Justification

Gemeinsamer Bundesausschuss

to the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Ibalizumab (Multidrug Resistant HIV-1 Infection)

of 18 February 2021

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 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 forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the first placing on the market of the active ingredient ibalizumab in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 1 September 2020. 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 31 August 2020.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 December 2020 on the website of the G-BA (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 ibalizumab 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 written statements submitted in the written and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has assessed the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative) according to 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 ibalizumab.

In light of the above and taking into account the written statements received and the oral hearing, the G-BA has arrived at 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 ibalizumab (Trogarzo) in accordance with the product information

Trogarzo, in combination with other antiretroviral(s), is indicated for the treatment of adults infected with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive antiviral regimen.

Therapeutic indication of the resolution (resolution of 18 February 2021):

See approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults infected with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive antiviral regimen

Appropriate comparator therapy for ibalizumab in combination with other antiretroviral active ingredients:

> A patient-individual antiretroviral therapy using a selection of approved active ingredients; taking into account the previous therapy(ies) and the reason for the change of therapy, in particular therapy failure because of virological failure and possible associated development of resistance or because of side effects.

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 according to 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 5.0 dated 10 July 2017. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care), Cologne.

3. As comparator therapy, medicinal applications or non-medicinal treatments for which the patient-relevant benefit has already been determined by the Federal Joint Committee 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. Active ingredients approved in principle for the treatment of adults infected with human immunodeficiency virus 1 (HIV-1):

Protease inhibitors (PI): atazanavir, darunavir, fosamprenavir, indinavir[2], ritonavir, saquinavir, tipranavir, lopinavir

Nucleosidal and nucleotidal reverse transcriptase inhibitors (NRTI): abacavir, didanosine, emtricitabine, lamivudine, stavudine[2], tenofovir alafenamide, tenofovir disoproxil, zidovudine

Non-nucleosidal reverse transcriptase inhibitors (NNRTI): efavirenz, etravirine, nevirapine, rilpivirine, doravirine

Integrase inhibitors (INI): dolutegravir, elvitegravir, raltegravir, bictegravir

Other antiviral agents: enfuvirtide (entry inhibitor), maraviroc, (entry inhibitor)

Other therapeutic agents: cobicistat (pharmacokinetic amplifier)

On 2. Non-medicinal treatment is not considered.

On 3. There are no resolutions in this therapeutic indication.

Resolutions on procedure according to Section 35a SGB V in the therapeutic indication HIV infection:

- Dolutegravir/lamivudine of 6 February 2020
- Doravirine/lamivudine/tenofovir disoproxil of 4 July 2019
- Doravirine of 4 July 2019
- Bictegravir/emtricitabine/tenofovir alafenamide of 20 December 2018
- Dolutegravir/rilpivirine of 6 December 2018
- Darunavir/cobicistat/emtricitabine/tenofovir alafenamide of 16 March 2018, 3 May 2018, and 5 July 2018
- Emtricitabine/rilpivirine/tenofovir alafenamide of 5 January 2017
- Emtricitabine/tenofovir alafenamide of 3 November 2016
- Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide of 16 June 2016 and 5 July 2018
- Dolutegravir/abacavir/lamivudine of 19 March 2015
- Cobicistat of 18 September 2014 and 1 October 2020
- Dolutegravir of 7 August 2014 and 21 September 2017
- Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil of 5 December 2013 and 3 May 2018
- Emtricitabine/rilpivirine/tenofovir disoproxil of 5 July 2012 and 19 June 2014
- Rilpivirine of 5 July 2012 and 16 June 2016

[2] It is currently not on the market in Germany

On 4. The generally accepted state of medical knowledge for the present indication was established by means of a search for guidelines and systematic reviews of clinical studies.

For the treatment of infections with the human immunodeficiency virus type 1 (HIV-1) in adults, the active ingredients mentioned under 1. are available according to the respective approved therapeutic indication with the exception of the active ingredients currently not available on the German market: indinavir, didanosine, and stavudine. For the treatment of adult patients with multidrug resistant HIV-1 infection, there are neither explicitly approved active ingredients nor resolutions on an early benefit assessment.

