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)
Baricitinib (new therapeutic indication: atopic dermatitis, ≥ 2 to < 18 years)

of 2 May 2024

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of 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 trials the pharmaceutical company has 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 baricitinib (Olumiant) was listed for the first time on 1 April 2017 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 18 October 2023, baricitinib 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 13 November 2023, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient baricitinib with the

new therapeutic indication "Treatment of moderate to severe atopic dermatitis in paediatric patients 2 years of age and older who are candidates for systemic therapy" in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication).

The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on 15 February 2024 on the G-BA website (www.g-ba.de), therefore initiating the written statement procedure. In addition, an oral hearing was held.

Based on 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 (if necessary, also the addendum to the benefit assessment prepared by IQWiG), the G-BA decided on the question on whether an additional benefit of baricitinib compared with the appropriate comparator therapy could be determined – Annex XII - Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V. In order to determine the extent of the additional benefit, the G-BA has 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 IQWiG according to the General Methods was not used in the benefit assessment of baricitinib – Annex XII - Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V.

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

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

2.1.1 Approved therapeutic indication of Baricitinib (Olumiant) in accordance with product information

Baricitinib is indicated for the treatment of moderate to severe atopic dermatitis in adult and paediatric patients 2 years of age and older who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 2 May 2024):

Treatment of moderate to severe atopic dermatitis in children and adolescents 2 to 17 years of age who are candidates for systemic therapy.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Children 2 to 11 years of age with moderate atopic dermatitis who are candidates for systemic therapy

Appropriate comparator therapy:

A patient-individual optimised treatment regimen depending on the manifestation of the disease and taking into account the previous therapy and the following therapies:

- topical glucocorticoids of classes 1 to 3
- topical calcineurin inhibitors

The respective authorisation status of the medicinal products must be taken into account.

b) Children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy

Appropriate comparator therapy:

dupilumab (in combination with TCS and/or TCI if required)

c) Adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy

Appropriate comparator therapy:

Dupilumab (in combination with TCS and/or TCI if required)

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

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

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

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

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

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

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

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

on 1. Medicinal products with the following active ingredients are approved for the present therapeutic indication:
- topical glucocorticoids of classes 1 to 4
- pimecrolimus (moderate atopic eczema) and tacrolimus (moderate to severe atopic eczema)
- systemic glucocorticoids (severe eczema)
- ciclosporin (severe atopic dermatitis)
- antihistamines
- Dupilumab
- tralokinumab
- upadacitinib

on 2. UV treatments (UVA/ NB-UVB/ balneophototherapy) are eligible as non-medicinal treatments for atopic dermatitis, but UVA1 is not eligible as it is not a reimbursable treatment.

on 3. In the therapeutic indication under consideration here, the following resolutions of the G-BA are available:
- Therapeutic information on tacrolimus (resolution of 4 September 2003) and pimecrolimus (resolution of 4 September 2003); repeal resolution of 17 August 2023 not yet in force
- Resolutions on the benefit assessment according to Section 35a SGB V for the active ingredient dupilumab dated 17 May 2018, 20 February 2020, 1 July 2021 and 21 September 2023
- Resolution on the amendment of the Directive of Prescription of Medicinal Products in SHI-accredited Medical Care (MVV-RL): "Balneophototherapy for atopic eczema," dated 20 March 2020
- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient upadacitinib dated 17 February 2022

- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient tralokinumab dated 12 May 2023

on 4. The generally recognised state of medical knowledge on which the resolution of the G-BA is based, was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present therapeutic indication.

Patient population a)

Topical glucocorticoids of classes 1 to 3 and the calcineurin inhibitor tacrolimus (0.03%) and pimecrolimus are available as topical therapy options for a patient-individual optimised treatment regimen. The guidelines do not recommend class 4 topical glucocorticoids for children under 12 years of age and are only indicated in exceptional cases according to the marketing authorisation; there is a contraindication for children under 3 years of age. Therefore, these are not part of the appropriate comparator therapy.

