Justification

Gemeinsamer Bundesausschuss

to the Draft 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 Tezacaftor/Ivacaftor (Reassessment of an Orphan Drug after the € 50 Million Turnover Limit Was Exceeded: Cystic Fibrosis, Combination Regimen with Ivacaftor in Patients over 12 Years of Age (Heterozygous with Respect to F508del))

of 17 December 2020

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 based on 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 active ingredient combination tezacaftor/ivacaftor (Symkevi) was listed for the first time on 1 December 2018 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices. Symkevi for the treatment of cystic fibrosis is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999.

At its session on 16 May 2019, the G-BA passed a resolution on the benefit assessment of the active ingredient combination tezacaftor/ivacaftor in therapeutic indication “Symkevi is indicated in a combination regimen with ivacaftor 150 mg tablets for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are heterozygous for the F508del mutation and have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T” in accordance with Section 35a SGB V.

If the turnover of the orphan drugs with statutory health insurance at pharmacy sales prices as well as outside statutory medical care, including value added tax, exceeds € 50 million in the last twelve calendar months, the pharmaceutical company must, within three months of being requested to do so by the Federal Joint Committee, submit evidence according to Section 5,

paragraph 1 through 6 demonstrating the additional benefit compared with the appropriate comparator therapy.

In a letter dated 4 March 2020, the pharmaceutical company was requested to submit a dossier for a benefit assessment according to Section 35a SGB V by 1 July 2020 because the € 50 million turnover limit had been exceeded between December 2018 and November 2019. The pharmaceutical company submitted the final dossier to the G-BA in due time 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 6 VerfO on 26 June 2020.

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 October 2020, 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 tezacaftor/ivacaftor compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment (A20-55) prepared by the IQWiG, and the written statements made in the written and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit based on their therapeutic relevance (qualitative) according to the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of tezacaftor/ivacaftor.

In the 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 tezacaftor/ivacaftor (Symkevi) in accordance with the product information

Symkevi is indicated in a combination regimen with ivacaftor 150 mg tablets for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the F508del mutation or who are heterozygous for the F508del mutation and have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.

Therapeutic indication of the resolution (resolution of 17 December 2020):

Symkevi is indicated in a combination regimen with ivacaftor 150 mg tablets for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are heterozygous for the F508del mutation and have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

[1] General Methods, Version 6.0 dated 5 November 2020. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care), Cologne.

Patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation and who display one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.

- Best supportive care.

  Best supportive care (BSC) is defined as the therapy that ensures the best possible, patient-individual optimised, supportive treatment to alleviate symptoms and improve the quality of life (especially antibiotics for pulmonary infections, mucolytics, pancreatic enzymes for pancreatic insufficiency, physiotherapy (in the sense of the Heilmittel-Richtlinie (Remedies Directive)), making full use of all possible dietary measures).

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.
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. The following medicinal products are approved for symptomatic therapy of CF:

Aztreonam, carbocisteine[2], ceftazidim, ciprofloxacin, colistimethate, dornase alfa, levofloxacin[3], meronem, mannitol, pancreatin, tobramycin.

On 2. In the treatment of CF, nutritional measures, support of the respiratory function, and physiotherapy (in the sense of the Remedies Directive) are generally considered as non-medicinal treatment.

On 3. For the patient group to be considered in the present therapeutic indication “patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation and who display one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G, and 3849+10kbC→T”, the G-BA has passed the following resolution:

[2] Approved for adolescents from 13 years and adults with CF
[3] Approved only for adult patients with CF

- For ivacaftor, no additional benefit was determined for the patient group “Patients aged 12 years and older who are heterozygous for the F508del mutation and who have another mutation in the CFTR gene” (resolution of 20 February 2020).

