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: eosinophilic granulomatosis with polyangiitis)

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, GlaxoSmithKline GmbH & Co. KG 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 Commission of 24 November 2008 concerning the examination of amendments 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 eosinophilic granulomatosis with polyangiitis.

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 treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

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

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA)

The appropriate comparator therapy for mepolizumab as an add-on treatment is:

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

- A patient-individual therapy, taking into account the severity of the disease (organ or life-threatening manifestation), the symptomatology, the treatment phase and the course of the disease

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 addition to mepolizumab, systemic corticosteroids (prednisolone, prednisone and methylprednisone) are approved for the treatment of EGPA. The corticosteroids mentioned are approved for adults as well as for adolescents and children.

on 2. Plasmapheresis can be considered as a non-medicinal treatment.

on 3. For the treatment of EGPA, there are no resolutions from the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V.

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.

The robust evidence on medicinal treatment options in the present therapeutic indication is limited. In the absence of randomised controlled studies, recommendations for the treatment of EGPA are mainly based on the data on other

ANCA-associated vasculitides (AAV) and the clinical experience of experts in the field[2,3,4,5].

Guidelines distinguish between therapy for remission induction and subsequent remission-maintenance treatment. In addition, the respective treatment options essentially depend on the severity grade of the disease, i.e. whether or not an organ or life-threatening stage of the disease is present. Remission is normally induced using corticosteroids, which should initially be used in high doses, depending on the severity of the disease. The corticosteroids are also combined with immunosuppressive therapy, if necessary. Especially in the case of life-threatening or organ-damaging manifestations of EGPA, the use of cyclophosphamide and, under certain circumstances, rituximab is recommended.

The lowest possible dosage of oral corticosteroids (OCS) is aimed for in remission-maintenance treatment to avoid corresponding side effects. Immunosuppressive therapy is also recommended in this treatment phase, if necessary.

Cyclophosphamide, leflunomide, mycophenolate mofetil, methotrexate, azathioprine and rituximab are listed as possible active ingredients for immunosuppressive therapy of EGPA. Whether immunosuppressants are used and if so, which ones, depends not only on the severity and the treatment phase but also on the type of symptoms, in particular whether vasculitic or eosinophilic manifestations are predominant.

Furthermore, the course of the disease is taken into account in the treatment decision, i.e. whether it is a newly occurring, (repeatedly) relapsing or refractory disease. According to the German S1 guideline[2] non-severe recurrences can be treated by increasing the dose of OCS alone or also of immunosuppressive maintenance treatment. In the case of a recurrent, non-severe relapse, a dose increases of the existing remission-maintenance treatment or, if necessary, a change to another immunosuppressive substance should be made. The treatment of refractory or repeatedly relapsing EGPA is carried out on a patient-individual basis according to the decision of the doctor experienced in the treatment of vasculitides, taking into account all available therapy options described above.

In the overall assessment, for patients aged 6 years and older with relapsing-remitting or refractory EGPA, a patient-individual therapy, taking into account the severity of the disease (organ or life-threatening manifestation), the symptomatology, the treatment phase and the course of the disease is considered appropriate, in which corticosteroids should be combined with immunosuppressive therapy, if necessary, depending on the severity of the disease, the treatment phase and the course of the disease.

Only corticosteroids are approved in the present therapeutic indication. The immunosuppressants mentioned in guidelines - cyclophosphamide, leflunomide, mycophenolate mofetil, methotrexate, azathioprine and rituximab - are not approved

[2] Schirmer et al. for the German Society for Rheumatology (DGRh). S1 Guideline diagnostics and therapy of ANCA-associated vasculitis. Z Rheumatol 2017; 76 (Suppl 3): pp. 77–104

[3] Yates M, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis 2016;75(9):1583-1594.

[4] Mendel A, et al. CanVasc consensus recommendations for the management of antineutrophil cytoplasm antibody-associated vasculitis: 2020 update. J Rheumatol 2021;48(4):555-566.

[5] Chung SA, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Rheumatol 2021;73(8):1366-1383.

for the treatment of EGPA, but are considered suitable comparators in the context of patient-individual therapy.

However, the possibility of the off-label use of the active ingredients mentioned 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.

