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
Fostemsavir (multidrug resistant HIV-1 infection)

of 16 September 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 studies 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 benefits,
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. Costs of therapy for the statutory health insurance,
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 (German) market of the combination of active ingredient fostemsavir 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 April 2021. 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 24 March 2021.

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 1 July 2021, thus initiating the written statement procedure. In addition, an oral hearing was also held.

The G-BA came to a resolution on whether an additional benefit of fostemsavir compared to 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 addenda to the benefit assessment prepared by the 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 fostemsavir.

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 fostemsavir (Rukobia) in accordance with the product information

Rukobia, in combination with other antiretrovirals, is indicated for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen.

Therapeutic indication of the resolution (resolution from 16.09.2021):

"see the approved therapeutic indication"

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regime

Appropriate comparator therapy for fostemsavir 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 the 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 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.

[1] General Methods, version 6.0 of 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

2. If a non-medicinal treatment is considered 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 Federal Joint Committee has already determined the patient-relevant benefit shall be preferred.
4. Comparative therapy should be part of the appropriate therapy in the therapeutic indication according to the generally accepted state of medical knowledge.

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

Nucleoside and nucleotide reverse transcriptase inhibitors (NRTI): Abacavir, didanosine, emtricitabine, lamivudine, stavudine, [2]tenofovir alafenamide, tenofovir disoproxil, zidovudine

Non-nucleoside reverse transcriptase inhibitors (NNRTI): Efavirenz, etravirine, nevirapine, rilpivirine, doravirine

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

Other anti-virals: Enfuvirtide (fusion inhibitor), maraviroc (fusion inhibitor), ibalizumab (post-attachment inhibitor)

Other therapeutic agents: Cobicistat (pharmacokinetic amplifier)

on 2. A non-medicinal treatment cannot be considered as an appropriate comparator therapy in this therapeutic indication.

on 3. In the present therapeutic indication, there is the following resolution:

Ibalizumab from 18 February 2021

on 4. The generally accepted state of medical knowledge for the 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 listed under 1. are available in accordance with the respective approved therapeutic indication, with the exception of the active ingredients currently not available on the German market: indinavir, didanosine and stavudine. The active ingredient ibalizumab is explicitly approved for the treatment of adult patients with multidrug-resistant HIV-1 infection. In the benefit assessment according to Section 35a SGB V, it was determined that the additional benefit of ibalizumab compared to the appropriate comparator therapy is not proven.

In determining the appropriate comparator therapy for pretreated adult patients with multidrug-resistant HIV-1 infection, the aggregated evidence showed that after treatment failure of the previous therapies, depending on the active ingredients or product classes used and the reason for the treatment failure, a patient-individual

[2] Currently not placed on the German market

pharmacotherapy coordinated with the affected person is recommended. In subjects for whom no suppressive antiretroviral therapy (ART) can be composed of two to three fully active substances anymore, a combination of several substances with residual activity is frequently 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, as this may lead to the development of resistance among all active ingredients used in the therapeutic regimen. Although it is not possible to compose a fully 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 combination of active ingredients 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 combinations of approved and available active ingredients can therefore be regarded as appropriate.

With ibalizumab, an explicitly approved treatment option for the present therapeutic indication, has recently become available, the therapeutic significance of which cannot yet be conclusively assessed. However, ibalizumab may be an option in the context of patient-individual 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 fostemsavir is assessed as follows:

The additional benefit is not proven for adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regime adjunctive therapy.

Justification:

For adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regime adjunctive therapy, there are no directly comparative data of fostemsavir versus patient-individual antiretroviral therapy as an appropriate comparator therapy.

The BRIGHTE study submitted by the pharmaceutical company and the additionally submitted matching adjusted indirect comparisons (MAIC) are not suitable for assessing the additional benefit of fostemsavir, as explained below.

BRIGHTE study

The BRIGHTE study is an ongoing, multicentre phase III study with two cohorts over at least 96 weeks on the efficacy and safety of fostemsavir. The study included adults with multidrug-resistant HIV-1 infection (defined as HIV-1 RNA viral load ≥ 400 copies/mL and proven resistance, intolerance, and/or contraindications to antiretroviral agents in ≥ 3 product classes) who were assigned at the start of the study to either the randomised cohort if one to

two fully active ingredients from a maximum of two product classes were still available for them or to the non-randomised cohort if no more active ingredients were available.