In determining the appropriate comparator therapy for pre-treated adult patients with multidrug resistant HIV-1 infection, the aggregated evidence showed that after therapy failure of the previous therapies, depending on the active ingredients or active ingredient classes used and the reason for the therapy failure, a patient-individual pharmacotherapy coordinated with the patient is recommended. In patients for whom suppressive antiretroviral therapy (ART) can no longer be composed of two to three fully active substances, a combination of several substances with residual activity is often used in health care practice. It may also be necessary or useful to adjust the dose of active ingredients already in use. However, according to guidelines, no single remaining active ingredient should be added to a failing ART because this can lead to the development of resistance in all active ingredients used in the treatment regimen. Even if it is not possible to put together a completely suppressive ART, the goal of patient-individual antiretroviral therapy should be to maintain CD4 cell counts and prevent clinical progression.

The naming of a defined active ingredient combination in the sense of a therapy standard after therapy failure cannot be deduced based on the evidence available and because of the patient-individual selection of the therapy scheme depending on the previous therapy. In principle, all possible active ingredient combinations available can therefore be regarded as appropriate.

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

2.1.3 Extent and probability of the additional benefit

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

For adults with multidrug-resistant HIV-1 infection for whom no other suppressive antiviral regimen can be composed, the additional benefit is not proven.

Justification:

There are no direct comparative data for the use of ibalizumab in a manner compliant with the marketing authorisation compared with the appropriate comparator therapy. In addition, the indirect historical comparison presented by the pharmaceutical company is not suitable for deriving the additional benefit. Overall, no suitable data is available for the benefit assessment.

For the historical comparison, the pharmaceutical company uses individual arms of different studies and presents evaluations on the morbidity endpoint virological response at Week 48 and side effects. For ibalizumab, results from two non-comparative studies, TMB-301 and TMB-311, were pooled. For the appropriate comparator therapy, data from the placebo arm of the TNX-355.03 randomised controlled trial were used.

The TMB-301 study is a single-arm Phase III study of ibalizumab in combination with patient-individual optimised basic therapy for 25 weeks. Included were 40 patients with a multidrug

resistant HIV infection defined as a viral load > 1000 copies/ml and resistance to at least one medication from each of three active ingredient classes (three-class resistance). In addition, there should have been complete viral sensitivity to at least one antiretroviral active ingredient other than ibalizumab.

TMB-311 is a two-armed parallel group study of ibalizumab conducted over 110 weeks in patients with multidrug resistant HIV as defined in the TMB-301 study. For the indirect comparison, the pharmaceutical company submits data from patients who have already received ibalizumab in study TMB-301 (part of Cohort 1) or have not previously been treated with ibalizumab (Cohort 2) at study inclusion.

In both studies, patients received ibalizumab according to the instructions in the product information together with patient-individual optimised basic therapy (OBT). The fact that non-approved medicinal products were also used in the OBT is viewed critically. A high proportion of patients received a medicinal product that is still in clinical trials (e.g. fostemsavir). It is therefore not comprehensible whether study results can be attributed to the effect of ibalizumab or to the active ingredients not yet approved.

The double-blind, randomised controlled TNX-355.03 study compared ibalizumab and placebo, both of which were used in addition to patient-individual OBT. Patients with therapy failure on stable active ART were included in this study. In addition, there had to be complete viral sensitivity to at least one antiretroviral active ingredient other than ibalizumab. The blinded treatment duration was 16 to 48 weeks or until therapy failure. In the case of proven therapy failure, patients from all study arms were able switch to unblinded treatment with a new OBT and ibalizumab.

Because in both study arms ibalizumab was not used in a manner compliant with marketing authorisation, this direct comparative study is not suitable for the benefit assessment of ibalizumab compared with the appropriate comparator therapy. The pharmaceutical company uses the placebo arm for the indirect comparison.

However, the results of the study cannot be meaningfully interpreted and are therefore not suitable as a basis for an indirect comparison because more than two-thirds of the sub-population relevant for the indirect comparison switched from the placebo arm to treatment with ibalizumab.

However, above all, many of the active ingredients and active ingredient classes currently used in care were not yet available at the time the study was conducted. A comparison of ibalizumab with patient-individual therapy as it is used in everyday practice today is therefore not possible.

As the TMB-301 and -311 studies were conducted at a much later time period, it is also unclear whether the patient populations in the intervention and comparator arm are sufficiently comparable for the indirect comparison because differences (e.g. in disease duration and previous therapies) can be assumed.

It also remains unclear whether the patients included for the indirect comparison represent the present indication. For the comparison presented, the pharmaceutical company selects patients from different study arms who show viral sensitivity to a maximum of two antiretroviral active ingredients in addition to ibalizumab. Using the data available, it is not possible to assess whether it was indeed not possible to establish a suppressive antiviral regimen for the patients with the help of these active ingredients as intended by the therapeutic indication.