According to the S3 guideline "Atopic Dermatitis"[1] it is recommended using topical calcineurin inhibitors in case of non-response or contraindications of topical glucocorticoids. According to the guideline, the use of topical calcineurin inhibitors is particularly recommended for sensitive skin areas where the use of TCS is likely to be associated with side effects, or in areas where side effects from topical glucocorticoids have already occurred.

The use of antihistamines is not recommended for the treatment of atopic dermatitis.

Systemic glucocorticoids are available as a systemic therapy option within the framework of an optimised treatment regimen. Such an application is usually done as a short-term flare therapy. Particularly due to the severe side effects, the long-term use of systemic glucocorticoids in children is not recommended, so that they are not determined as part of the appropriate comparator therapy.

Based on the available evidence, phototherapeutic treatment forms are not recommended for children under 12 years of age and are therefore not part of the appropriate comparator therapy.

In the case of the defined appropriate comparator therapy, it is assumed that a patient-individually optimised treatment regimen is used, depending on the manifestation of the disease and taking into account the previous therapy. In case of intolerance, other, alternative active ingredients are used. Particularly as atopic dermatitis is a disease with fluctuating symptomatology - including seasonal - the treatment has to be individually adapted. A specific therapy that is appropriate for all patients cannot be determined.

Therapy adjustment during flares must be distinguished from therapy adjustment during chronic phases. Therapy adjustment during an flare (e.g. short-term administration of systemic glucocorticoids) may be necessary. This would be regarded as a component of the patient-individually optimised treatment regimen within the scope of the therapeutic indication. In addition to the treatment of the flares, it should also be possible to adjust the therapy in the chronic phases. Keeping the inadequate (prior) therapy unchanged does not correspond to the appropriate comparator therapy.

1 Werfel T. et al. S3 guideline Atopic Dermatitis (AD) [Neurodermitis; atopic eczema]. 2023. [Accessed: 25.03.2024] https://register.awmf.org/assets/guidelines/013-027l_S3_Atopische-Dermatitis-AD-Neurodermitis-atopisches-Ekzem_2023-08.pdf

In summary, for the treatment of moderate atopic dermatitis in children 2 to 11 years of age, a patient-individual optimised treatment regimen taking into account topical glucocorticoids of classes 1 to 3 and topical calcineurin inhibitors is determined as the appropriate comparator therapy for baricitinib.

Patient populations b) and c)

For the existing patient populations of adolescents 12 to 17 years of age with moderate to severe atopic dermatitis and children 2 to 11 years of age with severe atopic dermatitis who are candidates for continuous systemic therapy, the active ingredient dupilumab is available as a therapy option. Based on the benefit assessment resolution of 17 May 2018, dupilumab was able to show an indication of a considerable additional benefit compared with the appropriate comparator therapy in adults. In addition, non-quantifiable additional benefit of dupilumab for adolescents with moderate to severe atopic dermatitis and for children with severe atopic dermatitis was identified by resolutions of 20 February2020, 1 July 2021 and 21 September 2023. In the overall assessment of the available evidence, dupilumab is an adequate therapy option for adolescents 12 to 17 years of age with moderate to severe atopic dermatitis and children 2 to 11 years of age with severe atopic dermatitis who are candidates for continuous systemic therapy. Therefore, there is beneficial evidence for an active ingredient that has now also proven itself in practical application.

As part of the early benefit assessment, the JAK inhibitor upadacitinib and the monoclonal antibody tralokinumab were assessed by the G-BA in the therapeutic indication of moderate to severe atopic dermatitis in adolescents 12 years of age and older and adults. For both the active ingredient upadacitinib and the active ingredient tralokinumab, no additional benefit could be identified by the G-BA in adolescents with moderate to severe atopic dermatitis who are candidates for continuous systemic therapy, as no suitable data were available for this patient population. Therefore, upadacitinib and tralokinumab are not found to be appropriate comparator therapy for the present patient groups b) and c).

