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: polyarticular juvenile idiopathic arthritis (pJIA), ≥ 2 years)

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 13 January 2025, sarilumab received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 3 February 2025, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company have submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with

Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient sarilumab with the new therapeutic indication

Kevzara is indicated for the treatment of active polyarticular juvenile idiopathic arthritis (pJIA; rheumatoid factor positive or negative polyarthritis and extended oligoarthritis) in patients 2 years of age and older who have responded inadequately to previous therapy with conventional synthetic DMARDs (csDMARDs). Kevzara may be used as monotherapy or in combination with MTX.

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. 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 active polyarticular juvenile idiopathic arthritis (pJIA; rheumatoid factor positive or negative polyarthritis and extended oligoarthritis) in patients 2 years of age and older, who have responded inadequately to previous therapy with conventional synthetic DMARDs (csDMARDs).

Kevzara may be used as monotherapy or in combination with MTX.

Therapeutic indication of the resolution (resolution of 07.08.2025):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

a) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs

Appropriate comparator therapy for sarilumab, alone or in combination with MTX:

- Adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable, as monotherapy, taking into account the respective authorisation status in the case of MTX intolerance or unsuitability

b) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

Appropriate comparator therapy for sarilumab, alone or in combination with MTX:

- Abatacept or adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable, as monotherapy, taking into account the respective authorisation status in case of MTX intolerance or unsuitability, depending on prior therapy

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

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

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

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the

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

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

<u>Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:</u>

On 1. Besides sarilumab, glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; including MTX, sulfasalazine and hydroxychloroquine), biologic DMARDs (bDMARDs; here etanercept, adalimumab, golimumab, tocilizumab, abatacept) and the JAK inhibitors tofacitinib and baricitinib are approved for the treatment of polyarticular juvenile idiopathic arthritis (pJIA). For the approved therapeutic indications of csDMARDs and bDMARDs, some specifications on the approved age have to be additionally considered. Also, the active ingredient golimumab is only approved in combination with MTX.

On 2. Non-medicinal measures at the expense of the SHI are not considered as sole appropriate comparator therapy in the present therapeutic indication.

On 3. In the therapeutic indication to be considered here, there are two G-BA resolutions on the benefit assessment of medicinal products with new active ingredients for the active ingredients baricitinib from 2 May 2024 and tofacitinib from 3 March 2022.

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.

For the treatment of patients 2 years of age and older with pJIA, it can first be stated that different diseases can be distinguished within the therapeutic indication of JIA, whereby several subtypes can be characterised by a polyarticular course – including the polyarticular forms of rheumatoid factor positive [RF+] or rheumatoid factor negative [RF-] polyarthritis specified in the approved therapeutic indication of sarilumab, and also the extended oligoarthritis.

In addition, taking into account the comments of the clinical experts in the previous benefit assessment procedure for the active ingredient baricitinib[2], it is established that the diagnosis of JIA relates to children and adolescents and that it is not continued in adulthood. It is therefore assumed that the marketing authorisation of sarilumab in the therapeutic indication of pJIA covers children and adolescents aged 2 to 17 years.

The German S2k guideline[3] recommends the use of conventional synthetic DMARDs (csDMARDs) in the first-line therapy of pJIA after failure of (symptomatic) NSAIDs, including in particular a treatment with methotrexate. In the further course of the disease, it can be deduced from the recommendations that therapy of pJIA should be carried out with a (first) bDMARD after failure of csDMARDs. In addition, if a first bDMARD fails, therapy should be switched to another bDMARD. In this context, the aggregated evidence for bDMARDs gives evidence-based preference to combination with MTX over monotherapy with bDMARDs, if possible and if the authorisation status of the bDMARD does not conflict with this. If necessary, both the first and the other bDMARD can be given as monotherapy in the case of MTX intolerance or unsuitability, taking into account the respective authorisation status. Within the class of bDMARDs, the German guideline only differentiates in its recommendation on abatacept, while for the other approved bDMARDs, the specific recommendations of the guideline do not derive any priority or subordination among each other, neither within the TNFα inhibitors, nor between TNFα inhibitors and the IL-6R inhibitor tocilizumab. The recommendation level for the active ingredient abatacept is lowered compared to that of the other approved bDMARDs in the German S2k guideline, so that abatacept is regarded as subordinate to adalimumab, etanercept, golimumab and tocilizumab and, against this background, the use of abatacept is currently only considered appropriate for those patients who have failed or not tolerated a first bDMARD.