In the overall view, the indirect historical comparison presented is not considered suitable for the assessment of the additional benefit of ibalizumab compared with the appropriate comparator therapy. The main reason for the decision is that the appropriate comparator therapy was not implemented in the comparator arm and that active ingredients not yet approved in the context of OBT, which could distort the study results, were used in the intervention arm. Furthermore, it is unclear whether the study population reflects the indication.

There are thus no data relevant for the benefit assessment of ibalizumab. An additional benefit is therefore not proven.

2.1.4 Summary of the assessment

The present assessment refers to the benefit assessment of the new medicinal product "Trogarzo" with the active ingredient "ibalizumab". Ibalizumab, in combination with other antiretroviral(s), is indicated for the treatment of adults infected with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive antiviral regimen.

The G-BA determined an appropriate comparator therapy to be a patient-individual antiretroviral therapy using a selection of approved active ingredients taking into account the previous therapy(ies) and the reason for the change of therapy, in particular therapy failure because of virological failure and possible associated development of resistance or because of side effects.

There are no direct comparative studies of ibalizumab in a dosage compliant with the marketing authorisation versus the appropriate comparator therapy. The pharmaceutical company therefore presents a historical comparison from individual arms of different studies. For ibalizumab, results from two non-comparative studies, TMB-301 and TMB-311, were pooled. For the appropriate comparator therapy, data from the placebo arm of the TNX-355.03 randomised controlled trial were used.

Especially because the appropriate comparator therapy was not implemented in the comparator arm and active ingredients not yet approved were also used in the intervention arm as part of the optimised basic therapy, the indirect historical comparison presented is not taken into consideration. Moreover, it cannot be assessed from the data presented whether it was actually not possible to compile a suppressive antiviral regimen for the patients included as envisaged by the therapeutic indication. It therefore remains unclear whether the study population reflects the indication.

In the overall view, the additional benefit of ibalizumab compared with the appropriate comparator therapy is not proven.

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

The G-BA bases its resolution on the patient numbers stated by the pharmaceutical company in the dossier. The pharmaceutical company assumes that 75,721 patients with a diagnosed HIV infection will receive antiretroviral therapy in 2020. For the calculations, it uses the data of the Robert Koch Institute (RKI) for the end of 2018[3].

From the EuroSIDA study[4], the pharmaceutical company takes a proportional value of 6.5% for patients with three-class resistance (patients for whom activity is predicted only for 2 of 5 antiretroviral substance classes). This results in 4922 patients with a multidrug resistant HIV infection. These patient numbers will be further narrowed down to patients with three-class virological failure who require new treatment options. For this purpose, the pharmaceutical company refers to data[5] from patients with perinatally or heterosexually acquired HIV infection who start ART and cumulatively develop virological failure to active ingredients from at least three substance classes over a period of 5 years (approx. 4.5% and 10%, respectively). It

[3] Robert Koch Institute. Epidemiological Bulletin No. 46. 2019. URL: https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2019/Ausgaben/46_19.pdf?__blob=publicationFile.

[4] EuroSida-Centre of Excellence for Health, Immunity and Infections. Prevalence and characteristics of HIV-1 positive heavily treatment experienced (HTE) individuals in the EuroSIDA cohort. 2019.

[5] Judd A, et al. Higher rates of triple-class virological failure in perinatally HIV-infected teenagers compared with heterosexually infected young adults in Europe. HIV Med 2017; 18(3): 171–180.

transfers this proportion to the patients with multidrug resistant HIV infection (221 to 492 patients). Furthermore, based on Italian registry data[6], the pharmaceutical company estimates that viral suppression cannot be achieved in 26% with a viral load of < 50 RNA copies/ml.

Taking into consideration an expected SHI proportion among those affected of 88.1%[7], the pharmaceutical company determines 51 to 113 patients in the SHI target population.

Overall, the number of patients in the SHI target population estimated by the pharmaceutical company is subject to uncertainties. This is justified in particular by transferring the proportion of patients with virological three-class failure who need new treatment options to patients who already have three-class failure; however, this tends to lead to an underestimation. Further uncertainties arise from, among other things, the transfer of the Italian registry data to the German healthcare context and the methodological weaknesses in the derivation of the data on patients with already diagnosed HIV infection.