Even with permanent or continuous systemic therapy, topical glucocorticoids (TCS) in classes 2, 3 or 4 and the calcineurin inhibitor (TCI) tacrolimus and pimecrolimus may also be indicated as topical therapy options for individual lesions or in a limited period of time according to the guidelines.

In adolescents 12 to 17 years of age with moderate to severe atopic dermatitis and children 2 to 11 years of age with severe atopic dermatitis who are candidates for continuous systemic therapy is indicated, dupilumab (possibly in combination with TCS and/or TCI) is the appropriate comparator 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 baricitinib is assessed as follows:

a) Children 2 to 11 years of age with moderate atopic dermatitis who are candidates for systemic therapy

For children 2 to 11 years of age with moderate atopic dermatitis who are candidates for systemic therapy, the additional benefit is not proven.

b) Children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy

For children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy, the additional benefit is not proven.

c) Adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy

For adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy, the additional benefit is not proven.

Justification for patient populations a) to c):

No relevant study was identified for the assessment of the additional benefit of baricitinib compared to the appropriate comparator therapy.

In the BREEZE-AD-PEDS study, which was the basis for approval, a randomised comparison was carried out over 16 weeks against placebo. In accordance with the pharmaceutical company's approach in the dossier, this study is not considered for the present benefit assessment. No conclusions on the additional benefit of baricitinib compared to the appropriate comparator therapy can be derived from this study.

No suitable data are available for the assessment of the additional benefit of baricitinib compared to the appropriate comparator therapy in children and adolescents 2 to 17 years of age and older with moderate to severe atopic dermatitis who are candidates for continuous systemic therapy. This does not provide any hint for an additional benefit of baricitinib compared to the appropriate comparator therapy. An additional benefit is 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 baricitinib. The therapeutic indication assessed here is as follows: "Baricitinib is indicated for the treatment of moderate to severe atopic dermatitis in adult and paediatric patients 2 years of age and older who are candidates for systemic therapy."

In the therapeutic indication under consideration, 3 patient groups were differentiated on the basis of the patient's age and the severity of the disease:

Patient group a)

Children 2 to 11 years of age with moderate atopic dermatitis who are candidates for systemic therapy

As appropriate comparator therapy, the G-BA determined a patient-individually optimised treatment regimen, depending on the manifestation of the disease and under consideration of the previous therapy, taking into account topical glucocorticoids of the classes 1 to 3 and topical calcineurin inhibitors.

For this patient group, the pharmaceutical company does not submit any data on the assessment of the additional benefit of baricitinib compared to the appropriate comparator therapy, as no relevant study could be identified. An additional benefit of baricitinib compared to the appropriate comparator therapy is therefore not proven.

Patient group b)

Children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy

The G-BA determined a therapy with dupilumab (in combination with TCS and/or TCI if required) as the appropriate comparator therapy.

For this patient group, the pharmaceutical company does not submit any data on the assessment of the additional benefit of baricitinib compared to the appropriate comparator therapy, as no relevant study could be identified. An additional benefit of baricitinib compared to the appropriate comparator therapy is therefore not proven.

Patient group c)

Adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy

The G-BA determined a therapy with dupilumab (in combination with TCS and/or TCI if required) as the appropriate comparator therapy.

For this patient group, the pharmaceutical company does not submit any data on the assessment of the additional benefit of baricitinib compared to the appropriate comparator therapy, as no relevant study could be identified. An additional benefit of baricitinib compared to the appropriate comparator therapy is therefore not proven.

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

The information on the number of patients is based on the target population in statutory health insurance (SHI). The patient numbers stated by the pharmaceutical company in the dossier are considered to be underestimated. Therefore, the information is based on the data from the resolutions of the G-BA on dupilumab[2,3,4] in the therapeutic indication areas of moderate to severe atopic dermatitis in adolescents and severe atopic dermatitis in children who are candidates for systemic therapy. Despite the partially differing size of the patient populations, the patient numbers stated in the procedures for dupilumab are considered to be in a more plausible order of magnitude.

