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 Indacaterol Acetate/Glycopyrronium Bromide/Mometasone Furoate (Asthma)

of 4 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 indacaterol acetate/glycopyrronium bromide/mometasone furoate in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 August 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 5 August 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 16 November 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 indacaterol acetate/glycopyrronium bromide/mometasone furoate compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addenda to the benefit assessment prepared by the IQWiG. In order to determine the extent of the additional benefit, the G-BA 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 indacaterol acetate/glycopyrronium bromide/mometasone furoate.

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 indacaterol acetate/glycopyrronium bromide/mometasone furoate (Enerzair Breezhaler) in accordance with the product information

Enerzair Breezhaler is indicated as a maintenance treatment of asthma in adult patients not adequately controlled with a maintenance combination of a long-acting beta2-agonist and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year.

Therapeutic indication of the resolution (resolution of 4 February 2021):

See approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adult patients with asthma who are not adequately controlled with a maintenance combination of a LABA and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year

Appropriate comparator therapy:

High-dose ICS and LABA and LAMA

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 6.0 dated 5 November 2020. 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. In principle, active ingredients of different active ingredient classes are approved for the treatment of asthma:

- Selective beta-2 sympathomimetics: salmeterol, fenoterol, reproterol, salmeterol, formoterol, terbutaline, salbutamol, bambuterol, and clenbuterol
- Inhaled muscarinic antagonists: Tiotropium bromide
- Inhaled corticosteroids: beclometasone, budesonide, ciclesonide, fluticasone, and mometasone
- Oral corticosteroids: e.g.: Prednisolone and prednisone
- Combination preparations: Budesonide/formoterol, budesonide/formoterol, formoterol/fluticasone, salmeterol/fluticasone, vilanterol/fluticasone, ipratropium bromide/fenoterol, clenbuterol/ambroxol
- Others: theophylline, omalizumab, mepolizumab, reslizumab, benralizumab, dupilumab

On 2. For the treatment of inadequately controlled asthma, no non-medicinal measures can be considered as the sole appropriate comparator therapy.

On 3. The following resolutions on an amendment to the Pharmaceuticals Directive (AM-RL) have been adopted:
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Dupilumab (resolution 20 March 2020)
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Mepolizumab (resolution of 22 March 2019)
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Benralizumab (resolution of 2 August 2018)
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Reslizumab – repeal of the limitation of the period of validity (resolution of 6 December 2018)
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Mepolizumab – repeal of the limitation of the period of validity (resolution of 6 December 2018)
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Reslizumab (resolution of 6 July 2017)
- Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V: Mepolizumab (resolution of 21 July 2016)
- Annex IV: Therapeutic information on omalizumab (resolution of 17 December 2015).
- Annex XII / Annex IX: Fixed amount group formation fluticasone furoate/vilanterol

On 4. The generally accepted state of medical knowledge was illustrated by systematic research for guidelines and reviews of clinical studies in the present indication and is

presented in the “Research and synopsis of the evidence to determine the appropriate comparator therapy in accordance with Section 35a SGB V”.

The medicinal stage scheme for adults of the National Health Care Guideline Asthma (NVL Asthma, 4th edition, 2020 Version 1) must be considered. The wording of the intended therapeutic indication does not limit the therapeutic indication to a certain level of NVL Asthma. However, based on the active ingredient character of the combination of mometasone furoate, indacaterol acetate, and glycopyrronium bromide, the G-BA determines the appropriate comparator therapy for patients who are eligible for therapy in Stage 4 of the NVL Asthma 2020. Accordingly, it is assumed that the patients in the therapeutic indication received a dual combination (of high-dose ICS and LABA) as previous therapy and are thus not adequately controlled. It is also assumed that the patients are not yet eligible for the administration of antibodies. According to the guideline, in Stage 4 for adults with asthma who are not adequately treated with a two-dose combination of high-dose ICS and LABA, additional therapy with a long-acting inhaled anti-cholinergic (LAMA) is indicated.

If there is still the option of therapy escalation, the unchanged continuation of an inadequate therapy of asthma does not correspond to an appropriate comparator therapy in uncontrolled asthma.

Montelukast is approved only as an add-on treatment in patients suffering from mild to moderate persistent asthma. Because its narrow therapeutic range, theophylline is not a first-choice agent in asthma therapy and is therefore not determined to be an appropriate comparator therapy.

The marketing authorisations and product information of the medicinal products used in appropriate comparator therapy must be complied with.

