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 Sarilumab (new therapeutic indication: polymyalgia rheumatica)

of 7 August 2025

Contents

1. Legal basis

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

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

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

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

2. Key points of the resolution

The active ingredient sarilumab (Kevzara) was listed for the first time on 15 August 2017 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 22 March 2024, the pharmaceutical company submitted an application for postponement of the date for the start of the benefit assessment procedure for sarilumab in the therapeutic indication of polymyalgia rheumatica in accordance with Section 35a, paragraph 5b SGB V.

At their session on 16 May 2024, the G-BA approved the application pursuant to Section 35a paragraph 5b SGB V and postponed the relevant date for the start of the benefit assessment and the submission of a dossier for the benefit assessment for the therapeutic indication in question to four weeks after the marketing authorisation of the other therapeutic indication of the therapeutic indication covered by the application, at the latest six months after the first relevant date. The marketing authorisation for the other therapeutic indication covered by

the application according to Section 35a paragraph 5b SGB V were granted within the 6-month period.

On 25 November 2024, sarilumab received extension of the marketing authorisation for the therapeutic indication of polymyalgia rheumatica. The extension of the marketing authorisation for the therapeutic indication of polyarticular juvenile idiopathic arthritis (pJIA), ≥ 2 years, was granted on 13 January 2025. Both extensions of the marketing authorisation are classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 3 February 2025, the pharmaceutical company submitted a dossier in due time in accordance with Section 4, paragraph 3, number 3 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 2 of the Rules of Procedure of the G-BA (VerfO) for the active ingredient sarilumab with the therapeutic indication "Kevzara is indicated for the treatment of polymyalgia rheumatica (PMR) in adult patients who have had an inadequate response to corticosteroids or who experience a relapse during corticosteroid taper".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 May 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 sarilumab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA 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 sarilumab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have 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 Sarilumab (Kevzara) in accordance with the product information

Kevzara is indicated for the treatment of polymyalgia rheumatica (PMR) in adult patients who have had an inadequate response to corticosteroids or who experience a relapse during corticosteroid taper.

Therapeutic indication of the resolution (resolution of 07.08.2025):

see the approved therapeutic indication

[1]General Methods, version 7.0 from 19.09.2023. 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 polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper

Appropriate comparator therapy for sarilumab:

- An individualised therapy with selection of systemic glucocorticoids and the combination of glucocorticoids with methotrexate

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 the medicinal product to be assessed, systemic glucocorticoids (prednisolone, prednisone, methylprednisolone and triamcinolone) are explicitly approved for the treatment of PMR.

On 2. A non-medicinal treatment alone cannot be considered in the present therapeutic indication.

On 3. For the treatment of PMR, there are no resolutions according to Section 35a SGB V on the benefit assessment of medicinal products with new active ingredients.

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 therapeutic indication. 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.

Overall, the evidence for the indication of PMR can be categorised as limited. When conducting the evidence search to determine the appropriate comparator therapy, only one Italian guideline[2] could be included in the evidence synopsis. In addition, the German S3 guideline from 2017, which is based on the EULAR/ACR 2015[3] guideline and expired at the end of 2022, was used to determine the appropriate comparator therapy for the present procedure[4], as it reflects the therapy recommendations and therapy standard in Germany in accordance with the statements of the AkDÄ.

Systemic glucocorticoids are primarily recommended in the present therapeutic indication. These should be used as soon as PMR has been diagnosed. The initial therapy should be selected by individualisation within the dose range of 15 – 25 mg prednisone equivalent per day. When deciding on the specific glucocorticoid dose, comorbidities, disease activity and manifestation as well as the risk of occurrence of glucocorticoid-induced side effects should be taken into account. It is then

2 Ughi N, Sebastiani GD, Gerli R, et al. The Italian Society of Rheumatology clinical practice guidelines for the management of polymyalgia rheumatica. Reumatismo 2020;72(1):1-15.

3 Dejaco C, Singh YP, Perel P, et al. 2015 Recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Annals of the Rheumatic Diseases 2015;74:1799-1807.

