The medicinal product should be discontinued if visual and anatomical findings indicate that the patient will not benefit from continued treatment.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 August 2025).

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

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.

Due to the possible patient-individual approach regarding the adjustment of the treatment intervals according to the product information, the possible upper and lower limits of the costs are presented in the present resolution for the following years. In contrast to the previously approved VEGF inhibitors, there are no specific requirements in the product information for bevacizumab regarding the length of the treatment intervals in the context of individualisation, which is why the lower limit of the annual treatment costs for the first year of treatment with bevacizumab cannot be specified.

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

On bevacizumab: According to the requirements in the product information, treatment with bevacizumab is started 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. The treatment intervals can then be individualised on the basis of the disease activity, although the product information does not contain any specific requirements regarding the length of the treatment intervals in the context of individualisation.

On aflibercept: Treatment with aflibercept is initiated with three consecutive monthly injections; followed by a treatment interval of two months. Then, this treatment interval can be maintained or prolonged by 2 - 4 weeks in a "Treat & Extend" dosage regimen. Treatment intervals longer than 4 months were not investigated. This has no effect on the cost calculation, as prolongation of the dosing interval beyond 4 months is still possible according to the product information. If the functional and/or morphological findings deteriorate, the treatment interval should be shortened accordingly. Treatment intervals below 4 weeks were not studied. To calculate the upper limit of treatments, the 2-month treatment interval achieved according to the fixed initial scheme is taken as a basis.

On faricimab: According to the requirements in the product information, the treatment is initiated with three injections at intervals of 4 weeks. After 16 and/or 20 weeks, a treatment check-up is suggested, on the basis of which the physician can individually determine the treatment intervals based on the disease activity. In patients without disease activity, administering faricimab every 16 weeks is to be considered. For patients with disease activity, treatment every 8 weeks or 12 weeks is to be considered.

On ranibizumab: Treatment in adults 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 by up to two weeks at a time.

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

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. 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				
Bevacizumab 1st year	1x monthly[3] for 3 applications	3	1	Up to 12

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	Then 1x monthly[3] until individualised treatment intervals[2]	Up to 9		
Bevacizumab Subsequent years	1x monthly[3] until individualised treatment intervals[2]	12.0 – 0	1	0 – 12.0
Appropriate comparator therapy				
Aflibercept 1st year	1x monthly[3] for 3 applications and 1x every 2 months[3]	4	1	6 – 7
	Then 1x every 2 months[3] until Treat & Extend[4]	3 – 2		
Aflibercept Subsequent years	1x every 2 months[3] until Treat & Extend[4]	6.0 – 0	1	0 – 6.0
Faricimab 1st year	1x every 28 days for 3 applications	3	1	5 – 8
	Then 1x every 56 days until 1x every 112 days	5 – 2		
Faricimab Subsequent years	1x every 56 days until 1x every 112 days	6.5 – 3.3	1	3.3 – 6.5
Ranibizumab 1st year	1x monthly[3] for 3 applications	3	1	7 – 12
	Then 1x monthly[3] until Treat & Extend[5]	9 – 4		
Ranibizumab Subsequent years	1x monthly[3] until Treat & Extend[5]	12.0 – 0	1	0 – 12.0

[2] To calculate the lower limit: The interval duration is individualised based on the disease activity. The product information does not state how long the treatment interval should be extended in increments.
[3] One month corresponds to 30.4 days on average.
[4] To calculate the lower limit: The treatment interval is prolonged by 28 days for each treatment.
[5] To calculate the lower limit: The treatment interval is prolonged by 14 days for each treatment.

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					
Bevacizumab 1st year	1.25 mg	1.25 mg	1 x 1.25 mg	Up to 12	Up to 12 x 1.25 mg
Bevacizumab Subsequent years	1.25 mg	1.25 mg	1 x 1.25 mg	0 – 12.0	0 x 1.25 mg – 12.0 x 1.25 mg
Appropriate comparator therapy					
Aflibercept 1st year	2 mg	2 mg	1 x 2 mg	6 – 7	6 x 2 mg – 7 x 2 mg
Aflibercept Subsequent years	2 mg	2 mg	1 x 2 mg	0 – 6.0	0 x 2 mg – 6.0 x 2 mg
Faricimab 1st year	6 mg	6 mg	1 x 6 mg	5 – 8	5 x 6 mg – 8 x 6 mg
Faricimab Subsequent years	6 mg	6 mg	1 x 6 mg	3.3 – 6.5	3.3 x 6 mg – 6.5 x 6 mg
Ranibizumab 1st year	0.5 mg	0.5 mg	1 x 0.5 mg	7 – 12	7 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 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.

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					
Bevacizumab	1 SFI	€ 961.59	€ 1.77	€ 52.61	€ 907.21
Appropriate comparator therapy					
Aflibercept	1 SFI	€ 1,099.42	€ 1.77	€ 60.24	€ 1,037.41
Faricimab	1 SFI	€ 963.98	€ 1.77	€ 52.75	€ 909.46
Ranibizumab	1 SFI	€ 1,200.09	€ 1.77	€ 65.82	€ 1,132.50
Abbreviations: SFI = solution for injection					

LAUER-TAXE® last revised: 15 August 2025

Costs for additionally required SHI services:

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

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

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 four 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)].