Plasmapheresis is not considered a regular part of patient-individual therapy, as it can only be considered as acute therapy for severe renal function impairment due to active rapid progressive glomerulonephritis or pulmonary haemorrhage. In addition, the significance of plasmapheresis in the therapy of AAV is currently unclear.

There is no specific evidence for the treatment of children aged 6 years and older and adolescents with EGPA. The European paediatric guideline[6] refers to the general procedure for vasculitis in children for the present therapeutic indication. Taking into account the written statements of the scientific-medical societies on the determination of the appropriate comparator therapy, it can be deduced for children with EGPA that the therapy strategies are oriented towards those of adulthood. Accordingly, it is considered justified overall not to determine an appropriate comparator therapy for children and adolescents that differs from that for adults with EGPA.

It should be possible to adapt the therapy to the respective needs of the patients in both study arms. Therapy adjustment may include dosage adjustments as well as changes of therapy or therapy initiation for the treatment of new symptoms or for the deterioration of existing symptoms.

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:

The additional benefit is not proven for patients 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

Justification:

The pharmaceutical company submits the MIRRA study for the benefit assessment according to Section 35a SGB V. This is a randomised, controlled, double-blind study comparing mepolizumab with placebo in addition to oral glucocorticoid (OCS) and immunosuppressant, if any, in adults with EGPA diagnosed at least six months ago. EGPA diagnosis was based on history or presence of asthma and eosinophilia and at least two other EGPA characteristics.

[6] De Graeff N, et al. European consensus-based recommendations for the diagnosis and treatment of rare paediatric vasculitides - the SHARE initiative. Rheumatology (Oxford) 2019;58(4):656-671

Patients with active disease as well as those with a history of relapsed[7] or refractory[8] disease were included. 71% in the comparator arm and 54% in the mepolizumab arm had active EGPA at the start of the study (BVAS > 1).

Children and adolescents as well as patients with organ or life-threatening EGPA were excluded from study participation. Thus, no data are available on these sub-populations covered by the therapeutic indication.

A total of 136 patients were randomised to a 52-week treatment with mepolizumab (N = 68) or placebo (N = 68). In both arms, patients received a basic therapy consisting of OCS (≥ 7.5 mg/day), the dosage of which could be adjusted in the course of the study, and an immunosuppressant, if necessary. Immunosuppressants (e.g. leflunomide, mycophenolate mofetil, methotrexate, azathioprine) could only be used in the study if the dosage was kept stable for at least 4 weeks before the start of the study until its end. Treatment with cyclophosphamide and rituximab was not allowed.

Endpoints included the duration of remission and the percentage of patients in remission. Remission was defined in the MIRRA study as BVAS = 0 and OCS dose ≤ 4 mg/day. Other patient-relevant endpoints were assessed in the categories of morbidity, health-related quality of life and side effects.

Implementation of the appropriate comparator therapy

At the start of the study, all patients received OCS as part of the basic therapy. In addition, 60% and 46% of patients in the intervention and comparator arms, respectively, were treated with an immunosuppressant. Treatment with immunosuppressants was only allowed if the therapy was initiated before the start of the study and the dosage was kept stable. Accordingly, at the start of the study, the study doctor did not have a choice of several treatment options that would have enabled the patients who would have needed an adjustment at this point in time to optimise their therapy on a patient-individual basis. For how many patients, especially those with an active EGPA at the start of the study, an optimisation of the therapy would have been indicated cannot be estimated on the basis of the data provided by the pharmaceutical company.

Also, during the course of the study, an adjustment of the therapy, i.e. both a change of the dosage adjustments and a change or initiation of a therapy, for the treatment of newly occurring symptoms or in case of deterioration of existing symptoms without permanent discontinuation of the study medication was only permitted for the OCS and not for the immunosuppressants.

In addition, the subgroup analyses presented for the characteristic immunosuppressant as concomitant treatment (yes/no) indicate that immunosuppressive therapy might have prevented recurrences or led to remission. According to these subgroup analyses, the advantage of mepolizumab for the endpoint of remission is more pronounced in patients without immunosuppressants as concomitant treatment than in patients with immunosuppressants. However, complete data on subgroup analysis was not provided.

