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
Sparsentan (primary immunglobulin A nephropathy)

of 6 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.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V). Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5 Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of

the medicinal product concerned has exceeded the turnover threshold according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the G-BA must be completed within three months of the relevant date for submission of the evidence and published on the internet.

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

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient sparsentan on 1 August 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 1 VerfO on 30 July 2024.

Sparsentan for the treatment of adults with primary immunoglobulin A nephropathy (IgAN) is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the approval studies by the G-BA.

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 01 November 2024 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA has adopted its resolution on the basis of the dossier of the pharmaceutical company, the dossier evaluation carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G24-20) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA has evaluated the studies relevant for the marketing authorisation with regard to their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7, sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of sparsentan.

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

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

2.1.1 Approved therapeutic indication of Sparsentan (Filspari) in accordance with the product information

Filspari is indicated for the treatment of adults with primary immunoglobulin A nephropathy (IgAN) with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥ 0.75 g/g).

Therapeutic indication of the resolution (resolution of 6 February 2025):

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

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

Hint for a minor additional benefit

Justification:
For the benefit assessment, the pharmaceutical company submitted evaluations from the phase III PROTECT study. This is a multicentre, randomised, controlled, double-blind study to investigate the safety and efficacy of sparsentan compared to irbesartan.

Adults with primary IgAN who had persistent proteinuria and a high risk of disease progression despite treatment with a stable, maximum tolerated dose of an angiotensin-converting enzyme (ACE) inhibitor and/or angiotensin receptor blocker (ARB) were enrolled.

Among others, therapy-naïve patients with an eGFR < 30 ml/min/1.73 m^2 and those who had cellular glomerular crescents in > 25% of the glomeruli in the renal biopsy within 6 months prior to screening were excluded.

There was a 1:1 randomisation to treatment with sparsentan (N = 203) or irbesartan (N = 203), each applied orally. Stratification was based on eGFR (30 to < 60 ml/min/1.73 m^2 and ≥ 60 ml/min/1.73 m^2) and urine protein excretion (≤ 1.75 g/day and > 1.75 g/day) for screening.

Standard therapy (ACE inhibitor and/or ARB therapy) and all other non-permitted concomitant medications had to be discontinued prior to the randomisation visit (day 1).

The study comprises a 4-week screening phase, a 110-week active-controlled treatment phase and a 4-week double-blind study phase in which the standard therapy is resumed (overall, a 114-week double-blind study phase).

Following the double-blind study phase, patients could change over to an unblinded single-arm extension study (OLE (open-label extension) study), in which all patients receive sparsentan.

Mortality

Deaths were surveyed as part of the safety assessment. Overall, one death occurred in the comparator arm. No effect estimators were submitted with the dossier. Due to the number of events, no statistically significant difference between the treatment arms is assumed. However, a final assessment is not possible.

Morbidity

Progression of kidney disease: End-stage renal disease (ESRD)

In the present study, end-stage renal disease (ESRD) is defined as the start of renal replacement therapy or a sustained eGFR <15 ml/min/1.73 m^2. For the benefit assessment, the percentage of patients achieving a confirmed ESRD at week 110 is used and the time-to-event analysis is presented additionally.

For the endpoint of end-stage renal disease, there were no statistically significant differences between the treatment arms.

Progression of kidney disease: Reaching stage 4 or 5 CKD

The classification of CKD stages was based on the eGFR/GFR using objective and internationally recognised KDIGO criteria. Stage 4 CKD subjects have severely reduced renal function with a GFR of 15-29 ml/min/1.73 m^2. Stage 5 CKD is defined as a GFR < 15 ml/min/1.73 m^2.

Reaching stage 4 or 5 CKD is considered patient-relevant. For the benefit assessment, the percentage of subjects who reach stage 4 or 5 CKD at week 110 is used and the time-to-event analysis is presented additionally.

There was no statistically significant difference for the post-hoc evaluated endpoint of reaching stage 4 or 5 CKD without adjustment based on the randomisation strata. Following the oral hearing, the pharmaceutical company submitted the adjusted effect estimators. The evaluation considering the randomisation strata is estimated to be methodologically more adequate and is therefore taken into account in the benefit assessment.

For the endpoint of reaching stage 4 or 5 CKD, there was a statistically significant advantage in favour of sparsentan over irbesartan.

Change in renal function, measured by proteinuria

The primary endpoint of the study was the change in renal function, measured by proteinuria, and operationalised, among others, as the percentage change in the UP/C ratio from baseline to week 110.
The endpoint is a laboratory parameter without direct reference to symptoms. Within the G-BA, opinions differ as to whether proteinuria constitutes a patient-relevant endpoint per se. As was also addressed in the written statement procedure, proteinuria is a relevant parameter for therapy management in this therapeutic indication. The pharmaceutical company did not submit suitable investigations to validate proteinuria as a surrogate for a patient-relevant endpoint. In addition, there are uncertainties regarding the imputation of missing values for this endpoint. However, being the primary endpoint of the study, it is presented additionally.