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

The product information for bevacizumab, aflibercept, faricimab and ranibizumab recommend 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.

Designation of the therapy	Costs/ service	Number/ year	Costs/ year
Medicinal product to be assessed			
Bevacizumab			
Intravitreal administration of the medicinal product on the left or right eye (EBM 31372/ 36372 or 31371/ 36371)	€ 96.42 – € 206.35	1st year: Up to 12 Subsequent years: 0 – 12.0	1st year: up to € 2,476.20 Subsequent years: € 0 - € 2,476.20
Optical coherence tomography (EBM 06338 or 06339)	€ 50.07	Different from patient to patient	non-quantifiable
Postoperative treatment (EBM 31717 or 31716)	€ 20.70 – € 28.88	1st year: Up to 12 Subsequent years: 0 – 12.0	1st year: up to € 346.56 Subsequent years: € 0 – € 346.56
Further check-ups	non-quantifiable	Different from patient to patient	non-quantifiable
Appropriate comparator therapy			
Aflibercept			
Intravitreal administration of the medicinal product on the left or right eye (EBM 31372/ 36372 or 31371/ 36371)	€ 96.42 – € 206.35	1st year: 6 – 7 Subsequent years: 0 – 6.0	1st year: € 578.52 – € 1,444.45 Subsequent years: € 0 – € 1,238.10
Optical coherence tomography (EBM 06338 or 06339)	€ 50.07	Different from patient to patient	non-quantifiable
Postoperative treatment (EBM 31717 or 31716)	€ 20.70 – € 28.88	1st year: 6 – 7 Subsequent years: 0 – 6.0	1st year: € 124.20 - € 202.16 Subsequent years: € 0 - € 173.28
Further check-ups	non-quantifiable	Different from patient to patient	non-quantifiable
Faricimab			
Intravitreal administration of the medicinal product on the left or right eye (EBM 31372/ 36372 or 31371/ 36371)	€ 96.42 – € 206.35	1st year: 5 – 8 Subsequent years: 3.3 – 6.5	1st year: € 482.10 – € 1,650.80 Subsequent years: € 318.19 – € 1,341.28
Optical coherence tomography (EBM 06338 or 06339)	€ 50.07	Different from patient to patient	non-quantifiable
Postoperative treatment (EBM 31717 or 31716)	€ 20.70 – € 28.88	1st year: 5 – 8 Subsequent years: 3.3 – 6.5	1st year: € 103.50 - € 231.04 Subsequent years: € 68.31 - € 187.72
Further check-ups	non-quantifiable	Different from patient to patient	non-quantifiable

Designation of the therapy	Costs/ service	Number/ year	Costs/ year
Ranibizumab			
Intravitreal administration of the medicinal product on the left or right eye (EBM 31372/ 36372 or 31371/ 36371)	€ 96.42 – € 206.35	1st year: 7 – 12 Subsequent years: 0 – 12.0	1st year: € 674.94 – € 2,476.20 Subsequent years: € 0 – € 2,476.20
Optical coherence tomography (EBM 06338 or 06339)	€ 50.07	Different from patient to patient	non-quantifiable
Postoperative treatment (EBM 31717 or 31716)	€ 20.70 – € 28.88	1st year: 7 – 12 Subsequent years: 0 – 12.0	1st year: € 144.90 – € 346.56 Subsequent years: € 0 - € 346.56
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 designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

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

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve

antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

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

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

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

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

Concomitant active ingredient

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

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

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

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

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in

combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

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

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

Designation

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

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

Exception to the designation

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

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical

knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

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

Justification for the findings on designation in the present resolution:

Adults with neovascular (wet) age-related macular degeneration (nAMD)

- 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 bevacizumab (Lytenava); Lytenava 25 mg/ml solution for injection
Last revised: January 2025

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

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

The calculation is based on all studies that were submitted as part of the benefit assessment dossier in the therapeutic indication to be assessed in accordance with Section 35a, paragraph 1, sentence 3 SGB V in conjunction with Section 4, paragraph 6 AM-NutzenV. Approval studies include all studies submitted to the regulatory authority in the authorisation dossier for the assessment of the clinical efficacy and safety of the medicinal product in the therapeutic indication to be assessed.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5% (0.0%) of the total number of study participants.

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

3. Bureaucratic costs calculation

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

4. Process sequence

At their session on 23 July 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 29 April 2025 the pharmaceutical company submitted a dossier for the benefit assessment of bevacizumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 7 VerfO.

By letter dated 30 April 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient bevacizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 July 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 August 2025. The deadline for submitting statements was 22 August 2025.

The oral hearing was held on 8 September 2025.

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

The evaluation of the written statements received and the oral hearing was discussed at the session of the Subcommittee on 7 October 2025, and the proposed draft resolution was approved.

At their session on 16 October 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	23 July 2024	Determination of the appropriate comparator therapy
Working group Section 35a	2 September 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on	8 September 2025	Conduct of the oral hearing

Medicinal Products		
Working group Section 35a	16 September 2025 30 September 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	7 October 2025	Concluding discussion of the draft resolution
Plenum	16 October 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 16 October 2025

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

Prof. Hecken