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 Mepolizumab (new therapeutic indication: chronic rhinosinusitis with nasal polyps (CRSwNP))

of 19 May 2022

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 is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient mepolizumab (Nucala) was listed for the first time on 1 February 2016 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 12 November 2021, mepolizumab received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2 number 2 letter a to Regulation (EC) No. 1234/2008 of the European Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7).

On 24 November 2021, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-

BA on the active ingredient mepolizumab with the new therapeutic indication (chronic rhinosinusitis with nasal polyps).

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 March 2022, 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 mepolizumab 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 addendum to the benefit assessment prepared by 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 mepolizumab.

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 Mepolizumab (Nucala) in accordance with the product information

Nucala is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.

Therapeutic indication of the resolution (resolution of 19 May 2022):

See new therapeutic indication according to marketing authorisation

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control

Appropriate comparator therapy for mepolizumab:

- Dupilumab or omalizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate)

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

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.
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. In the therapeutic indication for the treatment of CRSwNP, corticosteroids—are approved: the active ingredients budesonide and mometasone furoate as intranasal (topical) corticosteroids (INCS) as well as (oral) corticosteroids (OCS). For short-term intervention on demand, antibiotics and analgesics are covered by the marketing authorisation. In addition, the biologic agents dupilumab, omalizumab and mepolizumab are approved for the treatment of CRSwNP.

on 2. A sole non-medicinal treatment cannot be considered in the therapeutic indication. Surgical measures represent an intervention on demand.

on 3. For chronic rhinosinusitis with nasal polyposis (CRSwNP), a resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V of 14 May 2020 is available for dupilumab.

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 therapeutic indication. 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.

In the overall assessment, a positive recommendation for INCS can be derived from the aggregated evidence. INCS are superior to both treatment with placebo and "no treatment". CRSwNP is a chronic disease with a fluctuating course. Patients who have failed previous therapies with systemic corticosteroids and/or surgery, or who have an appropriate contraindication or ineligibility, are generally suitable for medicinal therapy with INCS at the

time of initiation of mepolizumab treatment, whereas invasive treatment options alone are more likely to be an option on a case-by-case basis, if needed. The use of saline nasal rinses is also recommended on the basis of evidence.

OCS are approved in the therapeutic indication relevant here, but the evidence for the long-term use of OCS for standard/ maintenance treatment of nasal polyps - especially beyond flare therapy - is to be regarded as rather low; uniform positive recommendations for long-term OCS use are not available on the basis of the aggregated evidence. In fact, national and international guidelines conclude that systemic glucocorticoids should only be considered as "flare therapy" in combination with INCS maintenance treatment. Antibiotics as well as analgesics are not considered as standard or maintenance treatment, as these are only indicated for short-term treatment on demand (in case of complications, infections). Based on these considerations, the G-BA assumes that patients receive further supportive measures (e.g. nasal rinses) as well as a therapy for complications compliant with marketing authorisation (if necessary, short-term antibiotics, short-term systemic glucocorticoids as part of a flare therapy) in the context of a clinical study.

In the therapeutic indication for CRSwNP, a first biologic agent, dupilumab, has been approved since October 2019; the marketing authorisation of omalizumab followed in July 2020. By resolution of May 2020, the G-BA derived an indication of a considerable additional benefit for dupilumab compared to maintenance treatment with intranasal corticosteroids (in this case mometasone furoate), while omalizumab did not undergo an early benefit assessment according to Section 35a SGB V. High-quality guidelines are currently only available for 2020 (EPOS 2020[2]). Although the significance of dupilumab and omalizumab cannot be assessed conclusively in the indication to be assessed here for patients with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control due to the lack of current guidelines, taking into account the aggregated evidence based on systematic reviews and guidelines, the comparative benefit assessment of dupilumab versus intranasal mometasone furoate as well as the written and oral statements of the scientific-medical societies for adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control, overall a further development in the therapy algorithm of severe, not adequately controlled CRSwNP can be derived.

Change of the appropriate comparator therapy

For the patient collective with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control, the sufficiently safe recommendation for add-on therapy with dupilumab or omalizumab can be derived on the basis of the aggregated evidence at this time. Based on the written and oral statements of the scientific-medical societies presented in the proceedings, it is concluded that for this patient collective, therapy with intranasal corticosteroids and/or surgery alone is no longer an option due to the severity of the disease or the course of the disease with frequent recurrences. Thus,

[2] Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology 2020;58(Suppl 29):1-464.