4 German Society for Rheumatology, Austrian Society for Rheumatology and Rehabilitation, Swiss Society for Rheumatology. S3 guideline for the treatment of polymyalgia rheumatica [online]. 2017. URL: https://register.awmf.org/assets/guidelines/060-006l_S3_Polymyalgia-rheumatica_2018-05-abgelaufen.pdf.

recommended to gradually reduce the glucocorticoid dose while monitoring the disease activity and adverse effects of the therapy. General guide values of the glucocorticoid "taper" are given both in the product information and in the guidelines, but ultimately an individualised approach is recommended.

According to the now expired "S3 guideline for the treatment of PMR", the use of methotrexate should be considered for the treatment of PMR in patients with relapse(s), inadequate response to glucocorticoids or in the case of occurrence of glucocorticoid-induced side effects. The significance of methotrexate in healthcare was also pointed out in the oral and written statement procedure.

However, the marketing authorisation of new active ingredients - such as sarilumab in this case - will contribute to methotrexate becoming less important in the treatment of PMR. This is already reflected in the recently published "S2e guideline for the treatment of PMR: update 2024"[5], which only recommends methotrexate as an alternative to interleukin-6 inhibitors in patients with recurrent course of disease and in selected patients with new-onset disease and a high risk of glucocorticoid-induced side effects.

However, when determining the appropriate comparator therapy, the actual medical treatment situation as it would be without the medicinal product to be assessed must be taken into account (Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV)). As explained above, the active ingredient methotrexate assumed significance in the clinical treatment of patients with PMR at least until the marketing authorisation of sarilumab. However, it should be noted that methotrexate is not approved in the therapeutic indication of PMR. According to the "S3 guideline for the treatment of PMR", methotrexate should be considered in addition to glucocorticoids for the treatment of PMR in patients with relapse(s), inadequate response to glucocorticoids or in the case of occurrence of glucocorticoid-induced side effects. The recommendation is based on randomised and controlled studies, as well as a retrospective study. Although the results of these studies did not all point in the same direction, the studies that reported good efficacy of methotrexate (in terms of recurrence rate, cumulative glucocorticoid dose, possibility of discontinuation of glucocorticoids) were of significantly higher quality than the studies that led to negative results. The written statement of the AkdÄ also refers to the off-label use of methotrexate in order to reduce the use of glucocorticoids in certain patient populations.

The use of methotrexate as an unapproved therapy option is medically necessary in patients who have already received glucocorticoids and have had an inadequate response to them or who experience a relapse and require therapy escalation. According to the generally recognised state of medical knowledge in the therapeutic indication to be assessed, the off-label use is considered part of the therapy standard in the medical treatment situation for the patients named above. It is therefore appropriate in accordance with Section 6, paragraph 2, sentence 3, number 3 AM-NutzenV to determine the off-label use of methotrexate as part of an individualised therapy as the appropriate comparator therapy for this patient population.

[5] German Society for Rheumatology and Clinical Immunology, Austrian Society for Rheumatology and Rehabilitation, Swiss Society for Rheumatology. S2e guideline for the treatment of polymyalgia rheumatica; update 2024 [online]. 2024. URL: https://register.awmf.org/assets/guidelines/060-006l_S2e_Behandlung-der-Polymyalgia-rheumatica_2025-04.pdf.

In the overall assessment, an individualised therapy with selection of systemic glucocorticoids and the combination of glucocorticoids with methotrexate is therefore determined as the appropriate comparator therapy for adults with PMR who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper. Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

The term "individualised therapy" is used instead of previously used terms such as "patient-individual therapy" or "therapy according to doctor's instructions". This harmonises the terms used in the European assessment procedures (EU-HTA).

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 sarilumab is assessed as follows:

The additional benefit of sarilumab over the appropriate comparator therapy is not proven for adults with polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper.

