Gemeinsamer Bundesausschuss

Justification

of the Draft 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 Efgartigimod alfa (Myasthenia Gravis, AChR-antibody+)

of 16 February 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.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V). Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5, Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover threshold according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the G-BA 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 online and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was 1 September 2022 in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA for the first placing on the (German) market of the active ingredient efgartigimod alfa. 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 31 August 2022.

Efgartigimod alfa for the treatment of Myasthenia Gravis is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No 141/2000 of the European Parliament and the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the approval studies by the G-BA.

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 1 December 2022 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA made its resolution on the basis of the pharmaceutical company's dossier, the dossier assessment carried out by the G-BA, the IQWiG assessment of treatment costs and patient numbers (IQWiG G22-29) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA has assessed the studies relevant for the marketing authorisation considering their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods 1 was not used in the benefit assessment of efgartigimod alfa.

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

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Efgartigimod alfa (Vyvgart) according to the product information

Vyvgart is indicated as an add-on to standard therapy for the treatment of adult patients with generalised Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.

Therapeutic indication of the resolution (resolution of 16.02.2023):

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

In summary, the additional benefit of efgartigimod alfa as an add-on to standard therapy is assessed as follows:

For adults with generalised Myasthenia Gravis who are anti-acetylcholine receptor antibody positive, there is a hint for a considerable additional benefit of efgartigimod alfa.

Justification:

The pharmaceutical company presents the phase III ADAPT (ARGX-113-1704) study for the present benefit assessment procedure according to Section 35a SGB V.

The ADAPT study is a multicentre, double-blind, randomised controlled trial comparing the efficacy and safety of efgartigimod alfa (hereafter referred to as efgartigimod) with placebo in combination with standard therapy.

Adults with class II, III or IVa/b gMG according to the Myasthenia Gravis Foundation of America (MGFA) classification at the time of screening were enrolled in the study. The treatment of patients in MGFA class I, i.e. with pure ocular MG, and MGFA class V corresponding to gMG requiring intubation (i.e. myasthenic crisis) was not investigated in the ADAPT study. The study participants had to continue to have disease-specific symptoms (MG-ADL total score ≥ 5 points, more than 50% of the score due to non-ocular symptoms) with stable standard therapy. As standard therapy, acetylcholinesterase (AChE) inhibitors, steroids and non-steroidal immunosuppressants were allowed to be used either as mono or combination therapy. Patients who received eculizumab or rituximab within the last 6 months were excluded from the study. In addition, the use of these active ingredients was not allowed in the study. As these treatment options are recommended for refractory subjects with gMG, the question arises whether and to what extent refractory patients are included in the study population.

The study population of the ADAPT study includes both patients with positive and negative AChR antibody (AB) status. In accordance with the approved therapeutic indication, only the results of the sub-population of AChR-AK positive patients submitted by the pharmaceutical company are considered for the present benefit assessment. All the following data refer to this subgroup.

Subjects enrolled in the ADAPT study received either placebo (n = 64 AchR-AK$^+$) or efgartigimod (n = 65 AchR-AK$^+$) for at least one and up to three cycles of treatment, depending on individual response. Standard therapy was continued at stable doses in both study arms. A treatment cycle consisted of a 3-week treatment phase, during which 4 infusions of either placebo or efgartigimod alfa (10 mg/kg) were given at weekly intervals, and a 5-week follow-up period. The treatment with efgartigimod was carried out according to the requirements in the product information. A new treatment cycle was initiated depending on the patient's clinical response. Condition for a further cycle was loss of response, in case of response in the previous cycle, and a MG-ADL total score of ≥ 5 points, with more than 50% of the total score attributable to non-ocular symptoms. The duration of the study was up to 26 weeks. Patients who completed the study were eligible for enrolment in the open-label, single-arm extension study ARGX-113-1705 (ADAPT+). In addition, study participants could cross over early into the ADAPT+ study if they needed further treatment, depending on the above criteria but could not complete the treatment cycle within the time frame of the ADAPT study (i.e. after week 18). As a result, patients in both arms were observed for a median duration of only 142 days (20.3 weeks) instead of 26 weeks as planned.

Endpoints included disease-specific symptomatology, general health status, health-related quality of life and side effects.