the therapeutic indication for the biologic agent mepolizumab includes those patients for whom initial therapy with biologic agents is generally indicated.
In summary, the G-BA comes to the conclusion that, taking into account the aforementioned aspects and against the background of the considerable additional benefit of dupilumab compared to the basic therapy with intranasal corticosteroids that has been considered the therapy standard to date, it is considered appropriate to adjust the appropriate comparator therapy at this time. For omalizumab, there are also high-quality RCTs from the marketing authorisation, the results of which, in combination with the available aggregated evidence, support the use of omalizumab in the indication to be assessed here at the present time. In the overall assessment, the GBA concludes that for mepolizumab as add-on therapy to intranasal corticosteroids in adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control, dupilumab or omalizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate), is considered appropriate. The above-mentioned options dupilumab and omalizumab are considered equally appropriate comparator therapies for the add-on therapy; within the intranasal corticosteroids, budesonide and mometasone furoate are equally appropriate therapeutic alternatives.

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

2.1.3 Extent and probability of the additional benefit

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

Adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control

For adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control, the additional benefit of mepolizumab as an add-on therapy compared with the appropriate comparator therapy is not proven.

Justification:

The pharmaceutical company submitted the results of the double-blind, randomised SYNAPSE study with analyses at week 52 to prove the additional benefit of mepolizumab.

The SYNAPSE study is a randomised, double-blind phase III study comparing mepolizumab versus placebo, each in an add-on design to maintenance treatment with intranasal mometasone furoate. Adults with at least two symptoms of chronic rhinosinusitis persisting for ≥ 12 weeks with recurrent bilateral nasal polyps and at least one nasal polyp surgery within

the last 10 years prior to the time of enrolment were enrolled in the study. The adults enrolled in the study also had to have at least 8 weeks of treatment with intranasal corticosteroids (INCS) before screening.

In the SYNAPSE study, a total of 414 patients[3] randomised (1:1) to 52 weeks of treatment with mepolizumab (N = 206) or placebo (N = 201). Primary endpoints were mean change in VAS nasal obstruction at weeks 49-52 and change in nasal polyp score at week 52. In addition, patient-relevant endpoints of the endpoint categories of morbidity, health-related quality of life and side effects were collected.

Change of the appropriate comparator therapy

Against the background of the further development of medical knowledge in severe CRSwNP, the G-BA considers it appropriate to change the appropriate comparator therapy with this resolution (see also comments on the appropriate comparator therapy). According to this amendment, basic therapy with INCS alone is no longer the appropriate comparator therapy for the mepolizumab indication to be assessed. The comparison of mepolizumab + mometasone furoate versus placebo + mometasone furoate is therefore no longer relevant to the present assessment. Since the SYNAPSE study does not provide data compared to the currently determined appropriate comparator therapy, the study cannot be used to derive the additional benefit of mepolizumab. Nevertheless, the results of the SYNAPSE study (analyses without replacement strategy, taking into account the IQWiG addendum) are presented additionally below, as they show a comparison of mepolizumab + mometasone furoate versus placebo + mometasone furoate:

Mortality

In the SYNAPSE study, no deaths occurred until week 52.

Morbidity

For the endpoints on symptomatology (nasal obstruction, nasal discharge and loss of sense of smell, each assessed by a visual analogue scale (VAS)), the percentage of patients with an improvement of ≥ 1.5 points at week 52 showed a statistically significant difference in the benefit of mepolizumab + mometasone furoate versus placebo + mometasone furoate (nasal obstruction VAS: RR 0.87 [95% CI 0.75; 0.98] p value = 0.022; nasal discharge VAS: RR 0.87 [95% CI 0.75; 0.98] p value = 0.022; loss of sense of smell VAS: RR 0.73 [95% CI 0.57; 0.95] p value = 0.007).

For the endpoint SNOT-22 (symptomatology and social/emotional consequences of rhinosinusitis), a statistically significant advantage for mepolizumab + mometasone furoate

[3] Of the 414 randomised patients, 7 were randomised in error and subsequently excluded.

over placebo + mometasone furoate can also be derived for the percentage of patients with a relevant improvement in the total score by ≥ 16.5 points at week 52 (RR 0.80 [95% CI 0.69; 0.93] p value < 0.001).

For impairment of daily activities due to the disease, the SYNAPSE study showed a statistically significant difference to the advantage of mepolizumab + mometasone furoate over placebo + mometasone furoate. However, the 95% confidence interval of the standardised mean difference (Hedges' g) is not completely outside the irrelevance range of -0.2 to 0.2. Thus, it cannot be inferred that the observed effect is relevant.

The avoidance of repeated surgeries of nasal polyps after an initial surgery is a central therapeutic goal due to procedure-specific complications, among other things. In the present indication, the endpoint of nasal polyp surgeries (NP-OP) is basically a patient-relevant endpoint. There are different opinions on the suitability of the operationalisation of the endpoint in the present study.