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 indacaterol acetate/glycopyrronium bromide/mometasone furoate is assessed as follows:

For adult patients with asthma who are not adequately controlled with a maintenance combination of a LABA and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year, an additional benefit is not proven.

Justification:

For the assessment of the additional benefit of the active ingredient combination indacaterol acetate/glycopyrronium bromide/mometasone furoate (Ind/Glyc/Mom) compared with the appropriate comparator therapy, the pharmaceutical company presents the randomised, controlled ARGON Phase III study.

In the ARGON study, the active ingredient combination Ind/Glyc/Mom in 2 different dosages (150/50/80 µg or 150/50/160 µg) is compared with salmeterol/fluticasone (Sal/Flu) + tiotropium (Tio). The total treatment duration was 24 weeks. The patients as well as the study personnel were blinded only with respect to the dosage of the intervention arms. Of the two intervention arms, the Ind/Glyc/Mom arm at the 150/50/160 µg dosage corresponds to the marketing authorisation. The study arm with Ind/Glyc/Mom in the dosage of 150/50/80 µg is therefore not considered for the benefit assessment.

The study included 1426 adult patients with a *Global Initiative for Asthma* [GINA] asthma classification of ≥ 4, whose asthma was not adequately controlled despite treatment with moderate- or high-dose ICS and LABA. Inadequate control was defined as a score of at least

1.5 on the Asthma Control Questionnaire (ACQ)-7 at the time of screening and randomisation. Further inclusion criteria were the occurrence of a severe asthma exacerbation within the last 12 months before study inclusion, a one-second capacity (FEV1) of < 85% of the target value, and an increase in FEV1 of ≥ 12% in the reversibility test. Adjustment of asthma-related concomitant therapy was possible during the course of the study. The primary endpoint of the study is health-related quality of life as surveyed by the standardised *Asthma Quality of Life Questionnaire* (AQLQ-S).

The study was conducted at 166 study centres worldwide between February 2018 and July 2019.

In accordance with the product information, the administration of Ind/Glyc/Mom is approved only for patients who have previously been treated with a high-dose ICS and a LABA; therefore, only the correspondingly pre-treated patient population of the ARGON study is considered for the present benefit assessment. This corresponds to a total of 474 patients (242 patients in the intervention arm and 232 patients in the comparator arm).

Extent and probability of the additional benefit

Mortality

For the endpoint overall mortality, there was no statistically significant difference between the treatment groups.

Morbidity

Severe asthma exacerbations

In the ARGON study, a severe asthma exacerbation was defined as an asthma exacerbation requiring medical treatment by a physician, admission to an emergency department (or equivalent), or hospitalisation and treatment with OCS for at least 3 days. The evaluation was carried out as mean annual rate and number of patients with event.
Because it is assumed that the evaluation of severe asthma exacerbations as a mean annual rate is more relevant than the number of patients with the event of a severe asthma exacerbation, the latter is only presented additionally in the resolution.

For the endpoint severe asthma exacerbations, there was no statistically significant difference between the treatment groups in either of the evaluations.

Asthma symptomatology

In the ARGON study, asthma symptomatology was surveyed using the *Asthma Control Questionnaire* (ACQ-7) and an electronic patient diary. The ACQ was evaluated as ACQ-5, which includes a total of 5 questions on asthma symptomatology in the last 7 days and does not include 2 questions (“rescue medication use” and “limitation of lung function (FEV1)”) of the ACQ-7. The patient diary includes 7 questions about the symptomatology, 2 of which should patients should answer every morning and 5 of which patients should answer every evening. The questions relate to night-time symptoms, asthma symptomatology upon waking, activity limitations, shortness of breath, and wheezing.

Both instruments are suitable for assessing asthma symptomatology:
The questions of the patient diary were evaluated via different operationalisations as daily response or as change since the start of study, although the respective specific operationalisations and the question of whether the respective evaluation was pre-specified remained unclear. The missing information was submitted by the pharmaceutical company in the course of the written statement procedure; however, no significant differences were found in the pre-specified evaluations.

For asthma symptomatology, surveyed by ACQ-5, there was no statistically significant difference between the treatment groups based on the results.

Quality of life

In the ARGON study, health-related quality of life was assessed using the *Asthma Quality of Life Questionnaire* (AQLQ-S) and *St. George's Respiratory Questionnaire* (SGRQ). The pharmaceutical company shall submit responder analyses for both endpoints for the proportion of patients with an improvement of at least 0.5 (AQLQ-S) or 4 points (SGRQ).

