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)
Abrocitinib (new therapeutic indication: atopic dermatitis, ≥ 12 to ≤ 17 years)

of 17 October 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 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 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 abrocitinib (Cibinqo) was listed for the first time on 15 January 2022 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 21 March 2024, abrocitinib 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 from 12.12.2008, sentence 7).

On 18 April 2024, 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 abrocitinib with the new therapeutic

indication "for the treatment of moderate-to-severe atopic dermatitis in adolescents 12 years 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 assessment of the dossier. The benefit assessment was published on 1 August 2024 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 abrocitinib 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 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 the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of abrocitinib.

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 Abrocitinib (Cibinqo) in accordance with the product information

Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 17.10.2024):

Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adolescents 12 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:

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

Appropriate comparator therapy for abrocitinib:

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

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

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.

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:
- Antihistamines
- Baricitinib
- Ciclosporin (severe atopic dermatitis)
- Dupilumab
- Lebrikizumab
- Pimecrolimus (moderate atopic eczema) and tacrolimus (moderate-to-severe atopic eczema)
- Systemic glucocorticoids (severe eczema)
- Topical glucocorticoids of classes 2 to 4
- Tralokinumab
- Upadacitinib

on 2. UV treatments (UVA/ NB-UVB/ balneophototherapy) are eligible as non-medicinal treatments for atopic dermatitis. UVA1 is not a reimbursable therapy option in this indication.

on 3. In the therapeutic indication under consideration here, the following resolutions of the G-BA are available:
- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient dupilumab dated 20 February 2020
- 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
- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient baricitinib dated 2 May 2024
- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient lebrikizumab dated 6 June 2024

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.

For the present patient population of adolescents 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis who are candidates for a systemic therapy, the active ingredient dupilumab is available as a therapy option. By resolution of 20

February 2020, a non-quantifiable additional benefit of dupilumab was identified for adolescents with moderate-to-severe atopic dermatitis. In the patient population of adults, a considerable additional benefit was shown for dupilumab compared to the appropriate comparator therapy (resolution of 17 May 2018). In the overall assessment of the available evidence, the shown advantages make dupilumab an adequate therapy option for adolescents 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis who are candidates for systemic therapy. In addition, the use of dupilumab has proven itself in practical application.

Moreover, the JAK inhibitors baricitinib and upadacitinib were assessed by the G-BA as part of the early benefit assessment. For the active ingredient upadacitinib, an indication of a considerable additional benefit over the appropriate comparator therapy was shown in adults with moderate-to-severe atopic dermatitis. In contrast, the G-BA was unable to identify an additional benefit in the patient population of adolescents due to the absence of suitable data for these patient populations. An additional benefit of the active ingredient baricitinib was identified neither for adolescents nor adults because no suitable data were available for a comparison with the appropriate comparator therapy.

Compared to the JAK inhibitors, dupilumab continues to be of primary importance in the German healthcare context due to its longer market availability and good efficacy/safety profile. In addition, there are limitations in the safety profile of JAK inhibitors for sub-populations. Therefore, upadacitinib and baricitinib are currently not determined to be appropriate comparator therapy for the present patient group.

The G-BA identified no additional benefit of the active ingredients tralokinumab and lebrikizumab in adolescents 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy, as no suitable data were available for a comparison with the appropriate comparator therapy. In addition, the active ingredients concern a comparatively new therapy option whose significance cannot yet be conclusively assessed. Therefore, tralokinumab and lebrikizumab are not determined to be appropriate comparator therapy for the present patient group.

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 for a limited period of time according to the guidelines.

In adolescents 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis who are candidates for systemic therapy, dupilumab (possibly in combination with TCS and/or TCI) is determined to be 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 abrocitinib is assessed as follows:

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

Justification:

No RCT could be identified for the direct comparison of abrocitinib versus the appropriate comparator therapy dupilumab in adolescents 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy.