The study population comprises predominantly heavily pretreated subjects (75 and 83% with ≥ 3 prior therapies, respectively) with long disease duration (median 7.4 and 6.2 years, respectively) and mild-to-moderate generalised myasthenia (MGFA class II-III a/b). Only 3 or 5% of the patients had a severe gMG corresponding to a MGFA class IV. How many or whether refractory patients were examined within the scope of the study cannot be deduced from the baseline characteristics presented.

All study participants received the first treatment cycle. A second treatment cycle was given to 79% of subjects in the efgartigimod arm and 67% in the placebo arm. A third treatment cycle was given to 11% in the efgartigimod arm and 2% in the placebo arm. Since after the 1st treatment cycle only data from a select population are available (< 70% of the intention-to-treat population), which no longer corresponds to the randomised population, the responder analyses presented below can only be used for the 1st treatment cycle.

Mortality

The number of deceased patients was recorded as part of the safety assessment. No deaths occurred during the course of the study.

Morbidity

Disease-specific symptomatology using Myasthenia Gravis – Activities of Daily Living (MG-ADL)

The MG-ADL is an established patient-reported questionnaire used in care to assess the symptomatology of Myasthenia Gravis and its impact on activities of daily living such as talking, chewing, swallowing, breathing, combing hair or brushing teeth, arise from a chair, incidence of double vision and drooping eyelids.

The primary endpoint of the ADAPT study was defined as the percentage of AChR-AK-positive subjects with an improvement in MG-ADL total score of ≥ 2 points over a period of at least 4 consecutive weeks with the first improvement no later than one week after the last dose of

study medication in treatment cycle 1 compared to baseline values. In the context of the written statement procedure, the pharmaceutical company presented a *post hoc* analysis, based on the primary endpoint with a response criterion of 15% of the scale range (improvement of ≥ 4 points), which is used for the present benefit assessment.

For this endpoint, the study showed a statistically significant advantage of efgartigimod.

In addition, the pharmaceutical company presented evaluations of the *area under the* curve (AUC) in the dossier in order to better capture the fluctuating course. Due to the strongly reduced return rates (< 40%) after week 20, the results are only considered up to and including week 20. Based on the p value, a statistically significant difference to the advantage of efgartigimod can be derived. However, as the mean AUC values presented depend on the observation period and become larger the longer they are measured, the values cannot be interpreted and are therefore not presented in the resolution.

Disease-specific symptomatology using Quantitative Myasthenia Gravis (QMG)

The QMG is a doctor-assessed questionnaire used to quantitatively measure myasthenic symptomatology and assesses the strength of faciopharyngeal, limb and trunk muscles, as well as vital capacity and ocular symptoms. In the present therapeutic indication, the QMG is an established measurement tool in clinical care, which is used together with the MG-ADL and MG-Quality of Life 15 (MG-Qol-15r) questionnaire for the ongoing assessment of disease activity and severity as well as treatment response.

In the post hoc responder analysis with a responder threshold of 15% (≥ 6 points) in the 1st treatment cycle, there was a statistically significant difference to the advantage of efgartigimod over placebo. However, 6 points were reached only once instead of a response over at least four weeks according to the pre-specified analysis of the QMG. Against the background of the fluctuating course of the disease, the one-time assessment of response is fraught with uncertainty.

Overall, the results on disease-specific symptomatology (QMG and MG-ADL) suggest an advantage of efgartigimod over placebo.

Myasthenia gravis composite (MGC)

The MGC is another questionnaire on the symptomatology of MG and contains both patient-reported and doctor-reported sections.

Due to uncertainties in the operationalisation, the endpoint is not used for the present benefit assessment.

Health status (EQ-5D VAS)

Health status was assessed in the ADAPT study using the visual analogue scale of the European Quality of Life -5-Dimensions (EQ 5D-VAS). In the responder analyses conducted *post hoc* by the pharmaceutical company with a clinical relevance threshold of 15%, a significant advantage of efgartigimod over placebo is shown for this endpoint in treatment cycle 1.

Quality of life

Health-related quality of life was assessed in the ADAPT study using the patient-reported Myasthenia Gravis Quality of Life 15 questionnaire (MG-QoL15r). The MG-QoL15r measures the mental well-being and social activity of patients.