Health-related quality of life

Health-related quality of life was assessed in the present study using the SF-36. For the SF-36, the physical component score (PCS) and the mental component score (MCS) are considered individually. For the SF-36, the percentage of patients with an improvement in the total score by ≥ 9.4 points (PCS) and ≥ 9.6 points (MCS) (15% of the scale range) at week 52 showed a statistically significant difference for the benefit of mepolizumab + mometasone furoate compared with placebo + mometasone furoate (PCS: RR 0.55 [95% CI 0.39; 0.76] p value < 0.001; MCS: RR 0.68 [95% CI 0.47; 0.99] p value = 0.03).

Side effects

There was no statistically significant difference between the treatment arms for the endpoints AEs, SAEs and discontinuation due to AEs.

2.1.4 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the benefit assessment of mepolizumab finds its legal basis in Section 35a paragraph 3 sentence 4 SGB V. Thereafter, the G-BA may limit the validity of the resolution on the benefit assessment of a medicinal product. In the present case, the limitation is justified by objective reasons consistent with the purpose of the benefit assessment according to Section 35a paragraph 1 SGB V.

The pharmaceutical company has submitted the results of the double-blind, randomised, direct comparator SYNAPSE study with analyses at week 52 to demonstrate the additional benefit of mepolizumab for adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide

adequate disease control. In the dossier, the pharmaceutical company derives the additional benefit of mepolizumab compared to the originally determined appropriate comparator therapy of the intranasal corticosteroid mometasone furoate.

The G-BA considers it appropriate to change the appropriate comparator therapy at this point in time and to adapt it to the current state of medical knowledge (see also 2.1.2 “Change of the appropriate comparator therapy”).

Since the appropriate comparator therapy was adapted during the ongoing process, the pharmaceutical company is given the opportunity to submit a new benefit assessment dossier to the G-BA, taking into account the current appropriate comparator therapy. The aim of this assessment is to be able to make statements about the additional benefit of mepolizumab compared to therapy with dupilumab or omalizumab for adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.

For the renewed benefit assessment after the expiry of the deadline, the dossier should present a comparison of mepolizumab with the corresponding appropriate comparator therapy. For this purpose, the G-BA considers a limitation for the resolution until 1 December 2022 to be appropriate.

A change in the limitation can generally be granted if it is justified and clearly demonstrated that the limitation is insufficient or too long. In accordance with Section 3 paragraph 7 AM-NutzenV in conjunction with Chapter 5 Section 1, paragraph 2, number 6 VerfO, the procedure for the benefit assessment of the medicinal product with the active ingredient mepolizumab recommences when the deadline has expired. For this purpose, the pharmaceutical company must submit a dossier to the G-BA at the latest on the date of expiry to prove the extent of the additional benefit of mepolizumab (Section 4, paragraph 3, number 5 AM-NutzenV in conjunction with Chapter 5 Section 8, number 5 VerfO). If the dossier is not submitted or is incomplete, the G-BA may determine that an additional benefit is considered as being not proven. The possibility that a benefit assessment for the medicinal product with the active ingredient mepolizumab can be carried out at an earlier point in time due to other reasons (cf. Chapter 5, Section 1 paragraph 2, nos. 2 – 4 VerfO) remains unaffected hereof.

2.1.5 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient mepolizumab. The therapeutic indication assessed here is as follows: "as add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe

CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control".

For adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control, the G-BA has determined dupilumab or omalizumab, each in combination with intranasal corticosteroids (budesonide or mometasone furoate) as an appropriate comparator therapy.

However, the dossier did not provide any comparator data for the assessment of the additional benefit of add-on therapy with mepolizumab compared to the appropriate comparator therapy dupilumab or omalizumab, in each case in combination with intranasal corticosteroids (budesonide or mometasone furoate), which are suitable for the question of the benefit assessment.

In the overall assessment, an additional benefit is therefore not proven and the resolution is limited until 1 December 2022.

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

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

The data from the previous resolution of the G-BA in the therapeutic indication for CRSwNP from 2020[4] are used as a basis for the information. As already stated in the previous resolution in the CRSwNP, the stated patient numbers are, however, subject to uncertainties, since the pharmaceutical company, on the one hand, restricts itself to patients who have already been prescribed INCS and, on the other, takes a time interval of 4 quarters between the last documented diagnosis and a previous paranasal sinus operation as a basis. There is an underestimation in the overall assessment.

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 Nucala (active ingredient: mepolizumab) at the following publicly accessible link (last access: 17 February 2022):
https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf

Treatment with mepolizumab should only be initiated and monitored by doctors experienced in CRSwNP therapy.