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. According to the current state of medical knowledge, there is no specific standard therapy for patients from 12 years of age with CF who are heterozygous for the F508del mutation and have another mutation in the CFTR gene. For patients with CF aged 12 years and older, the aforementioned medicinal and non-medicinal therapy options are available for symptomatic therapy. In the evidence provided, these are recommended for symptomatic therapy of CF, in particular, antibiotic therapy of pulmonary infections (ceftazidine, colistimethate, tobramycin), inhalation of medicinal products (mannitol, dornase alfa), enzyme substitution for pancreatic insufficiency (pancreatin), and nutritional therapy and support of respiratory function (e.g. through physiotherapy). CF is thus treated individually for each patient to alleviate symptoms and improve the quality of life in the sense of best supportive care (BSC).

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 tezacaftor/ivacaftor in combination with ivacaftor (TEZ/IVA + IVA) has been assessed as follows:

Patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation and who display one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.

An additional benefit is not proven.

Justification:

To assess the additional benefit of TEZ/IVA + IVA in patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation in the CFTR gene and who have a mutation with a residual CFTR function (RF mutation) on the second allele, the pharmaceutical company presented the pivotal multi-centre, randomised, double-blind, placebo-controlled cross-over VX14-661-108 Phase III study (hereinafter referred to as Study 108).

The patients in Study 108 were distributed randomly in six groups. For the benefit assessment, the non-compliant intervention (IVA) is not relevant. Of a total of 248 patients, 167 patients were randomised to the intervention arm (TEZ/IVA + IVA + BSC) and 165 patients to the comparator arm (placebo + BSC) in one of two treatment periods. The dosage of TEZ/IVA and IVA followed the specifications in the product information.

The stratification was based on age (< 18 years vs ≥ 18 years), FEV_1 (< 70% vs ≥ 70%) and type of RF mutation. The patients 12 years of age and older with a confirmed CF diagnosis and a heterozygous F508del mutation in the CFTR gene and an RF mutation in the CFTR gene included needed to display an FEV_1 ranging from ≥ 40% to ≤ 90% of the standard values for age, sex, and height as well as a sweat chloride value of ≥ 60 mmol/l at the time of the screening.

The data presented in the dossier shows that the patients included in the study received comprehensive symptomatic medical treatment during the course of the study containing among others: dornase alfa, sodium chloride, pancreatin and salbutamol as well as antibiotics,

food supplements and corticosteroids. Overall, it is to be assumed that at least one appropriate (stable) basic therapy with mucolytics and pancreas enzymes was carried out.

As a primary endpoint in Study 108, the "absolute change in FEV_1%" (percentage of forced expiratory one-second volume) was surveyed. In addition, endpoints in the categories mortality, morbidity, quality of life, and side effects were surveyed.

The study comprised an eight-week treatment period with a subsequent cross-over to an additional eight-week treatment period. The wash-out period between the treatment periods was eight weeks. After the two treatment periods, there was a four-week safety follow-up. For patients included in the Extension Study VX14-661-110, the safety follow-up was omitted.

The eight-week treatment phase chosen by the pharmaceutical company was considered sufficient for marketing authorisation to demonstrate the efficacy or the efficacy profile of tezacaftor/ivacaftor in combination with ivacaftor and was used by the G-BA in the benefit assessment under orphan criteria for which an additional benefit is generally considered proven.

However for evaluating the effects on patient-relevant endpoints of a medicinal product that is now subject to an unrestricted benefit assessment, this study duration is too short in order to be able to make a valid assessment of the additional benefit for a chronic disease.

Cystic fibrosis is a chronic disease without a cure and with progressive disease progression and lifelong therapeutic obligation. The guideline of the European Medicines Agency (EMA)[4] stipulates a minimum duration of 6 months for the investigation of a clinical endpoint in the present indication.

A treatment phase of only eight weeks does not take into account the patient-individual fluctuations in clinical symptomatology, which can be modified by various factors. Furthermore, no statements can be made on the basis of short-term studies as to whether the short-term effects persist in the longer term. Nor can any effects that only become apparent in the longer term (e.g. pulmonary exacerbations and their consequences or AEs) be recorded. Pulmonary exacerbations are a common cause of lung damage or death in patients with cystic fibrosis.