In addition, the JAK inhibitors tofacitinib and baricitinib are approved for the treatment of pJIA in the therapeutic indication. In the early benefit assessment, the G-BA identified no additional benefit of the JAK inhibitors tofacitinib and baricitinib over the appropriate comparator therapy for the treatment of pJIA. Tofacitinib and baricitinib are relatively new therapy options in the therapeutic indication, which are not yet explicitly mentioned in the guidelines. Their significance cannot yet be conclusively assessed. Tofacitinib and baricitinib are not determined as the appropriate comparator therapy for the present procedure.

Taking into account the aggregated evidence and the respective authorisation status, the G-BA considers in the overall assessment the use of adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable as monotherapy, as appropriate for children and adolescents 2 years of age and older with active pJIA, who have responded inadequately to previous therapy with conventional synthetic DMARDs (patient population a), taking into account the respective authorisation status in the case of MTX intolerance or unsuitability.

For children and adolescents 2 years of age and older with active pJIA who have had an inadequate response to one or more biologic DMARDs (patient population b), the G-BA

[2] Resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V for baricitinib dated 3 May 2024.
[3] German Society of Paediatrics and Adolescent Medicine. Therapy of Juvenile Idiopathic Arthritis; S2k guideline, long version, 3rd edition [online]. AWMF registry number 027-020. Last revised: 30.11.2019. Berlin (GER): Association of the Scientific Medical Societies (AWMF); 2019.
[valid until 29.11.2024 (currently under revision)]

considers change to abatacept or adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if necessary, as monotherapy, as appropriate comparator therapy, taking into account the respective authorisation status in case of MTX intolerance or unsuitability, depending on prior therapy. It is assumed that when selecting the comparator, it is switched to an active ingredient that has not yet been used as part of the prior therapy. An unchanged retention of the inadequate (prior) therapy does not correspond to the appropriate comparator therapy.

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

It is assumed that the patients covered by the therapeutic indication are not (or no longer) eligible for (symptomatic) therapy with NSAIDs and/or glucocorticoids alone. Irrespective of this, the use of glucocorticoids (systemic and/or intra-articular) should always be possible in the context of flare therapy.

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

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

2.1.3 Extent and probability of the additional benefit

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

a) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs

An additional benefit is not proven.

b) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

An additional benefit is not proven.

Justification for patient populations a) and b):

In their dossier, the pharmaceutical company did not present any relevant study for the assessment of the additional benefit of sarilumab in comparison with the appropriate comparator therapy.

They identified the label-enabling SKYPP study in the present therapeutic indication and presented it in the dossier. This is a non-randomised, uncontrolled, open-label phase IIb study comprising a dose-ranging phase and an extension phase. In accordance with the

pharmaceutical company's approach in the dossier, this study is not considered for the present benefit assessment due to the lack of comparison with the appropriate comparator therapy. An additional benefit is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient sarilumab. The therapeutic indication assessed here is as follows:

"Kevzara is indicated for the treatment of active polyarticular juvenile idiopathic arthritis (pJIA; rheumatoid factor positive or negative polyarthritis and extended oligoarthritis) in patients 2 years of age and older who have responded inadequately to previous therapy with conventional synthetic DMARDs (csDMARDs). Kevzara may be used as monotherapy or in combination with MTX."

In the therapeutic indication to be considered, two patient groups were distinguished:

Patient group a)

Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs

As the appropriate comparator therapy, the G-BA determined adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if necessary, as monotherapy, taking into account the respective authorisation status in the case of MTX intolerance or unsuitability. For this patient group, the pharmaceutical company presented the non-randomised, uncontrolled, open-label phase IIb SKYPP study, which, however, does not allow a comparison of sarilumab with the appropriate comparator therapy. Thus, no adequate data are available to assess the additional benefit of sarilumab. In the overall assessment, the additional benefit of sarilumab compared to the appropriate comparator therapy is not proven for this patient group.

Patient group b)

Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

As the appropriate comparator therapy, the G-BA determined abatacept or adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if necessary, as monotherapy, taking into account the respective authorisation status in the case of MTX intolerance or unsuitability, depending on the prior therapy. For this patient group, the pharmaceutical company presented the non-randomised, uncontrolled, open-label phase IIb SKYPP study, which, however, does not allow a comparison of sarilumab with the appropriate comparator therapy. Thus, no adequate data are available to assess the additional benefit of sarilumab. In the overall assessment, the additional benefit of sarilumab compared to the appropriate comparator therapy is not proven for this patient group.

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 information is based on the data of the pharmaceutical company from the dossier and the patient numbers from the resolution on the benefit assessment of the active ingredient tofacitinib[4]. The calculation of the size of the target population was based on routine data analyses and is subject to uncertainties in the overall picture. These result, among other things, from the methodology used for the percentage values to distinguish between treatment with csDMARDs and bDMARDs .