Justification:

For the present benefit assessment, the pharmaceutical company presented the SAPHYR study. This is a randomised, double-blind, parallel, multicentre study comparing sarilumab + prednisone with placebo + prednisone. The comparative treatment phase lasted 52 weeks overall.

Adults with a diagnosis of active PMR who experienced at least one relapse during the attempt to taper off glucocorticoid therapy were enrolled. Patients without relapse who have had an inadequate response to corticosteroids were not examined in the SAPHYR study.

As a prerequisite for study participation, patients had to have received treatment with ≥ 10 mg/day prednisone equivalent for at least 8 weeks before the start of the study, and treatment with at least 7.5 mg/day and a maximum of 20 mg/day prednisone equivalent at screening and during the screening phase.

Patients with a diagnosis of giant cell arteritis, concomitant rheumatoid arthritis or other connective tissue disorders or active fibromyalgia were excluded from the SAPHYR study. In addition, patients with an unstable or high (>15 mg/week) methotrexate (MTX) dose were not allowed to take part in the study.

A total of 118 patients were enrolled in the study. 60 subjects in the sarilumab + prednisone intervention arm and 58 in the placebo + prednisone control arm.

Glucocorticoid therapy should be optimised in both study arms before the start of the study in order to reduce the risk of serious adverse events (SAEs) during glucocorticoid taper. As a

starting dose for the first 2 weeks of treatment with prednisone, 15 mg/day prednisone was then used for all patients in both treatment arms. This was followed by prednisone taper according to fixed tapering regimens, with the prednisone dose in the intervention arm being gradually reduced to 1 mg/day by week 13, followed by placebo from week 14, while in the control arm it was gradually tapered off to 1 mg/day by week 52. In the event of PMR recurrence by week 12, treatment with unblinded additional prednisone (max. 5 mg/day) could be given in both study arms at the principal investigator's discretion. In the event of PMR relapse during regular prednisone taper (up to week 12) despite the administration of additional prednisone, the tapering regimen had to be discontinued, and the patient received an emergency glucocorticoid as decided by the principal investigator. In this case, blinded treatment with sarilumab or placebo should be continued, unless this was contraindicated due to safety concerns. In the event of persistent symptomatology during treatment with emergency glucocorticoids, other treatment options including conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) could be used.

Treatment with MTX could be continued in the SAPHYR study in patients who were already receiving treatment at a stable dose before the start of the study. However, the MTX dose had to be kept stable for the duration of the study. Nevertheless, it was possible to reduce the MTX dose and discontinue MTX for safety reasons. In the event of PMR relapse and inadequate effect of additional prednisone and if applicable emergency glucocorticoids, treatment with csDMARDs, which include MTX, was also permitted as emergency medication. In these cases, the study medication had to be discontinued.

The primary endpoint of the study was sustained remission at week 52. In addition, endpoints in the categories of morbidity, health-related quality of life and adverse events (AEs) were assessed.

On the implementation of the appropriate comparator therapy

Glucocorticoids

The use of glucocorticoids in the SAPHYR study corresponds to the determined appropriate comparator therapy. However, in accordance with the recommendations of the German guideline,[6,7] the dosage of glucocorticoids should be patient-individually adapted. In contrast, in the SAPHYR study, glucocorticoid therapy was started for all patients with a starting prednisone dose of 15 mg/day. Although this corresponds to the lower limit of the starting dose recommended in the guidelines, it cannot be ruled out on the basis of the available information that this starting dose was too high or too low for individual patients.

4 patients in the sarilumab arm and 7 patients in the comparator arm were treated with additional prednisone. The prednisone taper in both study arms was carried out according to a fixed tapering regimen with a fixed treatment duration.

The option of additional prednisone of a maximum of 5 mg/day up to week 12 and the administration of emergency medication over the entire treatment phase made individual

[6] German Society for Rheumatology, Austrian Society for Rheumatology and Rehabilitation, Swiss Society for Rheumatology. S3 guideline for the treatment of polymyalgia rheumatica [online]. 2017. URL: https://register.awmf.org/assets/guidelines/060-006l_S3_Polymyalgia-rheumatica_2018-05-abgelaufen.pdf.