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 Trogarzo (active ingredient: ibalizumab) at the following publicly accessible link (last access: 10 December 2020):

https://www.ema.europa.eu/en/documents/product-information/trogarzo-epar-product-information_de.pdf

Treatment with ibalizumab should only be initiated and monitored by specialists who are experienced in the treatment of patients with HIV infections.

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: 1 February 2021).

For the cost representation, only the dosages of the general case are considered. If the treatment duration is unlimited, initial induction regimens are to be disregarded in the representation of costs. Patient-individual dose adjustments (e.g. because of side effects or co-morbidities) are not taken into account when calculating the annual treatment costs.

For the appropriate comparator therapy and the basic therapy for ibalizumab, the range of treatment costs incurred depending on the individual therapy choice is shown. Because of the different combination options in individual therapy, not all possible combination therapies are presented; however, one low-cost therapy (nevirapine + lamivudine/tenofovir disoproxil) and one high-cost therapy (enfuvirtide + abacavir + emtricitabine) are presented as an example.

In accordance with the German guideline[8], different alternatives (“backbone” and combination partners) are recommended; these were taken into account for the cost presentation. Although enfuvirtide is not specifically mentioned in this guideline, it is a possible treatment option in the present therapeutic indication and is therefore taken into consideration for the treatment cost calculation.

[6] Prestigio Register. Study report of the PRESTIGIO Registry: demographic, clinical, laboratory and virological. 2019.
[7] SHI central association – source: official statistics health insurance management 1 on 1 December 2018, Statistisches Bundesamt [German Federal Office for statistics] (Last revised September 2019)
[8] German-Austrian guidelines on antiretroviral therapy of HIV-1 infection, AWMF 055-001, Version 8 of 10 April 2019 and Version 9 of 1 September 2020.

Treatment duration:

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 different for each individual patient and/or is shorter on average. The time unit “days” is used to calculate the “number of treatments/patient/year”, the time between individual treatments, and the maximum treatment duration if specified in the product information.

Designation of the therapy	Treatment mode	Number of treatments/patient/year	Treatment duration/treatment (days)	Treatment days/patient/ year
Medicinal product to be assessed				
Ibalizumab	Continuously, every 14 days	26.1	1	26.1
Nevirapine + lamivudine/tenofovir disoproxil				
Nevirapine	continuously, 2 × daily	365	1	365
Lamivudine + tenofovir disoproxil	continuously, 1 × daily	365	1	365
Enfuvirtide + abacavir + emtricitabine				
Enfuvirtide	continuously, 2 × daily	365	1	365
Abacavir	continuously, 2 × daily	365	1	365
Emtricitabine	continuously, 1 × daily	365	1	365
Appropriate comparator therapy				
Nevirapine + lamivudine/tenofovir disoproxil				
Nevirapine	continuously, 2 × daily	365	1	365
Lamivudine/tenofovir disoproxil	continuously, 1 × daily	365	1	365
Enfuvirtide + abacavir + emtricitabine				
Enfuvirtide	continuously, 2 × daily	365	1	365
Abacavir	continuously, 2 × daily	365	1	365
Emtricitabine	continuously, 1 × daily	365	1	365

Usage and 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					
Ibalizumab	800 mg	800 mg	4 × 200 mg	26.1	104.4 × 200 mg
Nevirapine + lamivudine/tenofovir disoproxil					
Nevirapine	200 mg	400 mg	2 × 200 mg	365	730 × 200 mg
Lamivudine/tenofovir disoproxil	245 mg/300 mg	245 mg/300 mg	1 × 245 mg/300 mg	365	365 × 245 mg/300 mg
Enfuvirtide + abacavir + emtricitabine					
Enfuvirtide	90 mg	180 mg	2 × 90 mg	365	730 × 90 mg
Abacavir	300 mg	600 mg	2 × 300 mg	365	730 × 300 mg
Emtricitabine	200 mg	200 mg	1 × 200 mg	365	365 × 200 mg
Appropriate comparator therapy					
Nevirapine + lamivudine/tenofovir disoproxil					
Nevirapine	200 mg	400 mg	2 × 200 mg	365	730 × 200 mg
Lamivudine/tenofovir disoproxil	245 mg/300 mg	245 mg/300 mg	1 × 245 mg/300 mg	365	365 × 245 mg/300 mg
Enfuvirtide + abacavir + emtricitabine					
Enfuvirtide	90 mg	180 mg	2 × 90 mg	365	730 × 90 mg
Abacavir	300 mg	600 mg	2 × 300 mg	365	730 × 300 mg
Emtricitabine	200 mg	200 mg	1 × 200 mg	365	365 × 200 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 Sections 130 and 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined based on consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated based on the costs per pack after deduction of the statutory rebates.

