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 Vutrisiran (new therapeutic indication: wild-type or hereditary transthyretin amyloidosis with cardiomyopathy)

of 22 January 2026

Contents

1. Legal basis

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

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirement 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 pass a resolution 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 vutrisiran (Amvuttra) was listed for the first time on 15 October 2022 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

Amvuttra is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999.

On 5 June 2025, vutrisiran 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).

The pharmaceutical company has irrevocably notified the Federal Joint Committee that, despite the orphan drug status for vutrisiran, a benefit assessment is to be carried out with

the submission of evidence in accordance with Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V. In addition, the turnover limit of EUR 30 million had already been exceeded at the time the resolution was adopted.

On 2 July 2025, the pharmaceutical company has submitted a dossier 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 vutrisiran with the new therapeutic indication "Amvuttra is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM)" in due time (i.e. at the latest within four weeks of informing the pharmaceutical company about the approval for a new therapeutic indication).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 October 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 vutrisiran 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 the addendum drawn up by the G-BA on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of vutrisiran.

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

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

2.1.1 Approved therapeutic indication of Vutrisiran (Amvuttra) in accordance with the product information

Amvuttra is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM).

Therapeutic indication of the resolution (resolution of 22.01.2026):

See the approved therapeutic indication

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

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM)

Appropriate comparator therapy for vutrisiran:

- Tafamidis

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 they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

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

On 2. In principle, liver or heart transplantation can be considered as a non-medicinal treatment option in the present therapeutic indication.

On 3. For the therapeutic indication of wild-type or hereditary transthyretin amyloidosis with cardiomyopathy, the following resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Tafamidis (resolution of 20 May 2021)
- Acoramidis (resolution of 18 September 2025)

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

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

The guidelines and scientific-medical societies recommend a therapy with the disease-modifying active ingredient tafamidis for adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy.

For the present therapeutic indication, liver or heart transplantation is basically considered as non-medicinal treatments. However, the treatment decision to perform a causal therapy of the underlying disease in the form of a liver and/or heart transplantation is strongly dependent on a patient-individual risk-benefit assessment and is only considered for patients who meet defined criteria regarding their degree of disease, general condition and age. It is assumed that liver or heart transplantation will not be considered at the time of therapy with vutrisiran. Accordingly, these procedures are not included in the appropriate comparator therapy.

The active ingredient acoramidis is a new treatment option in the present therapeutic indication (marketing authorisation on 10 February 2025). No additional benefit thereof compared with tafamidis was identified in the benefit assessment procedure. According to the generally recognised state of medical knowledge, acoramidis is not determined to be an appropriate comparator therapy for the present resolution.

Based on the evidence and taking into account the considerable additional benefit of tafamidis in the present therapeutic indication identified in the early benefit assessment, a therapy with tafamidis is therefore determined to be the appropriate

comparator therapy for adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM).

It is assumed that in both study arms a patient-individual adequate treatment of the respective organ manifestation (such as heart failure and/or polyneuropathy) is carried out according to the generally recognised state of medical knowledge, taking into account the special features of the disease ATTR amyloidosis.

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 vutrisiran is assessed as follows:

The additional benefit is not proven for adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM).

Justification:

The present assessment is based on the label-enabling HELIOS-B study which is a double-blind RCT comparing vutrisiran with placebo. Adult patients aged 18 to 85 years with hereditary (hATTR-CM) or wild-type transthyretin amyloidosis (wtATTR-CM) with cardiomyopathy were enrolled.

In the study, a total of 655 patients were assigned in a 1:1 ratio to treatment with 25 mg vutrisiran (N = 326) or placebo (N = 329). Randomisation was stratified by tafamidis treatment at baseline (yes vs no), ATTR disease type (hATTR-CM vs wtATTR-CM), and NYHA class (NYHA class I or II and age < 75 years vs all others).

Treatment with vutrisiran was carried out over a planned period of up to 36 months in accordance with the product information. Patients in both study arms were then able to continue treatment with vutrisiran in an open-label extension phase for up to 2 years.

Patients who have already been treated on-label with tafamidis at the start of the study should continue this treatment for the entire duration of the study, if possible, according to the principal investigator's decision. Patients who were not treated with tafamidis at the start of the study and for whom tafamidis therapy was not planned either during the screening phase or in the next 12 months after randomisation were enrolled in the study as a tafamidis-naïve sub-population in accordance with the study inclusion criteria. In the course of the study, this patient group was also able to start treatment with tafamidis according to the principal investigator’s decision.

The primary endpoint of the study is a composite endpoint of overall mortality and recurrent cardiovascular events.

In the benefit assessment dossier, the pharmaceutical company additionally presented results on the endpoint categories of mortality, morbidity, health-related quality of life and side effects both for the total population and for the sub-population without background

treatment with tafamidis. In contrast, the pharmaceutical company did not present results for the sub-population with background treatment with tafamidis.

The pharmaceutical company considered the HELIOS-B study identified by them to be unsuitable for the benefit assessment. They justified this by stating that the appropriate comparator therapy of tafamidis in the HELIOS-B study was not used as a comparator for a direct comparison with vutrisiran.

It is therefore true that the study does not allow any conclusions to be drawn for the benefit assessment of vutrisiran as monotherapy compared to monotherapy with tafamidis.

However, a relevant percentage of the patients enrolled (40% of the study participants in total, i.e. 130 out of 326 subjects in the vutrisiran arm and 129 out of 329 subjects in the placebo arm) were already receiving background treatment with tafamidis at the time of randomisation, which was continued in the further course of the study. Patients who received either vutrisiran + tafamidis or placebo + tafamidis over a period of at least 30 months were therefore enrolled in the HELIOS-B study. The study would thus allow comparative conclusions to be drawn about vutrisiran in combination with tafamidis versus tafamidis as monotherapy for a sub-population of the enrolled study participants.