The 272 study participants in the randomised cohort were treated with either fostemsavir or placebo for 8 days while failing antiretroviral therapy (ART) continued. Thereafter, like the patients in the non-randomised cohort, they received fostemsavir along with an optimised basic therapy (OBT) composed at the principal investigator's discretion. Thus, no comparative data for the benefit assessment is available from the non-randomised and randomised cohorts from day 9.

Endpoints collected were viral load and other endpoints on morbidity, health-related quality of life, and side effects.

The BRIGHTE study is not suitable for the present benefit assessment because the comparative study phase of 8 days is clearly too short for the assessment of the additional benefit in the present therapeutic indication, and the continuation of a failing therapy does not correspond to the specific appropriate comparator therapy. In addition, the study did not determine how many partially active ingredients were still available for the patients. Therefore, it is not possible to assess whether a patient-individual suppressive anti-viral regimen could actually not be put together, as intended by the therapeutic indication. Thus, it is unclear whether the study population represents the present therapeutic indication.

Indirect comparisons

The indirect comparisons presented are MAIC analyses comparing the single-arm phase of the BRIGHTE (fostemsavir plus OBT) study with single studies or study arms without a bridge comparator. For this purpose, the pharmaceutical company uses the single-arm studies TMB-301 (ibalizumab plus OBT) and VIKING-3 (OBT including dolutegravir) on the side of the comparative therapy as well as the comparator arm of the studies BENCHMRK-1 and BENCHMRK-2 (pooled data on placebo plus OBT).

For various reasons, the available MAIC analyses are not suitable for deriving conclusions on the additional benefit of fostemsavir compared to the appropriate comparator therapy.

On the one hand, MAIC analyses are generally not an adequate way to adjust for confounders. Even if an adjustment for potentially relevant effect modifiers or prognostic factors was made in the analysis, it cannot be ruled out that relevant adjustment and matching factors remain unconsidered and lead to distortions in the results.

On the other hand, the pharmaceutical company did not sufficiently prepare the methodology of the studies presented on the side of the comparative therapy nor of the patient characteristics. Thus, it is not possible to assess whether the BRIGHTE study and the BENCHMRK-1, BENCHMRK-2, TMB-301 and VIKING-3 studies are sufficiently comparable. Based on the information presented, it is also unclear whether the data included in the MAIC analysis is complete.

Regardless of this, the comparator arms of BENCHMRK-1 or BENCHMRK-2 and the VIKING-3 study do not represent the appropriate comparator therapy. When the studies were conducted (2006 - 2015), some of the active ingredients and product classes currently used in care were not yet available. Therefore, a comparison of fostemsavir versus patient-individual therapy as used in today's practice is not possible. For the VIKING-3 or TMB-301 study, it is also unclear whether dolutegravir (as part of OBT) or ibalizumab (plus OBT) represents the patient-individual therapy for all patients in the sense of the appropriate comparator therapy. In addition, the TMB-301 study is not suitable for comparator therapy for the indirect comparison because fostemsavir was used as part of OBT in nearly half of the study population.

Conclusion

Overall, the BRIGHTE study presented and the MAIC analyses additionally presented by the pharmaceutical company are not considered suitable for assessing the additional benefit of fostemsavir compared to the appropriate comparator therapy. The main reason for the decision is that the duration of the comparative study phase in the BRIGHTE study is clearly too short, and no comparison was made with the appropriate comparator therapy. The studies of the MAIC analyses presented on the side of the comparator therapy also do not correspond to the appropriate comparator therapy, so that no statements on the additional benefit can be derived based on the indirect comparisons presented. In addition, due to the insufficient workup of the MAIC analyses, it remains unclear whether the data included in the indirect comparisons are complete and whether the included studies are comparable with each other.

Therefore, no data relevant for the benefit assessment of fostemsavir are available, so an additional benefit is not proven.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "Rukobia" with the active ingredient fostemsavir. Fostemsavir, in combination with other antiretrovirals, is indicated for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral 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 the possible associated development of resistance or because of side effects.