[2] Resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V of 20 February 2020

[3] Resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V of 01 July 2021

[4] Resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V of 21 September 2023

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 Olumiant (active ingredient: baricitinib) at the following publicly accessible link (last access: 24 April 2024):

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

Treatment with baricitinib should only be initiated and monitored by doctors experienced in treating atopic dermatitis.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (incl. patient identification card).

In particular, the training material contains information and warnings on the risk of serious and opportunistic infections including tuberculosis and herpes zoster. It also points out the need for an effective contraceptive method.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 April 2024).

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.

Only proprietary prescription-only medicinal products were included in the cost representation. In the topical treatment with glucocorticoids frequently formulations are used which have not been considered here.
Topical therapy options are used on a patient-individual basis depending on the manifestation and localisation of the disease. In particular, the therapy is adapted to the patient-individual occurrence of the flares, so that the treatment duration is patient-individual.
As an example, one active ingredient each from topical glucocorticoids of class II (hydrocortisone butyrate) and class III (methylprednisolone) is presented.

Treatment period:

a) Children 2 to 5 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Baricitinib	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Topical glucocorticoids of classes 1 to 3 or tacrolimus (topical)				
Prednisolone	1 x daily for 2 weeks		Different from patient to patient	
Hydrocortisone butyrate	1-2 x daily for 1-2 weeks		Different from patient to patient	
Methylprednisolone	1 x daily for 2 weeks		Different from patient to patient	
Tacrolimus	1 x daily – 2 x weekly		Different from patient to patient	

b) Children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy

and

c) Adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Baricitinib	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Dupilumab in combination with TCS and/or TCI if required				
Dupilumab	< 12 years Continuously 1 x every 28 days	13.0	1	13.0
	≥ 12 years Continuously 1 x every 14 days	26.0	1	26.0
Prednisolone	1 x daily for 2 weeks		Different from patient to patient	
Hydrocortisone butyrate	1-2 x daily for 1-2 weeks		Different from patient to patient	
Methylprednisolone	1 x daily for 2 weeks		Different from patient to patient	
Pimecrolimus	2 x daily		Different from patient to patient	
Tacrolimus	1 x daily – 2 x weekly		Different from patient to patient	

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 dosages depending on body weight (BW), 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, 5-year-olds at 20.8 kg, 6-year-olds at 23.6 kg, 11-year-olds at 42.1 kg and 12-year-olds at 47.1 kg) were applied. The "Microcensus 2021 – body measurements of the population[6]" was applied for the ≤ 17-year-olds (average body weight: 67.2 kg).

a) Children 2 to 5 years of age with moderate to severe atopic dermatitis who are candidates for systemic 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
Medicinal product to be assessed					
Baricitinib	< 30 kg 2 mg	2 mg	1 x 2 mg	365.0	365.0 x 2 mg
	≥ 30 kg 4 mg	4 mg	4 mg	1 x 4 mg	365.0 x 4 mg
Appropriate comparator therapy					
Topical glucocorticoids of classes 2 to 3 or tacrolimus (topical)					
Hydrocortisone butyrate		Different from patient to patient			
Methylprednisolone		Different from patient to patient			
Tacrolimus		Different from patient to patient			

[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

b) Children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy

and

c) Adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic 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
Medicinal product to be assessed					
Baricitinib	< 30 kg 2 mg	2 mg	1 x 2 mg	365.0	365.0 x 2 mg
	≥ 30 kg 4 mg	4 mg	1 x 4 mg	365.0	365.0 x 4 mg
Appropriate comparator therapy					
Dupilumab in combination with TCS and/or TCI if required					
Dupilumab	< 12 years 300 mg	300 mg	1 x 300 mg	13.0	13.0 x 300 mg
	≥ 12 years < 60 kg 200 mg ≥ 60 kg 300 mg	200 mg or 300 mg	1 x 200 mg or 1 x 300 mg	26.0	26 x 200 mg or 26 x 300 mg
Hydrocortisone butyrate		Different from patient to patient			
Methylprednisolone		Different from patient to patient			
Pimecrolimus		Different from patient to patient			
Tacrolimus		Different from patient to patient			