[7] German Society for Rheumatology and Clinical Immunology, Austrian Society for Rheumatology and Rehabilitation, Swiss Society for Rheumatology. S2e guideline for the treatment of polymyalgia rheumatica; update 2024 [online]. 2024. URL: https://register.awmf.org/assets/guidelines/060-006l_S2e_Behandlung-der-Polymyalgia-rheumatica_2025-04.pdf.

adjustments possible, but relevant limitations in the selected operationalisation must be taken into account. The use of prednisone as an emergency medication led to subjects being categorised as non-responders in the endpoint of sustained remission (see section below).

The additional prednisone had to be discontinued by week 12. According to the guideline, in the event of a relapse during taper, the dose should at least be increased to the dose prior to occurrence of the relapse and then gradually reduced to the dose at which the relapse occurred within 4 to 8 weeks after remission of symptomatology. However, the SAPHYR study did not allow a slow taper, which is intended to reduce the risk of new recurrences, depending on when the additional prednisone was used.

Add-on therapy with methotrexate

In the SAPHYR study, 20% of patients in the intervention arm and 29%[8] thereof in the control arm received additional treatment with MTX. However, MTX therapy could only be continued in stable dosage or used as emergency medication. According to information provided by the pharmaceutical company in the written statement procedure, MTX was used as an emergency medication in 3.3% of subjects in the sarilumab arm and in 8.6% thereof in the placebo arm.

However, it remains uncertain to what extent an additional administration of MTX to treat the relapse would have been indicated for some of the study participants as MTX was not available as a treatment option, for example at the start of the study.

Against the background that a relevant percentage of study participants was further treated with MTX, and that MTX is also only suitable for part of the study population particularly due to the older age of the patient population and the limited body of evidence on the specific indication, adequate implementation of the appropriate comparator therapy in the SAPHYR study was assumed overall.

Extent and probability of the additional benefit

Mortality

The results on overall mortality are based on the data on fatal adverse events. No deaths occurred. For the endpoint of overall mortality, there was no statistically significant difference between the treatment arms.

Morbidity

Remission

Achieving and maintaining remission is a key therapeutic goal in this therapeutic indication. In the dossier, the pharmaceutical company presented evaluations on the composite endpoint "sustained remission at week 52" and on its individual components as separate endpoints. The sustained remission at week 52 comprises the following individual components:

- remission by week 12 at the latest,

[8] It is unclear whether these figures only include patients who have continued treatment with MTX as an add-on therapy or also subjects who have received additional treatment with MTX as part of emergency medication.

- no relapse from week 12 to 52,
- sustained CRP reduction from week 12 to 52 and
- successful prednisone taper from week 12 to 52 (no need for emergency medication).

The single component "remission by week 12 at the latest" is defined as the remission of signs and symptoms of PMR in conjunction with normalisation of C-reactive protein (CRP). Relapse was defined as a recurrence of signs and symptoms or an increase in ESR associated with active PMR requiring an increase in glucocorticoid dose.

The composite endpoint "sustained remission" therefore includes results for the laboratory parameters CRP and ESR, which are not patient-relevant per se. Against the background of the active ingredient character of the medicinal product to be assessed, the data on these parameters in particular cannot be interpreted, or can only be interpreted to a very limited extent. With interleukin-6 receptor antagonists, inflammation parameters such as the CRP value or the ESR can be within the normal range, regardless of the disease activity.

As part of the written statement procedure, the pharmaceutical company also submitted sensitivity analyses without the inclusion of CRP and ESR values for the endpoint "sustained remission". These show that the two laboratory parameters do not significantly influence the results.

However, there are uncertainties for the composite endpoint as well as for the individual components of remission, no relapse and successful prednisone taper, as the achievement of these endpoints was linked to adherence to the prednisone tapering regimen.