The pharmaceutical company submits the BRIGHTE study and supplementary matching adjusted indirect comparisons (MAIC). However, these are not suitable for assessing the additional benefit of fostemsavir compared with the appropriate comparator therapy. The main reason for this is that the duration of the comparative study phase in the BRIGHTE study is clearly too short, and no comparison was made with the appropriate comparator therapy. The studies of the MAIC analyses presented on the side of the comparator therapy also do not correspond to the appropriate comparator therapy, so that no statements on the additional benefit can be derived on the basis of the indirect comparisons presented. In addition, due to the insufficient workup of the MAIC analyses, it remains unclear whether the data included in the indirect comparisons are complete and whether the included studies are comparable with each other.

Therefore, no data relevant for the benefit assessment of fostemsavir are available, so an additional benefit is not proven.

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

The information on the number of patients (approx. 80 – 240) is based on the target population in statutory health insurance (SHI).

The data follow the representations of the pharmaceutical company and the assessment of IQWiG. Overall, the number of patients in the SHI target population estimated by the pharmaceutical company can be assumed to be an underestimate, in particular, due to the

double consideration of a percentage for three-class resistance. In addition, the data are subject to uncertainties in individual calculation steps.

The number of patients indicated in the present case differs from the number indicated in the identical therapeutic indication (resolution on ibalizumab of 18 February). The patient numbers reported there were also assessed as an underestimate. Since the estimated number is higher in the present procedure for fostemsavir and since the number of patients was operationalised not only by virological failure but also by the presence of side effects, it is assumed that the present patient numbers are a better approximation of the actual numbers to be expected, despite an assumed underestimation.

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 Rukobia (active ingredient: fostemsavir) at the following publicly accessible link (last access: 2 July 2021):
https://www.ema.europa.eu/en/documents/product-information/rukobia-epar-product-information_en.pdf

Treatment with fostemsavir should only be initiated and monitored by doctors experienced in treating patients with HIV infection.

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 September 2021).

For the cost representation, only the doses of the general case are considered. If the treatment duration is not limited, initial induction schemes are not considered for the cost representation. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

For the appropriate comparator therapy and basic therapy with fostemsavir, the range of treatment costs incurred depending on the individual choice of therapy is shown. Because of the different combination possibilities in individual therapy, not all possible combination therapies are presented but a cost-effective (nevirapine + lamivudine / tenofovir disoproxil) and a cost-intensive therapy (ibalizumab + abacavir + emtricitabine) as examples.

According to the current German-Austrian guidelines[3], different alternatives ("backbone" with combination partners) are recommended that were taken into account for the cost representation. Although ibalizumab is not yet specifically mentioned in these guidelines, it represents a possible treatment option in the present therapeutic indication and is therefore considered for the treatment cost calculation.

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 patient-

German-Austrian guidelines on antiretroviral therapy for HIV-1 infection, AWMF 055-001, version 8 of 10.04.2019 and version 9 of 01.09.2020.

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 for 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)	Days of treatment/ patient/ year
Medicinal product to be assessed				
Fostemsavir	continuously, 2 times a day	365	1	365
Nevirapine + lamivudine / tenofovirdisoproxil				
Nevirapine	continuously, 2 times a day	365	1	365
Lamivudine + tenofovirdisoproxil	continuously, 1 time a day	365	1	365
Ibalizumab + abacavir + emtricitabine				
Ibalizumab	Continuously, every 14 days	26.1	1	26.1
Abacavir	continuously, 2 times a day	365	1	365
Emtricitabine	continuously, 1 time a day	365	1	365
Appropriate comparator therapy				
Nevirapine + lamivudine / tenofovirdisoproxil				
Nevirapine	continuously, 2 times a day	365	1	365
Lamivudine / tenofovirdisoproxil	continuously, 1 time a day	365	1	365
Ibalizumab + abacavir + emtricitabine				
Ibalizumab	Continuously, every 14 days	26.1	1	26.1
Abacavir	continuously, 2 times a day	365	1	365
Emtricitabine	continuously, 1 time a day	365	1	365

Consumption:

Designation of the therapy	Dosage/ application	Dosage/ patient/ days of treatment	Usage by potency/ day of treatment	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Fostemsavir	600 mg	1200 mg	2 x 600 mg	365	730 x 600 mg
Nevirapine + lamivudine / tenofovirdisoproxil					
Nevirapine	200 mg	400 mg	2 x 200 mg	365	730 x 200 mg
Lamivudine / tenofovirdisoproxil	245 mg / 300 mg	245 mg / 300 mg	1 x 245 mg / 300 mg	365	365 x 245 mg / 300 mg
Ibalizumab + abacavir + emtricitabine					
Ibalizumab	800 mg	800 mg	4 x 200 mg	26.1	104.4 x 200 mg
Abacavir	300 mg	600 mg	2 x 300 mg	365	730 x 300 mg
Emtricitabine	200 mg	200 mg	1 x 200 mg	365	365 x 200 mg
Appropriate comparator therapy					
Nevirapine + lamivudine / tenofovirdisoproxil					
Nevirapine	200 mg	400 mg	2 x 200 mg	365	730 x 200 mg
Lamivudine / tenofovirdisoproxil	245 mg / 300 mg	245 mg / 300 mg	1 x 245 mg / 300 mg	365	365 x 245 mg / 300 mg
Ibalizumab + abacavir + emtricitabine					
Ibalizumab	800 mg	800 mg	4 x 200 mg	26.1	104.4 x 200 mg
Abacavir	300 mg	600 mg	2 x 300 mg	365	730 x 300 mg
Emtricitabine	200 mg	200 mg	1 x 200 mg	365	365 x 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 on the basis of

consumption. The required number of packs of a particular potency was first determined based on consumption to calculate the annual treatment costs. 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 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					
Fostemsavir 600 mg	180 RET	€ 11,778.13	€ 1.77	€ 669.38	€ 11,106.98
Nevirapine + lamivudine / tenofovirdisoproxil					
Nevirapine 200 mg	120 TAB	€ 266.99	€ 1.77	€ 12.74	€ 252.48
Lamivudine / tenofovirdisoproxil 245 mg / 300 mg	30 FCT	€ 47.05	€ 1.77	€ 1.71	€ 43.57
Ibalizumab + abacavir + emtricitabine					
Ibalizumab 200 mg	2 CIS à 1,33 mL	€ 2508.78	€ 1.77	€ 140.00	€ 2367.01
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 / tenofovirdisoproxil					
Nevirapine 200 mg	120 TAB	€ 266.99	€ 1.77	€ 12.74	€ 252.48
Lamivudine / tenofovirdisoproxil 245 mg / 300 mg	30 FCT	€ 47.05	€ 1.77	€ 1.71	€ 43.57
Ibalizumab + abacavir + emtricitabine					
Ibalizumab 200 mg	2 CIS à 1,33 mL	€ 2,508.78	€ 1.77	€ 140.00	€ 2,367.01
Abacavir 300 mg	180 FCT	€ 1,107.09	€ 1.77	€ 52.01	€ 1,053.31

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
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; RET = retard tablets; TAB = tablets					

LAUER-TAXE® last revised: 1 September 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 evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be considered 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 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, no costs for additionally required SHI services had to be taken into account.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe)(Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic drugs a maximum amount of € 81 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 71 per ready-to-use unit are to be payable. These additional other costs do not add to the pharmacy sales price but follow the rules for calculation in the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe). The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy sales price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

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

On 24 March 2021, the pharmaceutical company submitted a dossier for the benefit assessment of fostemsavir to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 1 VerfO.

By letter dated 26 March 2021 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 fostemsavir.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 June 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 01 July 2021. The deadline for submitting written statements was 22 July 2021.

The oral hearing was held on 10 August 2021.

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 the 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 7 September 2021, and the proposed resolution was approved.

At its session on 16 September 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Sub-committee Medicinal product	28 January 2020	Determination of the appropriate comparator therapy
Working group Section 35a	3 August 2021	Information on statements received; preparation of the oral hearing
Sub-committee Medicinal product	10 August 2021	Conduct of the oral hearing

Working group Section 35a	17 August 2021; 31 August 2021	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Sub-committee Medicinal product	7 September 2021	Final discussion of the draft resolution
Plenum	16 September 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 16 September 2021

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

Prof. Hecken