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 (atopic dermatitis)

of 7 July 2022

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 relevant date for the first placing on the (German) market of the active ingredient abrocitinib in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 January 2022. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 14 January 2022.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de) on 19 April 2022, 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, the statements

submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. 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 who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 07.07.2022):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy

Appropriate comparator therapy for abrocitinib:

Dupilumab (in combination with topical glucocorticoids and/or topical calcineurin inhibitors if required)

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

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.

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. Medicinal products with the following active ingredients are approved for the present therapeutic indication:

- topical glucocorticoids of classes 2 to 4
- pimecrolimus (moderate atopic eczema) and tacrolimus (moderate to severe atopic eczema)
- systemic glucocorticoids (severe eczema)
- ciclosporin (severe atopic dermatitis)
- antihistamines
- dupilumab
- baricitinib
- tralokinumab
- upadacitinib

on 2. UV treatments (UVA/NB-UVB/balneophototherapy) are eligible as non-medicinal treatments, 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)
- Resolutions on the benefit assessment according to Section 35a SGB V for the active ingredient dupilumab dated 17 May 2018, 20 February 2020 and 1 July 2021
- 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 baricitinib dated 6 May 2021
- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient tralokinumab dated 6 January 2022
- Resolution on the benefit assessment according to Section 35a SGB V for the active ingredient upadacitinib dated 17 February 2022

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.

According to the marketing authorisation, those patients are included in the therapeutic indication who are eligible for a systemic therapy.

For the present benefit assessment, adults with moderate-to-severe atopic dermatitis for whom continuous systemic therapy is indicated are considered, as the active ingredient abrocitinib is administered as a continuous therapy and is therefore only considered in adults for whom continuous systemic therapy is indicated.

For the present patient population of adults with moderate-to-severe atopic dermatitis eligible for continuous systemic therapy, the active ingredient dupilumab is available as further 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 the overall assessment of the available evidence, dupilumab represents an adequate therapy option for patients with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy. Therefore, there is beneficial evidence for an active ingredient that has now also proven itself in practical application.

The G-BA identified no additional benefit of the active ingredient tralokinumab in adults 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 ingredient is a comparatively new therapy option whose significance cannot yet be conclusively assessed. Therefore, tralokinumab is not found to be appropriate comparator therapy for the present patient group.

The JAK inhibitors baricitinib and upadacitinib were assessed by the G-BA as part of the early benefit assessment. For the active ingredient upadacitinib, the G-BA identified an indication of a considerable additional benefit in adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy and for whom 30 mg upadacitinib is the appropriate dose. The G-BA did not determine an additional benefit of baricitinib because no suitable data were available for a comparison with the appropriate comparator therapy. These active ingredients are also new treatment options whose significance cannot yet be conclusively assessed. In addition, against the background of the ongoing EMA PRAC procedure, the safety profile of the JAK inhibitors cannot be conclusively assessed at present. Therefore, upadacitinib and baricitinib are not found to be appropriate comparator therapy for the present patient group.

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

For patients for whom continuous systemic therapy is indicated, dupilumab (in combination with TCS and/or TCI if required) is the appropriate comparator therapy.

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

2.1.3 Extent and probability of the additional benefit

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

For the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for a continuous systemic therapy, there is a hint for a considerable additional benefit of abrocitinib compared with the appropriate comparator therapy dupilumab.

Justification:

For the benefit assessment, the pharmaceutical company submits the randomised controlled JADE DARE study, in which abrocitinib is compared with dupilumab.

The JADE DARE study investigated adults with chronic atopic dermatitis that had been present for at least 6 months. Disease severity grade was defined by the following criteria at the start of the study: affected body surface area ≥ 10%; Investigator Global Assessment (IGA) ≥ 3, Eczema Area and Severity Index (EASI) ≥ 16 and itching with a score of ≥ 4 on the Peak Pruritus Numerical Rating Scale (NRS). For the present benefit assessment, the severity definition via the affected body surface area, the IGA and the EASI is considered to be a sufficient representation of moderate-to-severe atopic dermatitis.