Although the option of using glucocorticoids as needed in the SAPHYR study enabled a certain degree of individualisation of the therapy, this reactive adjustment option - with the exception of the one-off additional administration of prednisone up to week 12 - was classified as emergency medication, which led to the classification as a non-responder for the endpoints mentioned. This operationalisation potentially disadvantages the comparator arm in particular, in which patients were particularly dependent on optimally selected, flexible glucocorticoid therapy due to the lack of a standardised additional therapy (such as sarilumab).

In principle, the classification as a non-responder due to an adjustment of the glucocorticoids in the sense of emergency medication means that subjects who achieved a remission after deviating from the fixed tapering regimen could no longer be included in the analysis as responders at a later point in time. This means that the number of responders is underestimated, especially in the comparator arm.

As part of the addendum, data on the endpoints "steroid-free clinical remission at week 52" and "clinical remission at week 52" were also additionally presented, based on the publication of the SAPHYR study. The endpoint "steroid-free clinical remission at week 52" covers those patients with a clinical remission, i.e. remission of the signs and symptoms of PMR, and steroid avoidance at week 52.

However, the results are not considered in the assessment of the additional benefit as these operationalisations were submitted by the pharmaceutical company neither in the dossier nor as part of the written statement procedure for the derivation of the additional benefit.

It is therefore not possible to deduce from the available information how many patients ultimately achieved the main goal in this therapeutic indication, i.e. remission, when using a patient-individual, adjustable tapering regimen, if applicable with a sustained low (e.g. < 5 mg/day) glucocorticoid dosage or even steroid avoidance.

In the overall assessment, the endpoint "sustained remission" and its individual components are not used against the background of the distorting aspects mentioned, which can have a particularly unfavourable effect on the comparator arm.

In addition, a high risk of bias can be assumed irrespective of the points of criticism already mentioned regarding the primary operationalisation of "sustained remission" presented by the pharmaceutical company. For the analysis, missing values were replaced as non-responders in study participants with missing values at the end of the study and in those who discontinued the study prematurely and had not suffered a relapse by then, so that the achievement of a sustained remission cannot be assessed.

Time to first PMR relapse after clinical remission

In the dossier, the pharmaceutical company presented an analysis of the time to first PMR relapse after clinical remission. Due to the high rate of censoring in the time-to-event analysis (52% versus 22%), the endpoint is not used for the present benefit assessment, despite the points of criticism mentioned in connection with the endpoint "sustained remission".

Change in the PMR activity score (PMR-AS) at week 52

The PMR activity score (PMR-AS) was collected to assess disease activity in the SAPHYR study. To this end, the pharmaceutical company submitted the change at week 52 for the total score and for the individual components as endpoints. The PMR-AS assesses the following individual components:

- pain assessment by the patient,
- disease assessment by the principal investigator,
- the CRP value,
- the duration of morning stiffness and
- the mobility of the upper limbs.

The individual components of duration of morning stiffness, mobility of the upper limbs and patient-reported pain assessment are patient-relevant endpoints and are used for the present benefit assessment (see below). The individual component of disease assessment by the principal investigator is not used, as the endpoint of patient-reported global assessment of disease activity using the VAS of the HAQ-DI already reflects the patient-relevant disease assessment. Against this background, the patient-relevant individual components are used, not the total score.

Duration of morning stiffness

For the assessment of the patient-relevant endpoint "change in duration of morning stiffness", the pharmaceutical company presented the mean difference determined using a mixed model

for repeated measures (MMRM). However, these analyses only consider randomised patients in the evaluation for whom a survey was available both at baseline and at week 52. Patients for whom both a value at the start of the study and a value at another time point (i.e. week 12 or week 24) were available were not considered. The analyses presented are used for the benefit assessment as the percentage of patients included in the evaluation is nevertheless sufficient.

For the endpoint "change in duration of morning stiffness", there was a statistically significant difference of 22.43 minutes between the treatment arms to the advantage of sarilumab when considering the mean differences over the study duration.