The pharmaceutical company presented the JADE DARE and JADE TEEN approval studies with the aim of transferring the evidence from study results of adults to adolescents. It is generally possible to transfer the data from adults to adolescents in the therapeutic indication of atopic dermatitis as the pathogenesis and clinical picture are sufficiently similar in adolescents and adults. However, the present data constellation is unsuitable for transferring the results of adults from the JADE DARE study to adolescents as there are significant uncertainties, which are explained below:

The JADE DARE study is a double-blind RCT comparing abrocitinib with dupilumab in adults. The treatment duration was 26 weeks. A total of 727 patients were assigned to treatment with abrocitinib 200 mg once daily (N = 362) or dupilumab 300 mg every 2 weeks (N = 365). The likewise approved 100 mg dose of abrocitinib was not investigated in the JADE DARE study. However, according to the product information, this is only suitable as a starting dose for specific risk groups. In the JADE DARE study - as well as in the subsequent JADE TEEN study - all patients had to apply emollients at least daily during the entire treatment duration and topical medicinal therapy at sites with active lesions. Based on evaluations of the JADE DARE study, a hint for a considerable additional benefit of abrocitinib over the appropriate comparator therapy dupilumab for adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy was identified by resolution of 7 July 2022.

The JADE TEEN study is a double-blind RCT comparing abrocitinib and placebo with a treatment duration of 12 weeks. 287 patients 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis were enrolled in the study. Randomisation was performed - without consideration of patient-individual characteristics such as weight or risk factors - in a ratio of 1:1:1 (abrocitinib 200 mg (N = 96), abrocitinib 100 mg (N = 95) or placebo (N = 96)). The JADE TEEN study considered in isolation is unsuitable for the present benefit assessment as there is no comparison with the appropriate comparator therapy. However, the pharmaceutical company is aiming for a transfer of evidence by presenting the 200 mg arm from the intervention side and the placebo arm of this study in the dossier.

For the transfer of evidence, it is assumed that there are consistent and sufficiently large effects across the various endpoints collected in the two JADE DARE and JADE TEEN studies. However, in the endpoints (EASI 100, SCORAD 100, SCORAD 90 and POEM 0), which formed the basis for deriving the additional benefit for adults by resolution of 7 July 2022, there were no statistically significant effects at week 12 in the JADE TEEN study. There were statistically significant advantages at week 12 in the POEM 0 to 2, SCORAD 75 and EASI 90 operationalisations. There were no statistically significant differences for these response thresholds at the final data cut-off of the JADE DARE study. Thus, there were no statistically significant differences in adolescents in the operationalisations of the endpoints that formed the basis for deriving an additional benefit in adults. Moreover, in view of the fact that the JADE TEEN study involved a placebo comparison, the combined effects in the POEM 0 to 2, SCORAD 75 and EASI 90 operationalisations at week 12 are considered to be inadequate to assume that the results can be transferred from adults to adolescents.

Furthermore, no data were presented for the 100 mg dose of abrocitinib, which would however have been relevant for the assessment of the additional benefit in adolescent patients. For adolescents 12 years and older with a body weight of less than 59 kg, the recommended starting dose of abrocitinib is 100 mg according to the product information. For adolescents weighing at least 59 kg, a starting dose of 100 mg or 200 mg once daily may be indicated, depending on tolerability and patient-individual risk factors. Regardless of the starting dose selected, the lowest effective dose should be considered for maintenance treatment. In principle, it can therefore be assumed that the lower (100 mg) dosage represents the adequate dose for a relevant percentage of the targeted patient population. A further uncertainty exists due to the assignment of patients to the two intervention arms (100 mg abrocitinib; 200 mg abrocitinib) in the JADE TEEN study, which was carried out without taking into account patient-individual characteristics such as weight or risk factors.

Taken together, it is not possible to transfer the results of adults from the JADE DARE study to adolescents in the present data constellation. In the overall assessment, no additional benefit of abrocitinib over the appropriate comparator therapy is identified for adolescents 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis who are candidates for systemic therapy.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient abrocitinib.

The therapeutic indication assessed here is as follows: Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adolescents 12 to ≤ 17 years of age who are candidates for systemic therapy.

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

The pharmaceutical company does not present suitable data for the patient population to be evaluated so that no statements on the additional benefit of abrocitinib compared to the appropriate comparator therapy can be derived.

In the overall assessment, no additional benefit of abrocitinib over the appropriate comparator therapy is identified for adolescents 12 to ≤ 17 years of age with moderate-to-severe atopic dermatitis who are candidates for systemic therapy.

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

The patient numbers stated by the pharmaceutical company in the dossier are considered to be underestimated. 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 from the resolutions of the G-BA on dupilumab in the therapeutic indication area of moderate-to-severe atopic dermatitis in adolescents[2], who are candidates for systemic therapy. The patient

[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.

numbers stated in the dupilumab procedures are estimated to be within a more plausible range.