[7] ≥ 1 confirmed EGPA relapse (i.e. need for OCS dose increase, initiation or dose increase of immunosuppressive therapy, or hospitalisation) within the last 2 years that occurred ≥ 12 weeks prior to screening, at an OCS dose ≥ 7.5 mg/day

[8] Failure to achieve remission (BVAS=0 and OCS dose ≤ 7.5 mg/day) within the last 6 months after induction therapy with standard treatment administered for at least 3 months or recurrence of EGPA symptoms during discontinuation of OCS (dose ≥ 7.5 mg/day) within 6 months prior to screening

Furthermore, due to the low remission rate in the control arm, it is assumed that an adjustment or initiation of immunosuppressive therapy would have been indicated in a relevant percentage of patients. According to the remission definition of EULAR, i.e. absence of disease activity (BVAS = 0) and OCS dose (≤ 7.5 mg/day), only six patients, two of them in the control arm, were in complete remission at the start of the study. The study description did not explain why no adjustment or new initiation of therapy with the other immunosuppressants would have been appropriate in the remaining patients beyond the adjustment of the OCS dose.

In the overall assessment, there is so much uncertainty as to whether an initiation or adjustment of immunosuppressive therapy would have been indicated for at least some of the enrolled patients that the appropriate comparator therapy is considered to be insufficiently implemented overall. Therefore, the MIRRA study cannot be used and no suitable data are available to assess the additional benefit of mepolizumab compared to the appropriate comparator therapy. An additional benefit is therefore not proven.

2.1.4 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 "add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA)"

The G-BA determined a patient-individual therapy as the appropriate comparator therapy, taking into account the severity of the disease (organ or life-threatening manifestation), the symptomatology, the treatment phase and the course of the disease. Glucocorticoids which may have to be combined with an immunosuppressant are considered suitable comparators in the context of a clinical study. It should be possible to adapt the therapy to the respective needs of the patients in both study arms.

The randomised, controlled, double-blind MIRRA study, comparing the efficacy and safety of mepolizumab with placebo in adults with EGPA without organ or life-threatening stage of the disease was presented. At the start of the study, all patients received OCS as part of the basic therapy. The dosage of OCS could be adjusted as needed during the course of the study. Treatment with immunosuppressants was allowed in the MIRRA study, but only on the condition that the immunosuppressive therapy was already started prior to time of enrolment in the study and the dosage was kept stable over the entire course of the study. Initiation or adjustment of immunosuppressive therapy was not possible both at the start of the study and during its course. In the overall analysis of the available information, there is so much uncertainty as to whether an initiation or adjustment of immunosuppressive therapy would have been indicated for at least some of the enrolled patients that the appropriate comparator therapy is considered to be insufficiently implemented overall. Therefore, the study cannot be used and no suitable data are available to assess the additional benefit of mepolizumab compared to the appropriate comparator therapy. An additional benefit is therefore not proven.

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

The G-BA bases its resolution on the estimate of patient numbers in the SHI target population derived by the pharmaceutical company in the dossier. However, the number of patients is assessed as uncertain. This is due to both overestimated and underestimated aspects of unclear magnitude and uncertain percentages from literature data for patients with relapsing-remitting or refractory EGPA from the total population with EGPA in 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 Nucala (active ingredient: mepolizumab) at the following publicly accessible link (last access: 13 May 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 EGPA therapy.

Mepolizumab is intended for long-term treatment. The need for continued therapy should be reviewed at least once a year. Patients who develop life-threatening manifestations of EGPA should also be assessed for the need for continued therapy as mepolizumab has not been studied in this patient group.

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:

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	1 x every 28 days	13.0	1	13.0
Patient-individual basic therapy[a]				
Methylprednisolone	1 x daily	Different from patient to patient	1	Different from patient to patient
Prednisolone	1 x daily	Different from patient to patient	1	Different from patient to patient

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Prednisone	1 x daily	Different from patient to patient	1	Different from patient to patient
Appropriate comparator therapy				
A patient-individual therapy, taking into account the severity of the disease (organ or life-threatening manifestation), the symptomatology, the treatment phase and the course of the disease[b]				
Methylprednisolone	1 x daily	Different from patient to patient	1	Different from patient to patient
Prednisolone	1 x daily	Different from patient to patient	1	Different from patient to patient
Prednisone	1 x daily	Different from patient to patient	1	Different from patient to patient
[a] In addition to corticosteroids and mepolizumab, patients may be treated with immunosuppressants. These are not approved in the therapeutic indication and are therefore not included in the costs. [b] In the context of patient-individual therapy, corticosteroids, if necessary with immunosuppressants (cyclophosphamide, rituximab, leflunomide, mycophenolate mofetil, methotrexate and azathioprine), are suitable comparators for the present benefit assessment. Immunosuppressants are not approved in the present therapeutic indication, which is why the costs are not presented.				