Change in renal function, measured by eGFR (slope)

The endpoint of change in renal function, measured by eGFR, was operationalised, among others, as the rate of change in eGFR after the start of randomised therapy (overall change) up to week 110.

The endpoint is a laboratory parameter without direct reference to symptoms. Within the G-BA, opinions differ as to whether renal function measured by eGFR (slope) represents a per se patient-relevant endpoint.

For the present benefit assessment procedure, the pharmaceutical company did not submit any suitable investigations to validate the eGFR (slope) as a surrogate for a patient-relevant endpoint. A final assessment of any surrogate validation of the eGFR slope can therefore not be made on the basis of the documents submitted in this procedure. There are also uncertainties regarding the imputation of missing values.

The endpoint is also presented additionally here against the background of the EMA's comments on the significance of the endpoint for the interpretation of the results of the primary endpoint "change in renal function measured by proteinuria".

Total hospitalisation

For the endpoint of total hospitalisation, the percentage of subjects with hospitalisations, the number of hospitalisations and the duration of hospitalisations for any reason were collected.

The operationalisation is not fully comprehensible. The pharmaceutical company did not provide a definition of the criteria according to which a hospital stay is considered hospitalisation. It is unclear whether this always had to include an inpatient admission with an overnight stay or whether outpatient and day-patient stays were also counted as hospitalisation.

Hospitalisations are generally estimated to be assessment-relevant as the reduction in hospital stays is considered patient-relevant. However, the endpoint "total hospitalisation" is only presented additionally here due to the limitations in operationalisation described above.

Systemic immunosuppressive therapy

The use of systemic immunosuppressants for kidney disease was documented in the PROTECT study by continuous review of concomitant medication and associated indication according to investigators throughout the double-blind study period and retrospectively up to 3 months prior to screening.

It is unclear to what extent the requirement or administration of systemic immunosuppressants was defined in terms of the treatment regimen (dosage, number of medication administrations and duration) in the analyses of the endpoint. Since no criteria were pre-specified or described post hoc in this regard, it is assumed that there were no minimum requirements regarding dosage, number of medication administrations and duration of administration of immunosuppressants in order to be included in the analyses.

Not every reduced consumption of immunosuppressants is directly patient-relevant. The relevance of the chosen operationalisation and the corresponding rationale were not explained by the pharmaceutical company. The advantages resulting from a reduced consumption of immunosuppressants should be reflected in patient-relevant endpoints, e.g. with regard to the reduction of disease symptoms, improvement in quality of life or reduction of (immunosuppressant-induced) side effects. Based on the described uncertainties regarding operationalisation, the endpoint is not assessed as patient-relevant here and is not used for the benefit assessment.

Quality of life

The data on quality of life are not assessable. The endpoint "Kidney Disease Quality of Life 36-item short version" (KDQOL-36) cannot be considered for the benefit assessment due to low (< 70%) return rates in the irbesartan treatment arm at all measurement time points post-baseline and due to sometimes widely differing return rates.

Side effects

Adverse events (AEs) in total

AEs occurred in around 90% of patients in each of the study arms. The results were only presented additionally.

Serious AEs (SAEs), severe AEs and therapy discontinuation due to AEs

There were no statistically significant differences between the treatment arms for the endpoints of SAEs, severe AEs and therapy discontinuation due to AEs.

Specific AEs

In detail, there was a statistically significant disadvantage to the disadvantage of sparsentan compared to irbesatan for the AEs of special interest in the endpoint "hypotension-related AEs (regardless of severity)".

Overall assessment

For the benefit assessment of sparsentan for the treatment of adults with primary IgAN, results of the randomised, double-blind PROTECT study which compared sparsentan with irbesartan are available.

One death occurred among patients treated with irbesartan. The data on mortality are not assessable due to the lack of effect estimators.

In the morbidity endpoint category, there was a slight statistically significant advantage in favour of sparsentan compared to irbesartan for the endpoint of reaching stage 4 or 5 CKD in the progression of kidney disease.

With regard to the quality of life endpoint category, the data cannot be assessed due to low return rates.

In the endpoint category of side effects, neither advantages nor disadvantages of sparsentan compared to irbesartan can be derived overall.

In the overall assessment of the available results on the patient-relevant endpoints, the G-BA classifies the extent of the additional benefit of sparsentan for the treatment of adults with primary IgAN, based on the criteria in Section 5, paragraph 8 in conjunction with Section 5, paragraph 7, sentence 1, numbers 1 to 4 AM-NutzenV.