For enrolment in the study, patients had to have either an inadequate response to topical medicinal therapies for atopic dermatitis for ≥ 4 consecutive weeks within 6 months prior to screening or the patients' disease required a systemic therapy within 1 year prior to start of the study. How an insufficient response was defined is not clear from the available information.

Patients were randomly assigned to the study arms. The stratification factor here was the severity of the disease (IGA 3, IGA 4). 362 patients were randomised to the abrocitinib arm and 365 patients to the dupilumab arm.

In the intervention arm, patients received 200 mg abrocitinib daily. This corresponds to both the recommended starting dose for patients < 65 years of age and the maximum daily dose. According to the product information, the dose can be reduced in the course of treatment depending on tolerability and efficacy. Furthermore, the lowest effective dose should be considered for maintenance treatment. However, a dose adjustment according to the product information depending on tolerability and efficacy was not allowed in the JADE DARE study.

The background therapy for the entire duration of the study was the use of emollients at least twice a day. TCS inhibitors with moderate efficacy were applied 1 time daily to sites with active lesions, or TCS, TCI or phosphodiesterase (PDE)4 inhibitors with low efficacy were applied to sites with intolerance or thin skin. Such therapies already administered prior to the start of the study could be continued. Background therapy with TCS, TCI or, if necessary, PDE4 inhibitors was de-escalated or re-initiated according to a set schedule. A therapy escalation (rescue therapy) with TCS inhibitors of high efficacy, systemic glucocorticoids or other systemic therapies could occur after week 4 at the principal investigator's discretion if necessary.

The treatment duration was 26 weeks. Patient-relevant endpoints on morbidity, health-related quality of life and side effects were collected in the study.

Extent and probability of the additional benefit

Mortality

For the endpoint of overall mortality, 2 deaths occurred in the abrocitinib arm and none in the dupilumab arm.

Morbidity

Morbidity in the present assessment is represented by disease severity and remission (assessed by EASI and SCORAD), itching (assessed by Peak Pruritus-NRS), pain (assessed by Skin Pain-NRS), sleep disorders (assessed by MOS Sleep Scale), patient-reported symptomatology (assessed by POEM) and health status (assessed by EQ-5D VAS).

Eczema Area and Severity Index (EASI 100 Remission, EASI 75 and EASI 90 Response)

In the German healthcare context, the EASI represents a standard instrument for the classification of severity by doctors and is relevant for the diagnosis and monitoring of disease severity in health care. The EASI is used in conjunction with other instruments to determine the severity of atopic dermatitis. The symptoms erythema, oedema/ papule formation, abrasions as well as lichenification of the skin are assessed by the doctor for each of the body regions head and neck, trunk, arms and legs with a score between 0 (not present) and 3 (very severe). The proportion of the body surface area affected is estimated by the principal investigator as a percentage of the total body surface area. Based on the evaluation of the symptoms and the assessment of the affected body surface area, an overall score is obtained. The EASI score can range from 0 (no evidence of atopic dermatitis) to 72.
The operationalisation of the EASI was based on the number of patients, who achieved a 90% (EASI 90) and 75% (EASI 75) improvement in EASI score from the start of the study to week 26, respectively. Furthermore, there are evaluations of the complete reduction of the external signs of dermatitis, i.e., a 100% reduction of the initial EASI value (EASI 100, remission).
The remission (EASI 100) as well as the response thresholds EASI 75 and EASI 90 are evaluated as patient-relevant. There is a statistically significant difference in remission (EASI 100) to the advantage of abrocitinib. The response thresholds EASI 90 and EASI 75 show no statistically significant differences between the treatment groups.