However, the medians and mean values of the baseline values of the patient characteristic of morning stiffness, as well as the observed standard deviations of the two treatment arms, differed significantly. There are therefore uncertainties as to the extent to which the present effect estimate was influenced by this. Furthermore, the specific operationalisation of the endpoint is unclear, i.e. whether the duration of morning stiffness assesses a patient-reported morning stiffness on the survey date or a patient-reported average morning stiffness over a period prior to the survey.

Overall, the uncertainties are so great that no additional benefit can be derived from the available results on the endpoint "duration of morning stiffness".

Mobility of the upper limbs

For the endpoint "mobility of the upper limbs" assessed using the PMR-AS, there was a statistically significant difference between the treatment arms to the advantage of sarilumab when considering the mean differences over the study duration. Overall, it cannot however be concluded that the effect is clinically relevant, as the 95% confidence interval of the standardised mean difference (SMD) is not completely below the irrelevance threshold of -0.2.

Pain

The endpoint of pain was assessed in the SAPHYR study using a visual analogue scale (VAS) of the Health Assessment Questionnaire - Disability Index (HAQ-DI). The scale range of the VAS was from 1 to 10. In the dossier, the pharmaceutical company presented responder analyses on the clinically relevant improvement of the pain VAS by ≥ 1.5 points. There was no statistically significant difference between the treatment arms.

Physical functional status

The endpoint "physical functional status" was assessed using the patient-reported questionnaire HAQ-DI. The pharmaceutical company presented responder analyses on the clinically relevant improvement of the HAQ-DI by ≥ 0.45 points. There was no statistically significant difference between the treatment arms.

Patient-reported global assessment of disease activity

In the SAPHYR study, the endpoint "patient-reported global assessment of disease activity" was assessed as a VAS as part of the HAQ-DI. The used responder analyses on the clinically relevant improvement in the VAS of the HAQ-DI by ≥ 15 points show no statistically significant difference between the treatment arms.

Fatigue

The endpoint of fatigue was assessed in the present study using the "Functional Assessment of Chronic Illness Therapy-Fatigue" (FACIT-Fatigue). There was no statistically significant difference between the treatment arms for the percentage of patients with a clinically relevant improvement in the FACIT-Fatigue by ≥ 7.8 points.

Health status

For the endpoint of health status, assessed using the VAS of the European Quality of Life Questionnaire 5 Dimensions (EQ-5D), there was no statistically significant difference between the treatment arms for the percentage of patients with a clinically relevant improvement by ≥ 15 points.

Quality of life

Health-related quality of life was assessed using the physical component and mental component summary scores of the generic Short Form 36-Item Health Survey Version 2 questionnaire. The responder analyses on the clinically relevant improvement by ≥ 10 points show no statistically significant differences between the treatment arms for either summary score.

Side effects

There was no statistically significant difference between the treatment groups for the endpoints of serious adverse events and discontinuation due to adverse events (AEs), as well as for the AEs of the system organ class of infections and serious infections.

Overall assessment

The results of the randomised, controlled SAPHYR study are available for the assessment of the additional benefit of sarilumab for the treatment of adults with polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper.

For the endpoint categories of mortality, health-related quality of life and side effects, there was neither an advantage nor a disadvantage of sarilumab + prednisone compared to placebo + prednisone.

For the endpoint category of morbidity, there was a statistically significant difference in favour of sarilumab for the endpoints "duration of morning stiffness" and "mobility of the upper limbs" respectively. For the endpoint "mobility of the upper limbs", however, it cannot be concluded that the observed effect is clinically relevant.

For the endpoint "duration of morning stiffness", an additional benefit cannot be derived due to uncertainties regarding the specific operationalisation and the differences in the baseline values.

For the endpoints of pain, physical functional status, patient-reported global assessment of disease activity, fatigue and health status, there were neither advantages nor disadvantages of sarilumab compared to the appropriate comparator therapy.

No operationalisations suitable for the benefit assessment were available for the endpoint "sustained remission".