Costs of the medicinal product:

Designation of the therapy	Package 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					
Ibalizumab 200 mg	2 CIS of 1.33 ml	€ 2,508.78	€ 1.77	€ 140.00	€ 2,367.01
Nevirapine + lamivudine/tenofovir disoproxil					
Nevirapine 200 mg	120 TAB	€ 266.99	€ 1.77	€ 12.74	€ 252.48
Lamivudine/tenofovir disoproxil 245 mg/300 mg	30 FCT	€ 47.05	€ 1.77	€ 1.71	€ 43.57
Enfuvirtide + abacavir + emtricitabine					
Enfuvirtide 90 mg	60 PSI	€ 2,349.76	€ 1.77	€ 198.36	€ 2,149.63
Abacavir 300 mg	180 FCT	€ 1,107.09	€ 1.77	€ 52.01	€ 1,053.31
Emtricitabine 200 mg	30 HC	€ 302.47	€ 1.77	€ 16.14	€ 284.56
Appropriate comparator therapy					
Nevirapine + lamivudine/tenofovir disoproxil					
Nevirapine 200 mg	120 TAB	€ 266.99	€ 1.77	€ 12.74	€ 252.48
Lamivudine/tenofovir disoproxil 245 mg/300 mg	30 FCT	€ 47.05	€ 1.77	€ 1.71	€ 43.57
Enfuvirtide + abacavir + emtricitabine					
Enfuvirtide 90 mg	60 PSI	€ 2,349.76	€ 1.77	€ 198.36	€ 2,149.63
Abacavir 300 mg	180 FCT	€ 1,107.09	€ 1.77	€ 52.01	€ 1,053.31
Emtricitabine 200 mg	30 HC	€ 302.47	€ 1.77	€ 16.14	€ 284.56
Abbreviations: HC = hard capsules, CIS = concentrate for the preparation of an infusion solution, FCT = film-coated tablets, PSI = powder and solvent for solution for injection; TAB = tablets					

Pharmaceutical selling price (LAUER-TAXE®) as last revised: 1 February 2021

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 assessed 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 standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary medical treatment or the prescription of other services when using the medicinal product to be assessed and the appropriate comparator therapy according to the product information, no costs for additionally required SHI services had to be taken into account.

Other services covered by SHI funds:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe; contract on price formation for substances and preparations of substances) is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131, paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the special agreement on contractual unit costs of retail pharmacist services (*Hilfstaxe*) (status: 11th Supplementary Agreement of 1 March 2020 to the contract on price formation for substances and preparations of substances), surcharges for the production of parenteral preparations containing cytostatic agents of a maximum of € 81 per ready-to-use preparation and for the production of parenteral solutions containing monoclonal antibodies of a maximum of € 71 per ready-to-use unit are to be payable. These additional costs are not added to the pharmacy sales price but rather follow the rules for calculating the *Hilfstaxe*. The cost representation is based on the pharmacy sales price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy sales price of the active ingredient, the invoicing of discards, the calculation of application containers and carrier solutions according to the regulations in Annex 3 of the *Hilfstaxe*.

3. Bureaucratic costs

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 6 August 2019, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 31 August 2020, the pharmaceutical company submitted a dossier for the benefit assessment of ibalizumab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 1 September 2020 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 ibalizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 26 November 2020, and the written statement procedure was initiated with publication on the website of the G-BA on 1 December 2020. The deadline for submitting written statements was 22 December 2020.

The oral hearing was held on 11 January 2021.

On 25 January 2021, the IQWiG submitted a new version of the IQWiG dossier assessment to the G-BA. Version 1.1 of 25 January 2021 replaces version 1.0 of the dossier assessment of 26 November 2020. The evaluation result was not affected by the changes in version 1.1 compared with version 1.0.

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 were discussed at the session of the subcommittee on 9 February 2021, and the proposed resolution was approved.

At its session on 18 February 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	6 August 2019	Determination of the appropriate comparator therapy
Working group Section 35a	6 January 2021	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	11 January 2021	Conduct of the oral hearing
Working group Section 35a	19 January 2021; 2 February 2021	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee on Medicinal Products	9 February 2021	Concluding discussion of the draft resolution
Plenum	18 February 2021	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 18 February 2021

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken