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 Inebilizumab (neuromyelitis optica spectrum disorders, anti-aquaporin-4 IgG seropositive)

of 19 January 2023

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and 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 active ingredient inebilizumab 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 August 2022. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 13 July 2022.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 November 2022 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of inebilizumab 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 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 inebilizumab.

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 Inebilizumab (Uplizna) in accordance with the product information

Uplizna is indicated as monotherapy for the treatment of adult patients with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 immunoglobulin G (AQP4-IgG) seropositive.

Therapeutic indication of the resolution (resolution of 19.01.2023):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 immunoglobulin G (AQP4-IgG) seropositive

Appropriate comparator therapy for inebilizumab as monotherapy:

Therapy according to doctor's instructions

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

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.

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

3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

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

on 1. The active ingredient eculizumab is approved for the treatment of adults with neuromyelitis optica spectrum disorders (NMOSD) who are positive for anti-aquaporin-4 (AQP4) antibodies and show a relapsing disease course. In addition, the active ingredient satralizumab is approved for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adults and adolescents aged 12 years and older who are anti-aquaporin-4 IgG (AQP4 IgG) seropositive.

on 2. Non-medical measures as sole appropriate comparator therapy are not considered in the present therapeutic indication.

on 3. In the therapeutic indication under consideration here, the following resolutions of the G-BA are available:

- Satralizumab (resolution according to Section 35a SGB V of 06.01.2022)

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic 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 according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a paragraph 7 SGB V.

According to the S2k guideline of the German Society of Neurology, the active ingredients eculizumab and rituximab should be used primarily in adults as part of long-term NMOSD therapy, while azathioprine and mycophenolate mofetil can be continued in stably adjusted patients or used if contraindicated. Tocilizumab has a second-line recommendation only.

The active ingredients azathioprine, mycophenolate mofetil, rituximab and tocilizumab are not approved for the present indication. The active ingredient eculizumab is only approved for NMOSD patients who are positive for anti-aquaporin-4 antibodies and show a relapsing disease course[2]. The active ingredient satralizumab is approved for adults and adolescents aged 12 years and older with NMOSD who are anti-aquaporin-4 IgG seropositive. Therefore, there is a discrepancy between medicinal products approved in the indication and those used in health care/ recommended in guidelines. The G-BA therefore determines a therapy according to the doctor's instructions as an appropriate comparator therapy.

Change of the appropriate comparator therapy

[2] approved from 2nd flare

So far, for adult patients with NMOSD who are anti-aquaporin-4 IgG seropositive, satralizumab has not been considered as part of the appropriate comparator therapy. In the opinion of the clinicians involved in the written statement procedure, this no longer corresponds to the current medical treatment situation. Even though satralizumab is not yet mentioned in the S2k guideline of the DGN, which is currently being revised, its importance in clinical practice should not be neglected. In addition, the non-approved active ingredients azathioprine and mycophenolate mofetil have only a subordinate significance in therapy according to the assessment of the clinicians and in accordance with the recommendation of the S2k guideline of the DGN. In patients who are stable on azathioprine or mycophenolate mofetil , therapy should be continued. If relevant comorbidities or contraindications speak against the use of the monoclonal antibodies (rituximab, eculizumab, satralizumab), the active ingredients azathioprine and mycophenolate mofetil can continue to be used in new settings.

Overall, the G-BA considers it appropriate to adapt the appropriate comparator therapy to the generally recognised state of medical knowledge. Accordingly, the active ingredient satralizumab is included as a therapy option in the therapy according to the doctor's instructions as a specific appropriate comparator therapy.

In a clinical study, the active ingredients azathioprine, eculizumab, mycophenolate mofetil, rituximab and satralizumab should be available for long-term immunosuppressive therapy.

However, the possibility of the off-label use of the active ingredients in a clinical study does not allow any conclusions to be drawn about their appropriateness in the off-label use in the standard care of insured persons in the SHI system. Such an assessment would be reserved for the decision according to Section 35c SGB V. This does not affect an off-label prescription in specific cases according to the criteria of the established case law of the Federal Social Court on off-label use not regulated in the Pharmaceuticals Directive.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5, Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

For adults with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 immunoglobulin G (AQP4-IgG) seropositive, the additional benefit is not proven.

Justification:

For adults with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 immunoglobulin G (AQP4-IgG) seropositive, there are no direct comparative studies of inebilizumab versus the appropriate comparator therapy. The pharmaceutical company therefore presents an adjusted indirect comparison with satralizumab via the bridge

comparator placebo. For inebilizumab he uses the N-MOmentum study and for satralizumab the SAkuraStar study.

The N-MOmentum study is a pivotal, double-blind, multicentre phase II/III RCT comparing inebilizumab and placebo, which included adults with AQP4 IgG-seropositive NMOSD with at least 1 acute flare in the previous year or at least 2 flares within the last 2 years requiring emergency treatment.

The SAkuraStar study is a pivotal, double-blind, multicentre phase III RCT with subsequent open-label extension phase comparing satralizumab and placebo, which included adults with AQP4 IgG-seropositive or -seronegative NMOSD with at least 1 flare in the previous year.

In the clinical care of NMSOD, the active agents eculizumab, rituximab and satralizumab play a crucial role. For the implementation of the therapy determined as the appropriate comparator therapy according to the doctor's instructions in a clinical study, it is expected that a selection from these active ingredients as well as azathioprine and mycophenolate mofetil, if applicable, should be available in the sense of a multi-comparator study.

Irrespective of whether the sole comparison with satralizumab can be regarded at all as the implementation of therapy according to doctor's instructions, it must be stated in the present case that for the patients in the SakuraStar study, however, it cannot be assumed with sufficient certainty on the basis of the available information that satralizumab is the only suitable therapy according to doctor's instructions. For example, no information is available on the active ingredients used to date in the patients, so that it cannot be assessed whether other therapy options (such as rituximab and eculizumab) are the appropriate therapy for the patients in the SakuraStar study according to the doctor's instructions at the time of enrolment.

The indirect comparison presented, which was carried out against only one comparator (satralizumab), is therefore not assessed as suitable for deriving an additional benefit compared to the therapy according to the doctor's instructions.

Therefore, no data relevant for the benefit assessment of inebilizumab 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 Uplizna with the active ingredient inebilizumab. Inebilizumab is approved as monotherapy for the treatment of adult patients with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 immunoglobulin G (AQP4 IgG) seropositive.

The appropriate comparator therapy was determined by G-BA to be a therapy according to doctor's instructions.

Due to the lack of directly comparative studies, the pharmaceutical company submits an adjusted indirect comparison with satralizumab via the bridge comparator placebo for the benefit assessment. For inebilizumab he uses the N-MOmentum study and for satralizumab the SAkuraStar study.

For the implementation of the therapy determined as the appropriate comparator therapy according to the doctor's instructions in a clinical study, it is expected that a selection from the active ingredients azathioprine, eculizumab, mycophenolate mofetil, rituximab and satralizumab should be available in the sense of a multi-comparator study. The presented

adjusted indirect comparison with satralizumab as the only comparator is not considered suitable to derive an additional benefit compared to therapy according to doctor's instructions.

Therefore, no data relevant for the benefit assessment of inebilizumab 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. 460 – 980) is based on the target population in statutory health insurance (SHI). The data follow IQWiG's presentations and calculations.

The meta-analysis calculated by the pharmaceutical company limits the uncertainty range more compared to the uncertainty range based on the prevalence estimators of the individual studies. Overall, a broader range for the target population therefore seems more appropriate in order to sufficiently address the existing uncertainty of the prevalence data with reference to Germany.

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 Uplizna (active ingredient: inebilizumab) at the following publicly accessible link (last access: 22 September 2022):

https://www.ema.europa.eu/en/documents/product-information/uplizna-epar-product-information_en.pdf

Treatment with inebilizumab should only be initiated and monitored by specialists be performed by a specialist in neurology or a specialist in neurology and psychiatry with experience in the treatment of neuromyelitis optica spectrum disorders.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (incl. patient identification card). The patient identification card contains, in particular, information and warnings about the risk of infections.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 January 2023).

Treatment period:

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 varies from patient to patient 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.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Inebilizumab	continuously, 1 x every 6 months	2.0	1	2.0
Appropriate comparator therapy				
Therapy according to doctor's instructions[3]				
Eculizumab	continuously, 1 x every 12-16 days	22.8 - 30.4	1	22.8 - 30.4
Satralizumab	continuously, 1 x every 28 days	13.0	1	13.0

Consumption:

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments, e.g., because of side effects or comorbidities, are not taken into account when calculating the annual treatment costs.

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					
Inebilizumab	300 mg	300 mg	3 x 100 mg	2	6 x 100 mg
Appropriate comparator therapy					
Therapy according to doctor's instructions[3]					
Eculizumab	1200 mg	1200 mg	4 x 300 mg	22.8 - 30.4	91.2 - -121.6 x 300 mg
Satralizumab	120 mg	120 mg	1 x 120 mg	13.0	13.0 x 120 mg

[3] In a clinical study, the active ingredients azathioprine, eculizumab, mycophenolate mofetil, rituximab and satralizumab should be available for long-term immunosuppressive therapy. However, the active ingredients azathioprine, mycophenolate mofetil and rituximab are not approved for the present indication, which is why these costs are not presented.

Costs:

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

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Inebilizumab 100 mg	3 CIS	€ 64,590.72	€ 1.77	€ 6,318.00	€ 58,270.95
Appropriate comparator therapy[3]					
Eculizumab 300 mg	1 CIS	€ 5,877.85	€ 1.77	€ 574.44	€ 5,301.64
Satralizumab 120 mg	3 SFI	€ 26,804.99	€ 1.77	€ 2,618.65	€ 24,184.57
Abbreviations: CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection					

LAUER-TAXE® last revised: 1 January 2023

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g., regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population" were used as a basis (average body height: 1,72 m; average body weight: 77 kg).

Premedication

According to the product information, premedication with a corticosteroid e.g., methylprednisolone 80-125 mg IV or equivalent is necessary approx. 30 min before the application of inebilizumab. Therefore, the costs for methylprednisolone with the dosage for premedication given in the product information are presented as an example. The costs may vary depending on the corticosteroid used and the dosage form.

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	Treatment days/ year	Costs/ patient/ year
Medicinal product to be assessed: Inebilizumab							
Premedication[4]							
Methylprednisolone 80 mg - 125 mg, IV	3 PII x 32 mg 1 PII x 125 mg	€ 21.31 € 23.97	€ 1.77 € 1.77	€ 2.99 € 2.97	€ 16.55 € 19.23	2.0 2.0	€ 33.10 € 38.46
Dimetindene IV 1 mg/10 kg	5 x 4 mg SFI	€ 23.67	€ 1.77	€ 5.81	€ 16.09	2.0	€ 12.87
Paracetamol[5,6] 500 – 1000 mg, oral	10 TAB x 500 mg 10 TAB x 1,000 mg	€ 2.96 € 3.32	€ 0.15 € 0.17	€ 0.13 € 0.14	€ 2.68 € 3.01	2.0	€ 0.54 € 0.60
Abbreviations: TAB = tablets, SFI = solution for injection, PII = powder and solvent for solution for injection or infusion							

Diagnosis of tuberculosis

For the medicinal product under assessment, inebilizumab, costs are regularly incurred for examining for both active and inactive ("latent") tuberculosis infections. The costs presented are a blood test (quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens specific for Mycobacterium tuberculosis-complex (except BCG)). In addition, a chest radiograph is usually required to detect pulmonary tuberculosis. The tuberculin skin test is not presented due to lack of sensitivity and specificity as well as the possibility of "sensitisation". These examinations are not required when using the appropriate comparator therapy .

Diagnosis of chronic hepatitis B and C

[4] According to the product information for Uplizna (last revised: June 2022)

[5] The dosage of 650 mg paracetamol in premedication stated in the product information cannot be achieved by tablets. Because of this, a dosage of 500 - 1,000 mg is used.

[6] Fixed reimbursement rate. Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Section 12, paragraph 7, of the AM-RL (information as concomitant medication in the product information of the prescription medicinal product) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5a SGB V, when a non-prescription medicinal product is dispensed invoiced according Section 300, a medicinal product sale price applies to the insured person in the amount of the sale price of the pharmaceutical company plus the surcharges according to Sections 2 and 3 of the Pharmaceutical Price Ordinance in the valid version of 31 December 2003.

Patients should be tested for HBV infection before starting treatment with inebilizumab. These examinations are not to be carried out regularly when using the appropriate comparator therapy. For the diagnosis of suspected chronic hepatitis B, sensibly coordinated steps are required[7,8]. A step-by-step serological diagnosis initially consists of the examination of HBs antigen and anti-HBc antibodies. If both are negative, a past HBV infection can be excluded. If HBs antigen is positive, an active HBV infection is detected.

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Medicinal product to be assessed				
Inebilizumab				
Tuberculosis	Quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens (at least ESAT-6 and CFP-10) specific for Mycobacterium tuberculosis-complex (except BCG) (GOP 32670)	1	€ 58.00	€ 58.00
	Chest radiograph (GOP 34241)	1	16.45	€ 16.45
Hepatitis B (HBV)	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50
	Anti-HBs antibody (GOP 32617)[9]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV-DNA (GOP 32817)	1	€ 89.50	€ 89.50
Hepatitis C (HCV)	HCV-RNA (GOP 32823)	1	€ 89.50	€ 89.50
	HCV antibody immunoblot (GOP 32661)	1	€ 44.10	€ 44.10
	HCV antibodies (GOP 32618)	1	€ 9.80	€ 9.80

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.

[7] "Update of the S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011" http://www.dgvs.de/fileadmin/user_upload/Leitlinien/Hepatitis_B/Leitlinie_Hepatitis_B.pdf

[8] „S3-Leitlinie Prophylaxe, Diagnostik und Therapie der Hepatitis-C-Virus HCV)-Infektion AWMF-Register-Nr.: 021/012" https://register.awmf.org/assets/guidelines/021-012l_S3_Hepatitis-C-Virus_HCV-Infektion_2018-07.pdf

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

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 € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the 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 purchase 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.

2.5 Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with Inebilizumab

According to Section 35a, paragraph 3, sentence 4, the Federal Joint Committee shall designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

In accordance with Section 2, paragraph 1, sentence 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), only medicinal products containing active ingredients whose effects are not generally known in medical science at the time of initial marketing authorisation are to be considered within the framework of the designation of medicinal products with new active ingredients that can be used in a combination therapy. According to Section 2, paragraph 1, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), a medicinal product with a new active ingredient is considered to be a medicinal product with a new active ingredient for as long as there is dossier protection for the medicinal product with the active ingredient that was authorised for the first time.

The designation of the combination therapies is based solely on the specifications according to Section 35a, paragraph 3, sentence 4. The G-BA does not conduct a substantive review based on the generally recognised state of medical knowledge. Thus, the designation is not associated with a statement as to the extent to which a therapy with the designated medicinal product with new active ingredient in combination with the medicinal product to be assessed corresponds to the generally recognised state of medical knowledge.

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 8 February 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 13 July 2022, the pharmaceutical company submitted a dossier for the benefit assessment of inebilizumab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 19 July 2022 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products 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 inebilizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 October 2022, and the written statement procedure was initiated with publication on the G-BA website on 1 November 2022. The deadline for submitting written statements was 22 November 2022.

The oral hearing was held on 5 December 2022.

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

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 10 January 2023, and the proposed resolution was approved.

At its session on 19 January 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	8 February 2022	Determination of the appropriate comparator therapy
Working group Section 35a	30 November 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	5 December 2022	Conduct of the oral hearing
Working group Section 35a	14 December 2022 4 January 2023	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	10 January 2023	Concluding discussion of the draft resolution
Plenum	19 January 2023	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 19 January 2023

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

Prof. Hecken