Scoring Atopic Dermatitis (SCORAD)

The SCORAD is another established tool for assessing the severity of atopic dermatitis. It is made up of three components:

- Assessment of the areal extent of the skin changes by the doctor.
- Assessment of the intensity of skin changes for 6 symptoms (erythema, oedema/ papule formation, oozing/ crusting, skin abrasion, lichenification as well as dryness of non-affected skin) by the doctor
- Patient-reported survey of symptoms of insomnia and itching during the last 3 days or nights, each on a VAS from 0 (no symptoms) to 10 (most severe symptoms)

An overall score is calculated from the three components of the SCORAD. The SCORAD can assume values between 0 and 103. Higher values mean a more severe clinical picture.
The operationalisation of the SCORAD was based on the number of patients, who achieved a 90% (SCORAD 90) and 75% (SCORAD 75) improvement in the SCORAD score from the start of the study to week 26, and a 100% reduction in baseline SCORAD score (SCORAD 100, remission). The total score includes the symptoms of insomnia and itching.
Remission (SCORAD 100) and response thresholds SCORAD 75 and SCORAD 90 are evaluated as patient-relevant. There is a statistically significant difference in remission (SCORAD 100) and SCORAD 90 response to the advantage of abrocitinib. The response threshold value SCORAD 75 shows no statistically significant difference between the treatment groups.

Itching (Peak Pruritus NRS)

Itching was assessed using the Peak Pruritus NRS scale. The Peak Pruritus NRS is a self-assessment tool to determine the maximum itching within the last 24 hours. The assessment is done using a numerical scale from 0 (no itching) to 10 (worst itching imaginable). In the JADE DARE study, itching was assessed daily via the Peak Pruritus NRS using an electronic patient diary.
On the one hand, the operationalisation peak pruritus NRS 0-1 (none or very low symptom burden) at week 26 and the improvement by ≥ 4 points up to week 26 are considered. There is no statistically significant difference between abrocitinib and dupilumab, neither for the

evaluation of the improvement by ≥ 4 points nor for the evaluation of the peak pruritus NRS 0-1.

Sleep disorders (MOS sleep scale)

The MOS Sleep Scale is a tool with a total of 12 items to assess sleep quality. In the JADE DARE study, the version that surveys sleep quality within the past 4 weeks was used. Evaluations of the Sleep Problem Index (SPI) I and II are available. The items and the scales each cover a range of values from 0 to 100, where a higher value means greater sleep disorders. Responder analyses for improvement by > 15 points are used for SPI I and II. There are no statistically significant differences between the treatment groups.

Pain (Skin Pain NRS)

Skin pain was assessed using the Skin Pain NRS scale. The Skin Pain NRS is a self-assessment tool to determine the maximum pain within the last 24 hours. The assessment is done using a numerical scale from 0 (no pain) to 10 (worst pain imaginable).
For the Skin Pain NRS, the operationalisation improvement of ≥ 4 points by week 26 is considered. There are no statistically significant differences between the treatment groups.

Patient-reported symptomatology (POEM)

The POEM is a tool for recording the symptomatology of patients with atopic dermatitis. The questionnaire records the frequency of occurrence of 7 different symptoms (itching, sleep disorders, bleeding skin, oozing skin, cracked skin, scaly skin, dry/rough skin) within the previous week. The frequency is recorded and the total score is formed (values between 0 and 28). Higher values mean more frequent symptomatology. The operationalisations POEM 0 and POEM 0-2 at week 26 are used for the present benefit assessment. This means that there is no symptom burden (POEM 0) or none to very low symptom burden (POEM 0-2). There is a statistically significant difference to the advantage of abrocitinib over dupilumab in both POEM 0 and POEM 0-2.
For the endpoint of patient-reported symptomatology (POEM 0), there is an effect modification due to the age characteristic. For patients ≥ 40 years of age, there is a statistically significant difference to the advantage of abrocitinib over dupilumab, while for patients < 40 years of age there is no statistically significant difference.
The effect modifications for the characteristic age are not shown for any other endpoints, which is why the significance of the subgroup analysis is assessed as too low overall to carry out a separate assessment of the additional benefit according to the age characteristic.

Health status (VAS of EQ-5D)

Health status was assessed using the visual analogue scale (VAS) of the EQ-5D questionnaire. On this, the subject rates their health status on a scale from 0 (worst conceivable health status) to 100 (best conceivable health status). For the endpoint of health status (EQ-5D-VAS), there is no statistically significant difference between the treatment groups for the mean change at week 26 compared to the start of the study.