The two response criteria do not correspond to the current methodological approach of the IQWiG (General Methods, Version 6.0 published on 5 November 2020), which, taking into consideration a currently missing standard for the quality assessment of studies on clinical relevance (MID) and the significance of determined MIDs, considers a response criterion of at least 15% of the scale range of an instrument (in the case of analyses conducted *post hoc*, exactly 15% of the scale range) to be necessary in order to reliably reflect a change that is noticeable for patients. No evaluations for this response criterion are available in the dossier.

Regardless of the question of which response criterion can be used for the benefit assessment, the evaluation of the responder analyses for the proportion of patients with an improvement of at least 0.5 (AQLQ-S) or 4 points (SGRQ) shows no significant difference between the treatment groups in the relevant sub-population.

For the evaluation of the two responder analyses, the pharmaceutical company applies an enhancement rule in which the treatment effect in the relevant sub-population can be tested at the increased significance level of 15% provided that (among other things) there is a statistically significant difference from the 5% level in the overall study population.

However, the approach of the pharmaceutical company is not followed regardless of whether the requirements for the application of the increase rule can be considered to be fulfilled in principle. For the benefit assessment, only the sub-population of the ARGON study compliant with the marketing authorisation is taken into consideration. Results of the total study population, which also include the data of the sub-population not compliant with the marketing authorisation, are not taken into consideration. For the benefit assessment, the evaluation of the mean change from the start of study is therefore used for the AQLQ-S and SGRQ.

In summary, for the endpoint health-related quality of life, based on the mean change from the start of study for the AQLQ-S and SGRQ, there was no statistically significant difference between the treatment groups.

Side effects

For both the endpoint SAEs and the endpoint discontinuation because of AEs, there was no statistically significant difference between the treatment groups. No specific AEs were selected based on frequency and differences between treatment arms.

Overall assessment/conclusion

For the benefit assessment of the active ingredient combination indacaterol acetate/glycopyrronium bromide/mometasone furoate for the treatment of adult patients with asthma who are not adequately controlled with a maintenance combination of a LABA and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year, results from the randomised, controlled ARGON Phase III study on mortality, morbidity, health-related quality of life, and side effects compared with treatment with salmeterol/fluticasone and tiotropium are available.

There are no significant differences between the treatment groups in any endpoint category.

An additional benefit for the active ingredient combination indacaterol acetate/glycopyrronium bromide/mometasone furoate for adult patients with asthma who are not adequately controlled with a maintenance combination of a LABA and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year compared with the appropriate comparator therapy salmeterol/fluticasone and tiotropium is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of the new medicinal product Enerzair Breezhaler with the active ingredient combination indacaterol acetate/glycopyrronium bromide/mometasone furoate. The active ingredient combination is approved for the treatment of asthma in adult patients not adequately controlled with a maintenance combination of a LABA and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year. A therapy consisting of high-dose ICS and LABA and LAMA was determined by the G-BA as an appropriate comparator therapy. The benefit assessment is based on the randomised, controlled ARGON Phase III study in which the active ingredient combination indacaterol acetate/glycopyrronium bromide/mometasone furoate in 2 different dosages (150/50/80 µg or 150/50/160 µg) was compared with salmeterol/fluticasone and tiotropium. Blinding was applied only to the dosage of the intervention arms. For the benefit assessment, only the authorisation-compliant intervention arm (dosage of 150/50/160 µg) and only the authorisation compliant sub-population (patients previously treated with a high-dose inhaled corticosteroid and a LABA) are considered.

Overall, the results do not show significant differences between the treatment groups in any endpoint category.

An additional benefit for the active ingredient combination indacaterol acetate/glycopyrronium bromide/mometasone furoate for adult patients with asthma who are not adequately controlled with a maintenance combination of a LABA and a high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous year compared with the appropriate comparator therapy salmeterol/fluticasone and tiotropium is therefore not proven.

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

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

The G-BA bases its resolution on the patient numbers provided by the pharmaceutical company in the dossier. However, these are subject to uncertainties in some places. The applicability criteria for identifying patients on LABA therapy and high-dose ICS therapy are partly not validated or differentiated. The criteria for identifying patients with inadequately controlled asthma with at least 1 exacerbation in the previous year 2017 may lead to an overestimation because of the inclusion of patients receiving therapy with biologics and to an underestimation because of the exclusion of patients who also received an OCS prescription in 2016.

On the basis of the information provided by the pharmaceutical company, it cannot be assessed whether the uncertainties mentioned in the applicability criteria or in the approach of the pharmaceutical company affect a relevant number of patients.