In the therapeutic indication of cystic fibrosis, short-term studies (with a treatment duration of less than 24 weeks) are therefore unsuitable for the benefit assessment here. Against this background, Study 108 cannot be used for the benefit assessment.

The pharmaceutical company also presented the results of the 24-week RCT VX14-661-106. The pharmaceutical company does not use Study VX14-661-106 to derive the additional benefit. Only patients with homozygous F508del mutation were included in this study. Study VX14-661-106 is therefore not considered for the present benefit assessment.

In addition, the pharmaceutical company also presented the supportive, ongoing, open-label, single-arm extension VX14-661-110 Phase III Study. Patients with the homozygous (Studies VX13-661-103, VX14-661-106, VX14-661-111) as well as the heterozygous F508del mutation (Studies VX14-661-107, VX14-661-108, VX14-661-109) in the CFTR gene were included in the study.

This single-arm study is not relevant for the present benefit assessment because no data are available for an assessment of tezacaftor/ivacaftor compared with the appropriate comparator therapy.

Thus, for this patient population, the pharmaceutical company did not present any study that would have been suitable for the assessment of the additional benefit of tezacaftor/ivacaftor compared with the appropriate comparator therapy.

[4] European Medicines Agency. Guideline on the clinical development of medicinal products for the treatment of cystic fibrosis [online]. 22 October 2009 [Accessed: 2 October 2019]. URL: https://www.ema.europa.eu/documents/scientific-guideline/guideline-clinical-development-medicinal-products-treatment-cystic-fibrosis-first-version_en.pdf.

2.1.4 Summary of the assessment

The present assessment is the renewed benefit assessment (because the € 50 million turnover limit was exceeded) of the active ingredient combination tezacaftor/ivacaftor (TEZ/IVA) in combination with/ivacaftor (IVA). The present assessment refers to the therapeutic indication "for the treatment of patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation and who display one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T."

Tezacaftor/ivacaftor has received marketing authorisation as an orphan drug.

Best supportive care (BSC) was determined as an appropriate comparator therapy by the G-BA.

For the benefit assessment of TEZ/IVA + IVA for the treatment of cystic fibrosis (CF, mucoviscidosis) in patients 12 years of age and older who are heterozygous for the F508del mutation in the CFTR gene and display an RF mutation the CFTR gene, the eight-week, multi-centre, randomised, double-blind, placebo-controlled cross-over phase III Study 108 was submitted.

This eight-week study (with subsequent cross-over) is too short for the benefit assessment. Thus, for this patient population, the pharmaceutical company did not present any study that would have been suitable for the assessment of the additional benefit of TEZ/IVA + IVA compared with the appropriate comparator therapy.

In the overall view, for patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation and who display one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T, an additional benefit is not proven for treatment with TEZ/IVA + IVA.

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

Patients 12 years of age and older with cystic fibrosis who are heterozygous for the F508del mutation and who display one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.

The G-BA uses the following derivation of patient numbers in order to enable a consistent examination of patient numbers, taking into account the most recent resolution (15 August 2019) on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V in the therapeutic indication of cystic fibrosis:

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

A total patient group of currently approx. 8,000 patients with cystic fibrosis in Germany is assumed[5].

This figure differs from the calculation in the dossier by the pharmaceutical company, which assumes a total population of 6,340 patients with cystic fibrosis. However, this figure is subject to uncertainties and represents an underestimate because patients without process data and up-to-date consent forms were not taken into account. Furthermore, there is currently no indication that the number of patients in the overall collective has changed significantly since

[5] https://www.muko.info/ (https://www.muko.info/englisch-version/) Website of Mukoviszidose e.V. (German Cystic Fibrosis Association) [accessed 27 June 2019]

the 2012 report (8,042 patients ever reported and still alive at that time). This number has already been adjusted to eliminate multiple responses in accordance with the information in the documentation).