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.

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.

The dosage of oral corticosteroids is adjusted patient-individual in the course of treatment of EGPA and does not follow a specific standard dosage. The potencies of 5 mg and 20 mg were shown as examples for prednisone and prednisolone. In addition, there are packs with a potency of 10 mg and 50 mg, as well as 1 mg and 2 mg for prednisolone. A similar approach was followed for methylprednisolone. Packs with 4 mg and 32 mg were taken into account here as examples. In addition, there are packs with 8 mg and 16 mg methylprednisolone.

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements were applied (average height: children aged 6 years: 1.22 m, average body weight of children aged 6 years: 23.6 kg).[9]

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	Patients ≥ 6 to < 12 years				
	< 40 kg				
	100 mg	100 mg	1 x 100 mg	13.0	13.0 x 100 mg
	≥ 40 kg				
	200 mg	200 mg	2 x 100 mg	13.0	26.0 x 100 mg
	Patients ≥ 12 years				
	300 mg	300 mg	3 x 100 mg	13.0	39.0 x 100 mg
Patient-individual basic therapy[a]					
Methylprednisolone	Different from patient to patient				
Prednisolone	Different from patient to patient				
Prednisone	Different from patient to patient				
Appropriate comparator therapy					
A patient-individual therapy, taking into account the severity of the disease (organ or life-threatening manifestation), the symptomatology, the treatment phase and the course of the disease[b]					
Methylprednisolone	Different from patient to patient				
Prednisolone	Different from patient to patient				
Prednisone	Different from patient to patient				
[a] In addition to corticosteroids and mepolizumab, patients may be treated with immunosuppressants. These are not approved in the therapeutic indication and are therefore not included in the costs. [b] In the context of patient-individual therapy, corticosteroids, if necessary with immunosuppressants (cyclophosphamide, rituximab, leflunomide, mycophenolate mofetil,					

[9] 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
methotrexate and azathioprine), are suitable comparators for the present benefit assessment. Immunosuppressants are not approved in the present therapeutic indication, which is why the 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					
Mepolizumab 100 mg	3 SFI	€ 3,731.89	€ 1.77	€ 0.00	€ 3,730.12
Methylprednisolone 4 mg[10]	100 TAB	€ 29.31	€ 1.77	€ 1.43	€ 26.11
Methylprednisolone 32 mg[10]	50 TAB	€ 123.31	€ 1.77	€ 0.00	€ 121.54
Prednisolone 5 mg[10]	100 TAB	€ 15.40	€ 1.77	€ 0.33	€ 13.30
Prednisolone 20 mg[10]	100 TAB	€ 21.59	€ 1.77	€ 0.82	€ 19.00
Prednisone 5 mg[10]	100 TAB	€ 16.71	€ 1.77	€ 0.43	€ 14.51
Prednisone 20 mg[10]	100 TAB	€ 29.25	€ 1.77	€ 1.42	€ 26.06
Appropriate comparator therapy					
Methylprednisolone 4 mg[10]	100 TAB	€ 29.31	€ 1.77	€ 1.43	€ 26.11
Methylprednisolone 32 mg[10]	50 TAB	€ 123.31	€ 1.77	€ 0.00	€ 121.54
Prednisolone 5 mg[10]	100 TAB	€ 15.40	€ 1.77	€ 0.33	€ 13.30
Prednisolone 20 mg[10]	100 TAB	€ 21.59	€ 1.77	€ 0.82	€ 19.00
Prednisone 5 mg[10]	100 TAB	€ 16.71	€ 1.77	€ 0.43	€ 14.51
Prednisone 20 mg[10]	100 TAB	€ 29.25	€ 1.77	€ 1.42	€ 26.06
Abbreviations: SFI = solution for injection; TAB = tablets					

LAUER-TAXE® last revised: 1 May 2022

[10] Fixed reimbursement rate

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.

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 24 November 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 2 VerfO.

By letter dated 30 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 30 November 2021, 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 11 April 2022, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 06 May 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	24 November 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