In the overall assessment, an additional benefit of sarilumab over the appropriate comparator therapy is not proven for adults with polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient sarilumab. The therapeutic indication assessed here is "Kevzara is indicated for the treatment of polymyalgia rheumatica (PMR) in adult patients who have had an inadequate response to corticosteroids or who experience a relapse during corticosteroid taper".

An individualised therapy with selection of systemic glucocorticoids and the combination of glucocorticoids with methotrexate was determined as the appropriate comparator therapy.

The results of the randomised, controlled, double-blind SAPHYR study, in which the efficacy and safety of sarilumab + prednisone was compared with placebo + prednisone over 52 weeks, are available for the assessment of the additional benefit of sarilumab. Prednisone was tapered off in both arms according to a defined dosage regimen. Although individual adjustments were generally possible by administering additional prednisone up to week 12 and emergency medication over the entire treatment phase, the chosen operationalisation resulted in relevant limitations, particularly in the assessment of the endpoint "sustained remission".

MTX therapy could either be continued at a stable dose or used as emergency medication. However, it is unclear whether additional administration of MTX to treat the relapse would have been indicated for some of the study participants.

For the endpoint categories of mortality, health-related quality of life and side effects, the SAPHYR study showed neither advantages nor disadvantages of sarilumab compared to placebo.

For the endpoint category of morbidity, there was a statistically significant difference in favour of sarilumab for the endpoints "duration of morning stiffness" and "mobility of the upper limbs" respectively. For the endpoint "mobility of the upper limbs", however, it cannot be concluded that the observed effect is clinically relevant. For the endpoint of morning stiffness, an additional benefit cannot be derived due to uncertainties regarding the specific operationalisation and the differences in the baseline values.

No operationalisations suitable for the benefit assessment were available for the endpoint "sustained remission". It is considered particularly critical that the endpoint could not be achieved if glucocorticoid therapy was adjusted in the sense of emergency therapy, as these patients were then categorised as non-responders. This operationalisation potentially disadvantages the comparator arm in particular, in which patients were particularly dependent on optimally selected, flexible glucocorticoid therapy due to the lack of a standardised additional therapy (such as sarilumab).

For the endpoints of pain, physical functional status, patient-reported global assessment of disease activity, fatigue and health status, there were neither advantages nor disadvantages of sarilumab compared to the appropriate comparator therapy.

In the overall assessment, an additional benefit of sarilumab over the appropriate comparator therapy is not proven for adults with polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper.

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 provided by the pharmaceutical company in the dossier. Overall, the specified number of patients in the SHI target population is subject to uncertainty. The main reasons for this are the lack of consideration of the steady increase in the prevalence rates of PMR and the unclear transferability of the percentage values of patients, who start treatment with corticosteroids, to prevalent patients. Likewise, there are uncertainties due to the unclear limitation to patients who respond to glucocorticoid therapy and the limited transferability of the percentage values to recurrences or inadequate response.

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 Kevzara (active ingredient: sarilumab) at the following publicly accessible link (last access: 2 April 2025):

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

Treatment with sarilumab should only be initiated and monitored by specialists who are experienced in the treatment of patients with polymyalgia rheumatica.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide a patient identification card. This contains instructions on how to deal with the possible side effects caused by sarilumab, in particular serious infections, neutropenia and gastrointestinal perforation.

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 July 2025).

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.

The (daily) doses recommended in the product information or in the labelled publications were used as the basis for calculation.

According to the product information for Kezvara, sarilumab is used in combination with a tapered therapy with systemic glucocorticoids, after which sarilumab can be continued as monotherapy. Glucocorticoids which are tapered off over time to the lowest possible dosage are also used as part of the appropriate comparator therapy.

The reduction of oral glucocorticoids should be adapted patient-individually during the course of treatment of polymyalgia rheumatica in accordance with the "S2e guideline for the treatment of polymyalgia rheumatica"[9].

As an initial glucocorticoid dose between 15 and 25 mg prednisone equivalent per day is recommended, prednisone in potencies of 5 mg and 20 mg are shown as examples for the group of oral glucocorticoids. There are also packs with a potency of 10 mg.