<u>Quality of life</u>

Dermatology Life Quality Index (DLQI)-Response

The DLQI is a validated questionnaire for the assessment of disease-specific health-related quality of life in adult patients with dermatological diseases. 10 items for 6 domains are recorded: Symptoms and well-being, daily activities, leisure time, work and school, personal

relationships and treatment; the questionnaire is completed by the patient. Each item has 4 response categories ranging from 0 (not at all) to 3 (very strongly). A total score is then formed (values from 0 to 30). The lower the score, the better is the health-related quality of life.
For the percentage of patients with a DLQI of 0 or 1, there is no statistically significant difference between the treatment groups at week 26.

Side effects

Overall rate of serious adverse events (SAEs), discontinuations due to AEs, infections, serious infections and eye diseases (SOC, AEs)

In the present benefit assessment, the endpoint of infections is used via the AEs occurring in the SOC infections and infestations and the endpoint of serious infections via the SAEs occurring in the aforementioned SOC.
For the endpoints of SAEs, discontinuation due to AEs, infections, serious infections and eye diseases (SOC, AEs), there was no statistically significant difference between the treatment groups.

Conjunctivitis (PT, AEs)

For the endpoint of conjunctivitis (PT, AEs), there is a statistically significant difference to the advantage of abrocitinib compared to dupilumab.

Nervous system disorders (SOC, AEs), nausea (PT, AEs) and acne (PT, AEs)

For the endpoints of nervous system disorders (SOC, AEs), nausea (PT, AEs) and acne (PT, AEs), there was a statistically significant difference to the disadvantage of abrocitinib versus dupilumab.

Overall assessment

The benefit assessment is based on the randomised controlled JADE DARE study, which compares abrocitinib with dupilumab at a dose of 200 mg. The study population includes adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy.
In the endpoint category of morbidity, there was a statistically significant difference to the advantage of abrocitinib compared to dupilumab in the endpoints of remission (EASI 100, SCORAD 100), SCORAD improvement by 90% (SCORAD 90), and patient-reported symptomatology (POEM 0; POEM 0-2). For the patient-reported symptomatology (POEM 0), there is an effect modification by the age characteristic.
In the other morbidity endpoints of itching, skin pain and health status, there is no statistically significant or relevant difference between the two treatment groups.
In the endpoint category of health-related quality of life, there is no statistically significant difference between the treatment groups in the endpoint DLQI 0-1.
In the endpoint category of side effects, there was no statistically significant difference between the treatment groups for the endpoints SAEs, discontinuation due to AEs, infections, serious infections and eye disorders (SOC, AEs). In detail, the specific AEs show both advantages (conjunctivitis) and disadvantages (nervous system disorders, nausea and acne) of abrocitinib compared to dupilumab.
In the overall assessment, the positive effects of abrocitinib on disease severity (EASI 100, SCORAD 100, SCORAD 90) and patient-reported symptomatology (POEM 0, POEM 0-2) compared with dupilumab are considered to be a significant improvement in the therapy-

relevant benefit that had not yet been achieved. In the context of specific side effects, there were both positive and negative effects of abrocitinib compared to dupilumab.
Thus, in adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy, a considerable additional benefit of abrocitinib over dupilumab can be derived overall.

Reliability of data (probability of additional benefit)

The assessment of the additional benefit is based on the randomised, double-blind JADE DARE study, in which abrocitinib was compared with dupilumab over 26 weeks.
In the JADE DARE study, dose adjustment of abrocitinib depending on tolerability and efficacy was not allowed according to the product information. Even though extensive dose adjustments may not yet be necessary for a treatment duration of 26 weeks as in the JADE DARE study, the lack of the possibility to adjust the dose, as provided for in the product information, leads to uncertainty. A further limitation is that, according to the product information, 100 mg should be used as the starting dose in patients aged 65 and above.
In the overall assessment, a hint is derived for the reliability of data of the JADE DARE study results.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Cibinqo with the active ingredient abrocitinib.
The active ingredient abrocitinib is used in adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy.
The G-BA determined dupilumab (in combination with TCS and/or TCI if required) as the appropriate comparator therapy. The benefit assessment is based on the randomised controlled JADE DARE study, which compares abrocitinib with dupilumab at a dose of 200 mg.
There are statistically significant advantages of abrocitinib over dupilumab in the endpoint category of morbidity. In the endpoint categories of health-related quality of life and side effects, there are no relevant differences between the treatment groups for the benefit assessment.
The positive effects of abrocitinib are assessed as a previously unachieved significant improvement in therapy-relevant benefit.
In the overall assessment, a hint for a considerable additional benefit of abrocitinib over dupilumab is identified in adults with moderate-to-severe atopic dermatitis who are candidates for a continuous systemic therapy.