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: 24 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 polyarticular juvenile idiopathic arthritis.

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).

Treatment period:

a) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs

[4] Resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V for tofacitinib dated 3 March 2022.

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
Methotrexate, if applicable	Continuously, 1 x every 7 days	52.1	1	52.1
Appropriate comparator therapy				
Adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable, as monotherapy, taking into account the respective authorisation status in case of MTX intolerance or unsuitability				
Adalimumab	Continuously, 1 x every 14 days	26.1	1	26.1
Etanercept	Continuously, 2 x in 7 days or Continuously, 1 x in 7 days	104.3 or 52.1	1 or 1	104.3 or 52.1
Golimumab	Continuously, 1 x monthly	12.0	1	12.0
Tocilizumab	Children ≥ 2 years (< 30 kg)			
	Continuously, 1 x every 28 days	13.0	1	13.0
	Adolescents ≤ 17 years (≥ 30 kg)			
	Continuously, 1 x every 14 days	26.1	1	26.1
Methotrexate, if applicable	Continuously, 1 x every 7 days	52.1	1	52.1

b) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

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
Methotrexate, if applicable	Continuously, 1 x every 7 days	52.1	1	52.1
Appropriate comparator therapy				
Abatacept or adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable, as monotherapy, taking into account the respective authorisation status in case of MTX intolerance or unsuitability, depending on prior therapy				
Abatacept	Continuously, 1 x every 7 days	52.1	1	52.1
Adalimumab	Continuously, 1 x every 14 days	26.1	1	26.1
Etanercept	Continuously, 2 x in 7 days or Continuously, 1 x in 7 days	104.3 or 52.1	1 or 1	104.3 or 52.1
Golimumab	Continuously, 1 x monthly	12.0	1	12.0
Tocilizumab	Children ≥ 2 years (< 30 kg)			
	Continuously, 1 x every 28 days	13.0	1	13.0
	Adolescents ≤ 17 years (≥ 30 kg)			
	Continuously, 1 x every 14 days	26.1	1	26.1
Methotrexate, if applicable	Continuously, 1 x every 7 days	52.1	1	52.1

Consumption:

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.

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

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

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population[5]" (average body weight of two-year-olds at 14.1 kg and average body height of two-year-olds at 0.93 m) were applied. This results in a body surface area of 0.59 m² for two-year-olds (calculated according to Du Bois 1916). The "Microcensus 2021 – body measurements of the population[6]" were applied for the 17-year-olds (average body weight: 67.2 kg, average body height: 1.74 m). This results in a body surface area of 1.81 m² for the 17-year-olds.

Methotrexate is approved for children 3 years of age and older. For cost representation, the dosage was calculated here as a function of body surface area for children 2 years of age and older. As it is not always possible to achieve the exact calculated dose per day with the commercially available dosage strengths, in these cases rounding up or down to the next higher or lower available dose that can be achieved with the commercially available dose potencies as well as the scalability of the respective dosage form.

Methotrexate is available on the market in both oral and parenteral dosage forms. For cost representation, it is assumed that patients 6 years of age and older generally receive the more economical option (tablets). Conversely, the parenteral form of administration is used to calculate the annual treatment costs for the lower limit of the range (children ≥ 2 years of age), as it is often not possible to administer tablets to children 2-5 years of age.

According to the product information, the use of abatacept is only approved with the dosage form of the injection solution as subcutaneous application for children 2 years and older. Intravenous administration is not indicated for this age group and is therefore not included in the calculation of annual treatment costs for children 2 years of age and older.

a) <u>Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs</u>

[5] Federal Health Reporting. Average body measurements of the population (2017, both sexes, 1 year and older), www.gbe-bund.de