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 Enerzair Breezhaler (active ingredient combination:

indacaterol acetate/glycopyrronium bromide/mometasone furoate) at the following publicly accessible link (last access: 21 January 2021):
https://www.ema.europa.eu/documents/product-information/enerzair-breezhaler-epar-product-information_de.pdf

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 January 2021).

The G-BA determined the costs for the appropriate comparator therapy based on the costs of the most cost-effective inhaled corticosteroids (ICS), long-acting beta-2 agonists (LABA), and ICS + LABA fixed combinations.

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				
Indacaterol acetate/glycopyrronium bromide/mometasone furoate	continuously, 1 × daily	365	1	365
Appropriate comparator therapy				
Inhaled corticosteroids (ICS, high-dose)				
Budesonide	continuously, 2 × daily	365	1	365
Long-acting beta-2 sympathomimetics (LABA)				
Formoterol	continuously, 2 × daily	365	1	365
ICS/LABA fixed combinations (high-dose)				
Fluticasone/salmeterol	continuously, 2 × daily	365	1	365
Long-acting muscarinic antagonists (LAMA)				

Designation of the therapy	Treatment mode	Number of treatments/ patient/year	Treatment duration/treatment (days)	Treatment days/patient/ year
Tiotropium	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					
Indacaterol acetate/ glycopyrronium bromide/ mometasone furoate	114 µg/ 46 µg/ 136 µg	114 µg/ 46 µg/ 136 µg	1 × 114 µg/ 46 µg/136 µg	365	365 × 114 µg/46 µg/ 136 µg
Appropriate comparator therapy					
Inhaled corticosteroids (ICS, high-dose)					
Budesonide	400 µg	800 µg	2 × 400 µg	365	730 × 400 µg
Long-acting beta-2 sympathomimetics (LABA)					
Formoterol	12 µg	24 µg	2 × 12 µg	730	730 × 12 µg
ICS/LABA fixed combinations (high-dose)					
Fluticasone/salmeterol	500 µg / 50 µg	1,000 µg/100 µg	2 x 500 µg/ 50 µg	365	730 × 500 µg/ 50 µg
Long-acting muscarinic antagonists (LAMA)					
Tiotropium	5 µg	5 µg	2 × 2.5 µg	365	730 × 2.5 µg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated based on the pharmacy sales price level as well as less 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. For the long-acting beta-2 agonists (LABA), inhaled corticosteroids (ICS), and ICS/LABA fixed combinations, the respective fixed reimbursement rate was applied.

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					
Indacaterol acetate/glycopyrronium bromide/mometasone furoate	90 SD	€ 296.66	€ 1.77	€ 15.81	€ 279.08
Appropriate comparator therapy					
Budesonide 400 µg[2]	300 SD	€ 63.59	€ 1.77	€ 4.16	€ 57.66
Formoterol 12 µg[2]	180 SD	€ 83.73	€ 1.77	€ 5.75	€ 76.21
Fluticasone/salmeterol 500 µg/ 50 µg[2]	180 SD	€ 133.65	€ 1.77	€ 9.70	€ 122.18
Tiotropium 2.5 µg	180 SD	€ 197.59	€ 1.77	€ 10.33	€ 185.49
Abbreviations: SD = single doses					

Pharmaceutical selling price (LAUER-TAXE®) as last revised: 15 January 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.

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.

[2] Fixed reimbursement rate

4. Process sequence

At its session on 11 February 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 5 August 2020, the pharmaceutical company submitted a dossier for the benefit assessment of indacaterol acetate/glycopyrronium bromide/mometasone furoate to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 7 August 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 indacaterol acetate/ glycopyrronium bromide/ mometasone furoate.

The dossier assessment by the IQWiG was submitted to the G-BA on 12 November 2020, and the written statement procedure was initiated with publication on the website of the G-BA on 16 November 2020. The deadline for submitting written statements was 7 December 2020.

The oral hearing was held on 21 December 2020.

By letter dated 22 December 2020, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by the IQWiG was submitted to the G-BA on 21 January 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 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 26 January 2021, and the proposed resolution was approved.

At its session on 4 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	10 September 2019	Determination of the appropriate comparator therapy
Working group Section 35a	16 December 2020	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	21 December 2020	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	7 January 2021 20 January 2021	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee on	26 January 2021	Concluding discussion of the draft resolution

Medicinal Products		
Plenum	4 February 2021	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 4 February 2021

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

Prof. Hecken