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 Cibinqo (active ingredient: abrocitinib) at the following publicly accessible link (last access: 5 September 2024):

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

Treatment with abrocitinib 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 September 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 co-morbidities) are not taken into account when calculating the annual treatment costs.

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

Abrocitinib is indicated for the treatment of patients 12 years and older with moderate-to-severe atopic dermatitis and may be used in combination with topical corticosteroids and/or topical calcineurin inhibitors. Thus, if applicable, the corresponding costs for the combination medicinal products are incurred both for the medicinal product under assessment and for the appropriate comparator therapy and are not listed separately.

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

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Abrocitinib	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Dupilumab	Continuously, 1 x every 14 days	26.1	1	26.1

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 dosages depending on body weight (BW), the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population[3]" (average body weight of 12-year-olds at 47.1 kg) were used as a basis: The "Microcensus 2021 – body measurements of the population[4]" was applied for the ≤ 17-year-olds (average body weight: 67.2 kg).

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

[4] 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					
Abrocitinib	100 mg or 200 mg	100 mg or 200 mg	1 x 100 mg or 1 x 200 mg	365.0	365 x 100 mg or 365 x 200 mg
Appropriate comparator therapy					
Dupilumab	< 60 kg: 200 mg ≥ 60 kg: 300 mg	200 mg or 300 mg	1 x 200 mg or 1 x 300 mg	26.1	26.1 x 200 mg or 26.1 x 300 mg

Costs of the medicinal products:

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.

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					
Abrocitinib 100 mg	91 FCT	€ 4,050.11	€ 2.00	€ 0.00	€ 4,048.11
Abrocitinib 200 mg	91 FCT	€ 4,733.11	€ 2.00	€ 0.00	€ 4,731.11
Appropriate comparator therapy					
Dupilumab 200 mg	6 SFI	€ 3,908.39	€ 2.00	€ 219.92	€ 3,686.47
Dupilumab 300 mg	6 SFI	€ 3,908.39	€ 2.00	€ 219.92	€ 3,686.47
Abbreviations: FCT = film-coated tablets; SFI = solution for injection					

LAUER-TAXE® last revised: 15 September 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.

For the use of abrocitinib, costs are regularly incurred for examining for both active and inactive ("latent") tuberculosis infections. The costs presented are a blood test (quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens specific for Mycobacterium tuberculosis-complex (except BCG)) and a chest radiograph. The tuberculin skin test is not presented due to lack of sensitivity and specificity as well as the possibility of "sensitisation".

Diagnostics to rule out chronic hepatitis B requires 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.[5]

In total, additionally required SHI services are required for the diagnosis of suspected chronic hepatitis B and examinations for tuberculosis infections which usually differ between the medicinal product to be assessed and the appropriate comparator therapy and are consequently considered as additionally required SHI services in the resolution.

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Abrocitinib	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

[5] S3 guideline on prevention, 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

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50
	Anti-HBs antibody (GOP 32617)[6]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV-DNA (GOP 32817)[7]	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 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

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

resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

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

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

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

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

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

Concomitant active ingredient

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

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

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

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

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

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

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

Designation

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

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

Exception to the designation

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

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit

had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

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

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

Justification for the findings on designation in the present resolution:

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 and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:
Product information for abrocitinib (Cibinqo); Cibinqo 50 mg/100 mg/200 mg film-coated tablets; last revised: March 2024

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 7 November 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 18 April 2024, the pharmaceutical company submitted a dossier for the benefit assessment of abrocitinib to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2, sentence 2 VerfO.

By letter dated 24 April 2024 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 abrocitinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 26 July 2024, and the written statement procedure was initiated with publication on the G-BA website on 1 August 2024. The deadline for submitting statements was 22 August 2024.

The oral hearing was held on 9 September 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 8 October 2024, and the proposed draft resolution was approved.

At its session on 17 October 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	7 November 2023	Determination of the appropriate comparator therapy
Working group Section 35a	4 September 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	9 September 2024	Conduct of the oral hearing
Working group Section 35a	18 September 2024 30 September 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	8 October 2024	Concluding discussion of the draft resolution

Plenum	17 October 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 17 October 2024

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

Prof. Hecken