Neither in the dossier nor in the written statement procedure did the pharmaceutical company submit data processed separately for this sub-population. The pharmaceutical company justified their approach by stating that the data cannot be used for the benefit assessment for methodological reasons. Following the oral hearing, the G-BA requested the pharmaceutical company to submit evaluations of the data for the sub-population that received tafamidis as background therapy. However, the pharmaceutical company again failed to provide this data despite being requested to do so. Overall, it can be stated that the HELIOS-B study contains potentially suitable data for the benefit assessment of vutrisiran in combination with tafamidis compared to tafamidis as monotherapy. The pharmaceutical company's approach of not providing separately processed data for the sub-population is viewed critically.

An additional benefit of vutrisiran over the appropriate comparator therapy tafamidis for the treatment of adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient vutrisiran. The therapeutic indication assessed here is as follows: "for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM)".

The G-BA determined tafamidis as the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company submitted the label-enabling HELIOS-B study in which vutrisiran was compared with placebo. The study therefore does not allow any conclusions to be drawn for the benefit assessment of vutrisiran as monotherapy compared to monotherapy with tafamidis. However, a relevant percentage of the enrolled patients (40% of the study participants in total) were already receiving background treatment with tafamidis at the time of randomisation, which was continued in the further course of the study. Patients who received either vutrisiran + tafamidis or placebo + tafamidis were therefore enrolled in the HELIOS-B study. The study would thus allow comparative conclusions to be drawn about vutrisiran in combination with tafamidis versus tafamidis as monotherapy for a sub-population of the enrolled study participants. However, the pharmaceutical company did not submit the data processed separately for this sub-population, despite being requested to do so. This approach of the pharmaceutical company is viewed critically.

An additional benefit of vutrisiran over the appropriate comparator therapy tafamidis for the treatment of adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy 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).

In the dossier, the pharmaceutical company presented a range for the number of patients, the calculation of which is based on the figures from the preliminary resolution on tafamidis[2] and which was updated using the current population figures and the percentage of subjects with statutory health insurance in 2024.

In the procedure for acoramidis[3] from 2025, a range for patients in the SHI target population was last specified for the present therapeutic indication, which is broader overall and fully covers the range specified by the pharmaceutical company.

The stated number of patients in the SHI target population is subject to uncertainty overall for all calculation approaches. The broader range on which the resolution on acoramidis is based takes these uncertainties into account to a greater extent and is therefore also used as the basis for this resolution on vutrisiran.

[2] Resolution on tafamidis from 20 May 2021
[3] Resolution on acoramidis from 18 September 2025

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 vutrisiran (Amvuttra) at the following publicly accessible link (last access: 2 October 2025):

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

Treatment with vutrisiran should only be initiated and monitored by specialists and general practitioners experienced in the treatment of patients with transthyretin amyloidosis with cardiomyopathy (ATTR-CM).

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 November 2025). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

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

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

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

Treatment period:

Adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM)

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Vutrisiran	Continuously, 1 x every 3 months	4.0	1	4.0
Appropriate comparator therapy				
Tafamidis	Continuously, 1 x daily	365.0	1	365.0

Consumption:

Adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM)

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					
Vutrisiran	25 mg	25 mg	1 x 25 mg	4.0	4.0 x 25 mg
Appropriate comparator therapy					
Tafamidis	61 mg	61 mg	1 x 61 mg	365.0	365.0 x 61 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:

Adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM)

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					
Vutrisiran	1 SFI	€ 79,799.01	€ 1.77	€ 4,556.74	€ 75,240.50
Appropriate comparator therapy					
Tafamidis	30 SC	€ 11,778.41	€ 1.77	€ 669.38	€ 11,107.26
Abbreviations: SFI = solution for injection; SC = soft capsules					

LAUER-TAXE® last revised: 1 November 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.

According to the product information, patients receiving vutrisiran should be administered daily oral vitamin A supplementation at a dosage of approximately 2,500 IU to 3,000 IU, or 2,500 IU per day. Vitamin A is not reimbursable, accordingly it is not considered in the cost representation.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

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

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

Basic principles of the assessed medicinal product

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

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

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

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

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

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

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or

- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

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

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

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

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

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

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

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

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients,

provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

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

Exception to the designation

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

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

Legal effects of the designation

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

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

Justification for the findings on designation in the present resolution:

Adults with wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM)

- 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 vutrisiran (Amvuttra); Amvuttra 25 mg solution for injection in a pre-filled syringe; last revised: June 2025

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 9 July 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

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

By letter dated 7 July 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 vutrisiran.

The dossier assessment by the IQWiG was submitted to the G-BA on 10 October 2025, and the written statement procedure was initiated with publication on the G-BA website on 15 October 2025. The deadline for submitting statements was 05 November 2025.

The oral hearing was held on 24 November 2025.

By letter dated 28 November 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 5 January 2026.

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

The evaluation of the written statements received and the oral hearing was discussed at the session of the Subcommittee on 13 January 2026, and the proposed draft resolution was approved.

At their session on 22 January 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	9 July 2024	Determination of the appropriate comparator therapy
Working group Section 35a	18 November 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	24 November 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	2 December 2025 16 December 2025 6 January 2026	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	13 January 2026	Concluding discussion of the draft resolution
Plenum	22 January 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 22 January 2026

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

Prof. Hecken