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 fixed reimbursement rates shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Patient groups a) to c)

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					
Baricitinib 2 mg	98 FCT	€ 4,043.77	€ 2.00	€ 227.65	€ 3,814.12
Baricitinib 4 mg	98 FCT	€ 4,043.77	€ 2.00	€ 227.65	€ 3,814.12
Appropriate comparator therapy					
Dupilumab 200 mg	6 SFI	€ 3,944.20	€ 2.00	€ 221.96	€ 3,720.24
Dupilumab 300 mg	6 SFI	€ 3,944.20	€ 2.00	€ 221.96	€ 3,720.24
Prednisolone 4 mg (topical)	100 CRE	€ 20.49	€ 2.00	€ 0.73	€ 17.76
0.1% hydrocortisone butyrate [7] (topical)	100 CRE	€ 12.41	€ 2.00	€ 0.09	€ 10.32
0.1% methylprednisolone[7] (topical)	100 EMU	€ 12.41	€ 2.00	€ 0.09	€ 10.32
Pimecrolimus 10 mg (topical)	100 CRE	€ 106.53	€ 2.00	€ 7.53	€ 97.00
0.03% tacrolimus (topical)	60 UNG	€ 65.72	€ 2.00	€ 4.30	€ 59.42
Abbreviations: FCT = film-coated tablets; CRE = cream; EMU = emulsion; SFI = solution for injection; UNG = unguentum (ointment)					

LAUER-TAXE® last revised: 15 April 2024

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.

Prior to administration of baricitinib, patients must be tested for active and inactive ("latent") tuberculosis infections and for the presence of an HBV infection.

[7] Fixed reimbursement rate

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Baricitinib	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	€ 58.00	€ 58.00
	Chest radiograph (GOP 34241)	1	€ 17.42	€ 17.42
Baricitinib	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50
	Anti-HBs antibody (GOP 32617)[8]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV-DNA (GOP 32817)[9]	1	€ 89.50	€ 89.50

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

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

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed

8 Only if HBs antigen negative and anti-HBc antibody positive.
9 Settlement of GOP 32817 for diagnosis of HBV reactivation or before, during, at the end of or after discontinuation of specific antiviral therapy.

therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

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

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

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

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

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

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

<u>Concomitant active ingredient</u>

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 information in the product information of the assessed medicinal product.

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

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

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

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

Designation

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

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

Exception to the designation

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

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

Legal effects of the designation

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

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

Justification for the findings on designation in the present resolution:

a) Children 2 to 11 years of age with moderate atopic dermatitis who are candidates for systemic therapy

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 baricitinib (Olumiant); Olumiant 1 mg/2 mg/4 mg film-coated tablets; last revised: October 2023

b) Children 2 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy

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 baricitinib (Olumiant); Olumiant 1 mg/2 mg/4 mg film-coated tablets; last revised: October 2023

c) Adolescents 12 to 17 years of age with moderate to severe atopic dermatitis who are candidates for systemic therapy

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 baricitinib (Olumiant); Olumiant 1 mg/2 mg/4 mg film-coated tablets; last revised: October 2023

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 its session on 22 November 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 13 November 2023 the pharmaceutical company submitted a dossier for the benefit assessment of baricitinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 14 November 2023 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits 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 baricitinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 7 February 2024, and the written statement procedure was initiated with publication on the G-BA website on 15 February 2024. The deadline for submitting statements was 07 March 2024.

The oral hearing was held on 25 March 2024.

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 23 April 2024, and the proposed resolution was approved.

At its session on 2 May 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	22 November 2022	Implementation of the appropriate comparator therapy
Working group Section 35a	19 March 2024	Information on written statements received, preparation of the oral hearing
Subcommittee Medicinal products	25 March 2024	Conduct of the oral hearing
Working group Section 35a	3 April 2024 16 April 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	23 April 2024	Concluding discussion of the draft resolution
Plenum	2 May 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 2 May 2024

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

Prof. Hecken