1. Of the 12,578 alleles with known mutations, 8384 alleles (68.98%) have an F508del mutation and 274 alleles (2.25%) have one of the following mutations: 2789+5G→A, 3272-26A, or 3849+10kbC→T[6]. Because 2.25% corresponds exclusively to 3 of the 14 mutations in the CFTR gene in this indication, this number is projected for the 14 mutations to be taken into account. For this purpose, information from a French and an American registry is taken into consideration. The percentage of 2,789+5G→A, 3272-26A, and 3,849+10kbC→T of all 14 mutations corresponds to approx. 64.9% in the American registry[7] and to approx. 60.3% in the French registry[8]. Based on this information, the result is 383 (= 8,000 × 68.98% × 2.25%/64.9% × 2) to 412 (= 8,000 × 68.98% × 2.25%/60.3% × 2) patients.
2. The percentage of patients 12 years and older in the entire patient group is approx. 73.1%[5] (280–301 patients).
3. Taking into account an 87.86% share of patients covered by statutory health insurance (SHI), the result is 246–264 patients in the target population.

The range of proportions for 2789+5G→A, 3272-26A, and 3849+10kbC→T in all 14 mutations used by the pharmaceutical company is subject to uncertainties.

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 Symkevi (active ingredient combination: tezacaftor/ivacaftor) at the following publicly accessible link (last access: 28 October 2020): https://www.ema.europa.eu/documents/product-information/symkevi-epar-product-information_de.pdf

Treatment with tezacaftor/ivacaftor may be initiated and monitored only by specialists who are experienced in the treatment of patients with cystic fibrosis.

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 December 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

[6] Nährlich L, Burkhart M, Wosniok J. German Cystic Fibrosis Registry: Annual Report 2018. 2019 https://www.muko.info/fileadmin/user_upload/angebote/qualitaetsmanagement/register/berichtsbaende/berichtsband_2018.pdf.
[7] Cystic Fibrosis Foundation Patient Registry. 2018 annual data report
[8] French Cystic Fibrosis Registry. Annual Data Report 2016, March 2018.

“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				
Tezacaftor/ ivacaftor	continuously, 1 × daily	365	1	365
Ivacaftor	continuously, 1 × daily	365	1	365
Best supportive care		different for each individual patient		
Appropriate comparator therapy				
Best supportive care		different for each individual patient		

Usage and consumption:

Designation of the therapy	Dosage/ application	Dose/patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Tezacaftor/ ivacaftor	100 mg/150 mg	100 mg/150 mg	1 × 100 mg/150 mg	365	365 × 100 mg/150 mg
Ivacaftor	150 mg	150 mg	1 × 150 mg	365	365 × 150 mg
Best supportive care			different for each individual patient		
Appropriate comparator therapy					
Best supportive care			different for each individual patient		

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates according to 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					
Tezacaftor/ivacaftor	28 FCT	€ 6,243.43	€ 1.77	€ 365.20	€ 5,876.46
Ivacaftor	56 FCT	€ 16,017.86	€ 1.77	€ 937.86	€ 15,078.23
Best supportive care		different for each individual patient			
Appropriate comparator therapy					
Best supportive care		different for each individual patient			
Abbreviations: FCT: film-coated tablets					

Pharmaceutical selling price (LAUER-TAXE®) as last revised: 1 December 2020

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.

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

On 26 June 2020, the pharmaceutical company submitted a dossier for the benefit assessment of tezacaftor/ivacaftor to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, Number 6 VerfO.

By letter dated 29 June 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 combination tezacaftor/ivacaftor.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 September 2020, and the written statement procedure was initiated with publication on the website of the G-BA on 1 October 2020. The deadline for submitting written statements was 22 October 2020.

The oral hearing was held on 9 November 2020.

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 8 December 2020, and the proposed resolution was approved.

At its session on 17 December 2020, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	10 March 2020	Determination of the appropriate comparator therapy
Working group Section 35a	4 November 2020	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	9 November 2020	Conduct of the oral hearing
Working group Section 35a	18 November 2020 2 December 2020	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee on Medicinal Products	8 December 2020	Concluding discussion of the draft resolution
Plenum	17 December 2020	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 17 December 2020

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

Prof. Hecken