[6] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

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	Children ≥ 2 years (< 30 kg)				
	4 mg/kg BW 56.4 mg	56.4 mg	1 x 270 mg	26.1	26.1 x 270 mg
	Adolescents ≤ 17 years (≥ 30 kg)				
	3 mg/kg BW 200 mg[7]	200 mg	1 x 270 mg	26.1	26.1 x 270 mg
Methotrexate, if applicable	10-15 mg/m² BSA 5.9 mg – 27.15 mg	5.9 mg – 27.15 mg	1 x 7.5 mg – 2 x 10 mg + 1 x 7.5 mg	52.1	52.1 x 7.5 mg – 104.2 x 10 mg + 52.1 x 7.5 mg
Appropriate comparator therapy					
Adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable, as monotherapy, taking into account the respective authorisation status in the case of MTX intolerance or unsuitability					
Adalimumab	Children ≥ 2 years (< 30 kg)				
	20 mg	20 mg	1 x 20 mg	26.1	26.1 x 20 mg
	Adolescents ≤ 17 years (≥ 30 kg)				
	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Etanercept	0.4 – 0.8 mg/kg BW 5.64 mg – 50 mg[8]	5.64 mg – 50 mg	1 x 10 mg – 1 x 50 mg	104.3 – 52.1	104.3 x 10 mg – 52.1 x 50 mg
Golimumab	Children ≥ 2 years (< 40 kg)				
	30 mg/m² BSA 17.7 mg	17.7 mg	1 x 45 mg	12.0	12 x 45 mg
	Adolescents ≤ 17 years (≥ 40 kg)				

[7] For patients weighing 63 kg or more, the sarilumab dose is limited to 200 mg, which is administered once every 2 weeks.
[8] The maximum daily dose of etanercept is 50 mg when administered once a week and 25 mg when administered twice a week.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	50 mg	50 mg	1 x 50 mg	12.0	12 x 50 mg
Tocilizumab	Children ≥ 2 years (< 30 kg)				
	10 mg/kg BW 141 mg	141 mg	2 x 80 mg	13.0	26.0 x 80 mg
	Adolescents ≤ 17 years (≥ 30 kg)				
	162 mg	162 mg	1 x 162 mg	26.1	26.1 x 162 mg
Methotrexate, if applicable	10-15 mg/m² BSA 5.9 mg – 27.15 mg	5.9 mg – 27.15 mg	1 x 7.5 mg – 2 x 10 mg + 1 x 7.5 mg	52.1	52.1 x 7.5 mg – 104.2 x 10 mg + 52.1 x 7.5 mg

b) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

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	Children ≥ 2 years (< 30 kg)				
	4 mg/kg BW 56.4 mg	56.4 mg	1 x 270 mg	26.1	26.1 x 270 mg
	Adolescents ≤ 17 years (≥ 30 kg)				
	3 mg/kg BW 200 mg[7]	200 mg	1 x 270 mg	26.1	26.1 x 270 mg
Methotrexate, if applicable	10-15 mg/m² BSA 5.9 mg – 27.15 mg	5.9 mg – 27.15 mg	1 x 7.5 mg – 2 x 10 mg + 1 x 7.5 mg	52.1	52.1 x 7.5 mg – 104.2 x 10 mg + 52.1 x 7.5 mg
Appropriate comparator therapy					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Abatacept or adalimumab or etanercept or golimumab or tocilizumab, each in combination with MTX; if applicable, as monotherapy, taking into account the respective authorisation status in the case of MTX intolerance or unsuitability, depending on prior therapy					
Abatacept	Children ≥ 2 years (< 25 kg)				
	50 mg	50 mg	1 x 50 mg	52.1	52.1 x 50 mg
	Adolescents ≤ 17 years (≥ 50 kg)				
	125 mg	125 mg	1 x 125 mg	52.1	52.1 x 125 mg
Adalimumab	Children ≥ 2 years (< 30 kg)				
	20 mg	20 mg	1 x 20 mg	26.1	26.1 x 20 mg
	Adolescents ≤ 17 years (≥ 30 kg)				
	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Etanercept	0.4 – 0.8 mg/kg BW 5.64 mg – 50 mg[8]	5.64 mg – 50 mg	1 x 10 mg – 1 x 50 mg	104.3 – 52.1	104.3 x 10 mg – 52.1 x 50 mg
Golimumab	Children ≥ 2 years (< 40 kg)				
	30 mg/m² BSA 17.7 mg	17.7 mg	1 x 45 mg	12.0	12 x 45 mg
	Adolescents ≤ 17 years (≥ 40 kg)				
	50 mg	50 mg	1 x 50 mg	12.0	12 x 50 mg
Tocilizumab	Children ≥ 2 years (< 30 kg)				
	10 mg/kg BW 141 mg	141 mg	2 x 80 mg	13.0	26.0 x 80 mg
	Adolescents ≤ 17 years (≥ 30 kg)				
	162 mg	162 mg	1 x 162 mg	26.1	26.1 x 162 mg
Methotrexate, if applicable	10-15 mg/m² BSA 5.9 mg –	5.9 mg – 27.15 mg	1 x 7.5 mg – 2 x 10 mg + 1 x 7.5 mg	52.1	52.1 x 7.5 mg – 104.2 x 10 mg +

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	27.15 mg				52.1 x 7.5 mg

Costs:

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

Costs of the medicinal products:

a) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs

and

b) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

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 270mg[9]	-	-	-	-	-
Methotrexate 7.5 mg[10]	12 SPF	€ 153.99	€ 1.77	€ 11.28	€ 140.94
Methotrexate 7.5 mg[10]	30 TAB	€ 33.75	€ 1.77	€ 1.77	€ 30.21
Methotrexate 10 mg[10]	30 TAB	€ 41.63	€ 1.77	€ 2.40	€ 37.46
Appropriate comparator therapy					
Abatacept 50 mg	4 SFI	€ 763.99	€ 1.77	€ 41.67	€ 720.55

[9] Sarilumab 270 mg vial with 175mg/ml solution for injection is currently unavailable on the German market, therefore a cost representation is not possible.

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
Abatacept 125 mg	12 PEN	€ 5,530.47	€ 1.77	€ 312.55	€ 5,216.15
Adalimumab 20 mg	2 SFI	€ 499.99	€ 1.77	€ 27.06	€ 471.16
Adalimumab 40 mg[10]	6 SFI	€ 2,804.97	€ 1.77	€ 224.14	€ 2,579.06
Etanercept 10 mg	4 DSS	€ 194.34	€ 1.77	€ 10.13	€ 182.44
Etanercept 50 mg[10]	12 SFI	€ 2,548.84	€ 1.77	€ 203.25	€ 2,343.82
Golimumab 45 mg	1 SFI	€ 1,845.93	€ 1.77	€ 102.13	€ 1,742.03
Golimumab 50 mg[10]	3 SPF	€ 2,548.84	€ 1.77	€ 203.25	€ 2,343.82
Tocilizumab 80 mg	4 CIS	€ 1,017.05	€ 1.77	€ 55.68	€ 959.60
Tocilizumab 162 mg	12 PEN	€ 5,135.91	€ 1.77	€ 290.02	€ 4,844.12
Methotrexate 7.5 mg[10]	12 SPF	€ 153.99	€ 1.77	€ 11.28	€ 140.94
Methotrexate 7.5 mg[10]	30 TAB	€ 33.75	€ 1.77	€ 1.77	€ 30.21
Methotrexate 10 mg[10]	30 TAB	€ 41.63	€ 1.77	€ 2.40	€ 37.46
Abbreviations: FCT = film-coated tablets; SPF = solution for injection in a pre-filled syringe; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PEN = solution for injection in a pre-filled pen					

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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 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.

Diagnosis of tuberculosis

For active ingredients of the appropriate comparator therapy of the patient populations a and b (adalimumab, etanercept, golimumab, abatacept, tocilizumab), costs are regularly incurred for examination of both active and inactive ("latent") tuberculosis infections. The additionally required SHI services for screening for tuberculosis infection are incurred equally for the medicinal product to be assessed and the appropriate comparator therapy, so that they are not presented.

Diagnosis of chronic hepatitis B

Patients must be tested for the presence of HBV infection prior to initiating treatment with abatacept or adalimumab or etanercept or golimumab. These examinations are not to be carried out regularly when using sarilumab. Diagnostics to rule out chronic hepatitis B requires

[10] Fixed reimbursement rate

sensibly coordinated steps. A step-by-step serological diagnosis initially consists of the examination of HBs antigen and anti-HBc antibodies. If both are negative, a past HBV infection can be excluded. In certain case constellations, further steps may be necessary in accordance with current guideline recommendations[11].

Designation of the therapy	Designation of the service	Number	Unit cost	Costs/ patient/ year
HBV screening				
Adalimumab Etanercept Golimumab Abatacept	HBV test Hepatitis B surface antigen status (GOP 32781)	1	€ 5.06	€ 5.06
	Anti-HBc antibody (FSI 32614)	1	€ 5.43	€ 5.43

[11] "Update of the S3 guideline on prophylaxis, diagnosis and therapy of hepatitis B virus infection AWMF Registry No.: 021/011 " https://register.awmf.org/assets/guidelines/021-011l_S3_Prophylaxe-Diagnostik-Therapie-der-Hepatitis-B-Virusinfektion_2021-07.pdf

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

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:

a) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to previous therapy with conventional synthetic DMARDs

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 175 mg/ml solution for injection
Last revised: 28 March 2025

b) Children and adolescents 2 years of age and older with active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), who have responded inadequately to one or more biologic DMARDs

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

References:
Product information for sarilumab (Kevzara); Kevzara 175 mg/ml solution for injection
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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 28 January 2025, 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 1, number 2 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.

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	28 January 2025	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
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