Significance of the evidence

The present assessment is based on the results of the double-blind, randomised-controlled phase III PROTECT study.

The risk of bias is assessed as high both at study level and at endpoint level. This is partly due to uncertainties regarding concomitant medication and subsequent therapies. In the case of subsequent therapies, there are in particular uncertainties regarding the subjects who were not switched back to the prior therapy after premature study discontinuation.

It should also be noted that the patients in the comparator arm of the PROTECT study received monotherapy with an angiotensin receptor blocker (irbesartan). The use of irbesartan alone does not meet the currently recognised standard of care for the treatment of primary IgAN. Taking into account the statements of clinical experts in the written statement procedure, patients with primary IgAN should also receive an SGLT2 inhibitor (e.g. dapagliflozin) in addition to medication with an angiotensin receptor blocker (such as irbesartan).

In the overall assessment, the significance of the evidence is categorised as a "hint" due to the uncertainties mentioned.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Filspari with the active ingredient sparsentan. Filspari was approved under "exceptional

circumstances" as an orphan drug. Sparsentan is approved for the treatment of adults with primary immunoglobulin A nephropathy (IgAN).

The benefit assessment is based on the results of the double-blind, randomised controlled PROTECT study, which compared sparsentan with irbesartan.

One death occurred among patients treated with irbesartan. However, the data on mortality are not assessable due to the lack of effect estimators.

In the morbidity category, there was a statistically significant advantage in favour of sparsentan compared to irbesartan in the endpoint of reaching stage 4 or 5 CKD in the progression of kidney disease. For the endpoint of end-stage renal disease (ESRD), there were no statistically significant differences between the treatment arms.

No assessable data on quality of life are available.

With regard to side effects, there were no relevant differences for the benefit assessment for the severe or serious adverse events and therapy discontinuation due to adverse events.

The risk of bias at study and endpoint level is considered to be high as there are in particular uncertainties regarding concomitant medication and subsequent therapies. It should also be noted that the patients in the comparator arm of the PROTECT study did not receive additional treatment with an SGLT2 inhibitor and therefore did not receive treatment for primary IgAN in line with the current standard of care. The significance of the data presented is therefore subject to uncertainties overall.

In the overall assessment, there is a hint for a minor additional benefit of sparsentan for the treatment of adults with primary IgAN.

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

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

The G-BA bases its resolution on the patient numbers from the dossier submitted by the pharmaceutical company. The pharmaceutical company's procedure for deriving the patient numbers is mathematically comprehensible. Overall, however, the range must be assessed as uncertain, particularly with regard to the implemented operationalisation of the existence of a potential primary IgAN. Furthermore, there are uncertainties regarding the procedure in the subsequent steps to further demarcate between primary and secondary IgAN as well as other diseases.

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 Filspari (active ingredient: sparsentan) at the following publicly accessible link (last access: 7 August 2024):

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

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

The concomitant use of sparsentan with angiotensin receptor blockers (ARB) is contraindicated.

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 January 2025).

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:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies

from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Sparsentan	Continuously, 1 x daily	365	1	365.0

Consumption:

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.

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					
Sparsentan	400 mg	1 x 400 mg	1 x 400 mg	365.0	365.0 x 400 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					
Sparsentan 400 mg	30 FCT	€ 4,935.94	€ 2.00	€ 278.60	€ 4,655.34
Abbreviations: FCT = film-coated tablets					

LAUER-TAXE® last revised: 1 January 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.

No additionally required SHI services are taken into account for the cost representation.

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:

Adults with primary immunoglobulin A nephropathy (IgAN) with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥ 0.75 g/g)

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 sparsentan (Filspari); Filspari 200/400 mg film-coated tablets; 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

On 30 July 2024, the pharmaceutical company submitted a dossier for the benefit assessment of sparsentan to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 1 November 2024 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting statements was 22 November 2024.

The oral hearing was held on 9 December 2024.

An amendment to the benefit assessment with a supplementary assessment of data submitted in the written statement procedure was submitted on 10 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 28 January 2025, and the proposed draft resolution was approved.

At its session on 6 February 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	29 October 2024	Information of the benefit assessment of the G-BA
Working group Section 35a	4 December 2024	Information on written statements received; preparation of the oral hearing
Subcommittee	9 December 2024	Conduct of the oral hearing

Medicinal products		
Working group Section 35a	18 December 2024 15 January 2025	Consultation on the dossier evaluation by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal products	28 January 2025	Concluding discussion of the draft resolution
Plenum	6 February 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 6 February 2025

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

Prof. Hecken