[4] Resolution of the GBA pursuant to Section 35a SGB V of 14 May 2020 for the active ingredient dupilumab.

Alternative treatments may be considered for patients who do not respond to treatment for CRSwNP after 24 weeks. Some patients with an initial partial response may benefit from continued treatment beyond 24 weeks.

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 May 2022).

Treatment period:

The annual treatment costs shown refer to the first year of treatment.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Mepolizumab	Continuously, 1 x every 28 days	13.0	1	13.0
Intranasal corticosteroids				
Budesonide	Continuously, 2 x daily	365	1	365
Mometasone	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Dupilumab	Continuously, 1 x every 14 days	26.1	1	26.1
Omalizumab	Continuously, every 14 days – every 28 days	13.0 – 26.1	1	13.0 – 26.1
Intranasal corticosteroids				
Budesonide	Continuously, 2 x daily	365	1	365

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Mometasone	Continuously, 1 x daily	365	1	365

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.

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.

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the calculation of omalizumab consumption, doses were based on body weight (bw) on the basis of average body measurements (average body height: 1,72 m; average body weight: 77 kg). This results in a body surface area of 1.90 m² (calculated according to Du Bois 1916)[5].

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					
Mepolizumab	100 mg	100 mg	1 x 100 mg	13.0	13.0 x 100 mg
Intranasal corticosteroids					
Budesonide	0.1 mg – 0.2 mg	0.2 mg – 0.4 mg	4 x 0.05 mg – 8 x 0.05 mg	365	1.460 strokes 0.05 mg each – 2,920 strokes 0.05 mg each

[5] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Mometasone	0.1 mg – 0.4 mg	0.1 mg – 0.4 mg	2 x 0.05 mg – 8 x 0.05 mg	365	730 strokes 0.05 mg each – 2,920 strokes 0.05 mg each
Appropriate comparator therapy					
Dupilumab	300 mg	300 mg	1 x 300 mg	26.1	26.1 x 300 mg
Omalizumab	150 mg – 600 mg	150 mg – 600 mg	1 x 150 mg – 4 x 150 mg	13.0 – 26.1	13.0 x 150 mg – 104.4 x 150 mg
Intranasal corticosteroids					
Budesonide	0.1 mg – 0.2 mg	0.2 mg – 0.4 mg	4 x 0.05 mg – 8 x 0.05 mg	365	1,460 strokes 0.05 mg each – 2,920 strokes 0.05 mg each
Mometasone	0.1 mg – 0.4 mg	0.1 mg – 0.4 mg	2 x 0.05 mg – 8 x 0.05 mg	365	730 strokes 0.05 mg each – 2,920 strokes 0.05 mg each

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					
Mepolizumab 100 mg	3 SFI	€ 3,731.89	€ 1.77	€ 0.00	€ 3,730.12
Budesonide 0.05 mg[6]	2 NDS (2 x 200 ED)	€ 30.83	€ 1.77	€ 1.55	€ 27.51
Mometasone 0.05 mg[6]	2 NAS (2 x 140 strokes)	€ 26.30	€ 1.77	€ 1.19	€ 23.34
Appropriate comparator therapy					
Dupilumab 300 mg	6 SFI	€ 4,337.25	€ 1.77	€ 244.41	€ 4,091.07
Omalizumab 150 mg	10 IFE	€ 5,019.23	€ 1.77	€ 283.36	€ 4,734.10
Budesonide 0.05 mg[6]	2 NDS (2 x 200 ED)	€ 30.83	€ 1.77	€ 1.55	€ 27.51
Mometasone 0.05 mg[6]	2 NAS (2 x 140 strokes)	€ 26.30	€ 1.77	€ 1.19	€ 23.34
Abbreviations: IFE = solution for injection in a pre-filled syringe; SFI = solution for injection, NDS = nasal dosing spray, NAS = nasal spray					

LAUER-TAXE® last revised: 1 May 2022

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.

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

[6] Fixed reimbursement rate

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

On 24 November 2021, the pharmaceutical company submitted a dossier for the benefit assessment of mepolizumab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 29 November 2021 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient mepolizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 25 February 2022, and the written statement procedure was initiated with publication on the website of the G-BA on 1 March 2022. The deadline for submitting written statements was 22 March 2022.

The oral hearing was held on 11 April 2022.

By letter dated 12 April 2022, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 29 April 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 May 2022, and the proposed resolution was approved.

At its session on 19 May 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	7 July 2020	Determination of the appropriate comparator therapy
Working group Section 35a	5 April 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	11 April 2022	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents

Working group Section 35a	20 April 2022 3 May 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal products	10 May 2022	Concluding discussion of the draft resolution
Plenum	19 May 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 19 May 2022

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

Prof. Hecken