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 from the resolutions of the G-BA on dupilumab in the therapeutic indication of moderate-to-severe atopic dermatitis in adults[2] who are candidates for a systemic therapy.

[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 17 May 2018

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: 24 June 2022):

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 specialists experienced in treating atopic dermatitis.

In patients in whom no therapeutic benefit can be demonstrated after 24 weeks of treatment, discontinuation of treatment should be considered.

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. The training material includes instructions on how to manage the potential side effects associated with abrocitinib, particularly severe and opportunistic infections including tuberculosis and herpes zoster. It also points out the need for an effective contraceptive method.

Furthermore, against the background of the ongoing EMA PRAC procedure, the safety profile of the JAK inhibitors such as abrocitinib cannot be conclusively assessed at present.

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 June 2022).

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 is patient-individual 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 the maximum treatment duration, if specified in the product information.

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 approved as such or in combination with other medicinal products for topical application for the treatment of moderate-to-severe atopic dermatitis in adults. The active ingredient of the appropriate comparator therapy, dupilumab can be used both as part of a monotherapy and 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 therefore not listed separately.

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	1	365
Appropriate comparator therapy				
dupilumab	continuously, 1 x every 14 days	26.1	1	26.1

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Abrocitinib	100 mg - 200 mg	100 mg - 200 mg	1 x 100 mg - 1 x 200 mg	365 365	365 x 100 mg - 365 x 200 mg
Appropriate comparator therapy					
dupilumab	300 mg	300 mg	1 x 300 mg	26.1	26.1 x 300 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Abrocitinib 100 mg	91 FCT	€ 4,299.60	€ 1.77	€ 242.26	€ 4,055.57
Abrocitinib 200 mg	91 FCT	€ 5,360.11	€ 1.77	€ 302.83	€ 5,055.51
Appropriate comparator therapy					
Dupilumab 300 mg	6 SFI	€ 4,337.25	€ 1.77	€ 244.41	€ 4,091.07
Abbreviations: FCT = film-coated tablets, SFI = solution for injection					

LAUER-TAXE® last revised: 15 June 2022

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".

In addition, patients receiving therapy with abrocitinib should be tested for the presence of HBV infection before initiating the respective treatment. For the diagnosis of suspected chronic hepatitis B, sensibly coordinated steps are required. 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. If HBs antigen is positive, an active HBV infection is detected.

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/ patient/ year
Medicinal product to be assessed				
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	€ 16.45	€ 16.45
	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50
	Anti-HBs antibody (GOP 32617)[3]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV-DNA (GOP 32823)[4]	1	€ 89.50	€ 89.50

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 28 July 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

The appropriate comparator therapy determined by the G-BA was reviewed. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at its session on 22 June 2021.

On 14 January 2022, 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 1, sentence 2 VerfO.

By letter dated 17 January 2022 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

[3] Only if HBs antigen negative and anti-HBc antibody positive.

[4] Invoicing for GOP 32823 possible before or during antiviral therapy with interferon and/or nucleic acid analogues.

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 13 April 2022, and the written statement procedure was initiated with publication on the website of the G-BA on 19 April 2022. The deadline for submitting written statements was 10 May 2022.

The oral hearing was held on 23 May 2022.

By letter dated 24 May 2022, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 10 June 2022.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 28 June 2022, and the proposed resolution was approved.

At its session on 7 July 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	28 July 2020	Determination of the appropriate comparator therapy
Subcommittee Medicinal products	22 June 2021	New determination of the appropriate comparator therapy
Working group Section 35a	17 May 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	23 May 2022	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	31.05.2022; 14.06.2022; 21.06.2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal products	28 June 2022	Concluding discussion of the draft resolution
Plenum	7 July 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 7 July 2022

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

Prof. Hecken