Methotrexate is not approved in the present therapeutic indication. Doses of 7.5-10 mg/week were used in clinical studies[10].

[9] https://register.awmf.org/assets/guidelines/060-006l_S2e_Behandlung-der-Polymyalgia-rheumatica_2025-04.pdf

[10] Dejaco C, Singh YP, Perel P, et al 015 Recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Annals of the Rheumatic Diseases 2015;74:1799-1807.

Adults with polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Sarilumab	Continuously, 1 x every 14 days	26.1	1	26.1
Prednisone	Different from patient to patient			
Appropriate comparator therapy				
Therapy according to doctor's instructions, taking into account systemic glucocorticoids and the combination of glucocorticoids with methotrexate				
Glucocorticoids monotherapy				
Prednisone	Different from patient to patient			
Glucocorticoids in combination with methotrexate				
Prednisone	Different from patient to patient			
Methotrexate	Continuously, 1 x every 7 days	52.1	1	52.1

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					
Sarilumab	200 mg	200 mg	1 x 200 mg	26.1	26.1 x 200 mg
Prednisone	Different from patient to patient				
Appropriate comparator therapy					
Therapy according to doctor's instructions, taking into account systemic glucocorticoids and the combination of glucocorticoids with methotrexate					
Glucocorticoids monotherapy					
Prednisone	Different from patient to patient				

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Glucocorticoids in combination with methotrexate					
Prednisone	Different from patient to patient				
Methotrexate	7.5 mg - 10 mg	7.5 mg - 10 mg	1 x 7.5 mg - 1 x 10 mg	52.1	52.1 x 7.5 mg - 52.1 x 10 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Sarilumab 200 mg	6 SFI	€ 4,216.42	€ 1.77	€ 237.51	€ 3,977.14
Prednisone 5 mg[11]	100 TAB	€ 16.74	€ 1.77	€ 0.43	€ 14.54
Prednisone 20 mg[11]	100 TAB	€ 29.29	€ 1.77	€ 1.42	€ 26.10
Appropriate comparator therapy					
Methotrexate 7.5 mg[11]	30 TAB	€ 33.75	€ 1.77	€ 1.77	€ 30.21
Methotrexate 10 mg[11]	30 TAB	€ 41.63	€ 1.77	€ 2.40	€ 37.46
Prednisone 5 mg[11]	100 TAB	€ 16.74	€ 1.77	€ 0.43	€ 14.54
Prednisone 20 mg[11]	100 TAB	€ 29.29	€ 1.77	€ 1.42	€ 26.10
Abbreviations: SFI = solution for injection in pre-filled pen; TAB = tablets					

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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

[11] Fixed reimbursement rate

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.

Prior to administration of the active ingredient sarilumab, patients must be examined for active and inactive ("latent") tuberculosis infections.

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Sarilumab	Quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens (at least ESAT-6 and CFP-10) specific for Mycobacterium tuberculosis-complex (except BCG) (GOP 32670)	1	€ 53.36	€ 53.36
	Chest radiograph (GOP 34241)	1	€ 18.09	€ 18.09

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 polymyalgia rheumatica who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper

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 sarilumab (Kevzara); Kevzara® 150 mg/200 mg solution for injection in a pre-filled syringe / pre-filled pen; last revised: January 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 12 December 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 3 February 2025, the pharmaceutical company submitted a dossier for the benefit assessment of sarilumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 2, sentence 6 VerfO.

By letter dated 4 February 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 sarilumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 15 May 2025. The deadline for submitting statements was 5 June 2025.

The oral hearing was held on 24 June 2025.

By letter dated 24 June 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 10 July 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 29 July 2025, and the proposed draft resolution was approved.

At their session on 7 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	12 December 2023	Determination of the appropriate comparator therapy
Working group Section 35a	18 June 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	24 June 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	1 July 2025 15 July 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	29 July 2025	Concluding discussion of the draft resolution
Plenum	7 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 August 2025

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

Prof. Hecken