The results on health-related quality of life, assessed by the MG-QoL15r, show a statistically significant difference to the advantage of efgartigimod over placebo in the post hoc responder analysis with a responder threshold of 15% in the 1st treatment cycle.

Side effects

Adverse events (AEs) that occurred from the first dose of study medication until the end of the last visit (for up to 26 weeks) were considered for the evaluations of the endpoints in the category "side effects". Subjects who discontinued treatment prematurely were followed up monthly until day 182 in the safety follow-up.

There were no statistically significant differences between treatment arms for the overall rates of serious AEs (SAEs), severe AEs and AEs leading to discontinuation of study medication, as well as AEs of special interest.

However, the results are subject to uncertainties as the pharmaceutical company did not present evaluations excluding disease-related events or events of the underlying disease and AEs and SAEs were observed that could also include events from the category "morbidity".

In addition, the risk of bias is increased due to the patient-individual treatment regimen and the study design with possible early transition to the ADAPT+ study. Overall, the risk of bias in the side effects category is therefore assessed as high.

Overall assessment

For the benefit assessment of efgartigimod alfa for the treatment of adults with generalised Myasthenia Gravis who are anti-acetylcholine receptor antibody positive, results of the randomised controlled trial ADAPT are available for the endpoint categories of mortality, morbidity, quality of life and side effects compared to placebo. In both study arms, patients received standard therapy consisting of AChE inhibitors, steroids and/or non-steroidal immunosuppressants, which was stable before the start of the study.

There were no deaths in the endpoint category of mortality.

In the morbidity category, the responder analyses show statistically significant advantages in favour of efgartigimod over placebo for the 1st treatment cycle, both for disease-specific symptomatology (MG-ADL and QMG) and for general health status (EQ5D VAS). In addition, there is a statistically significant, clinically relevant benefit for the morbidity endpoint "MG-ADL AUC", which takes into account the chronic fluctuating course of the disease over 20 weeks.

For health-related quality of life, there is an advantage of efgartigimod alfa based on MG-QoL15r.

With regard to side effects, neither an advantage nor a disadvantage of efgartigimod over placebo can be found, in each case in combination with the standard therapy.

In the overall assessment of the results, an additional benefit of efgartigimod can be derived on the basis of the positive effects in all available patient-relevant endpoints on morbidity -

i.e. on disease-specific symptomatology (MG-ADL, QMG) and general health status - and health-related quality of life, which is assessed as considerable in its extent.

Significance of the evidence

For the pivotal, double-blind randomised controlled trial ADAPT on which the present benefit assessment is based, the risk of bias at study level is assessed as low.

Uncertainties arise primarily from the short observation period of the data used. With the exception of the endpoint "MG-ADL AUC", which shows an advantage of myasthenic symptomatology over 20 weeks, the endpoints on morbidity and quality of life refer to the 1st treatment cycle, i.e. on an observation period of 8 weeks. Assessable data over a longer observation period would have been necessary to be able to map the sustainability of the effects.

Furthermore, there are uncertainties as to whether and to what extent refractory patients are included in the study population. It is thus unclear whether the effects observed in the ADAPT study can be unconditionally transferred to this patient group.

Overall, the above-mentioned uncertainties regarding the significance of the evidence result in a hint for an additional benefit.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "Vyvgart" with the active ingredient "efgartigimod alfa". Efgartigimod alfa t is indicated as an add-on to standard therapy for the treatment of adult patients with generalised Myasthenia Gravis who are anti-acetylcholine receptor antibody positive.

For the present benefit assessment, results of the randomised controlled phase III study ADAPT were used for the endpoint categories of mortality, morbidity, quality of life and side effects in comparison to placebo. In both study arms, patients received standard therapy consisting of AChE inhibitors, steroids and/or non-steroidal immunosuppressants, which was stable before the start of the study.

There were no deaths in the endpoint category of mortality.

In the morbidity category, the responder analyses show statistically significant advantages in favour of efgartigimod over placebo for the 1st treatment cycle, both for disease-specific symptomatology (MG-ADL and QMG) and for general health status (EQ5D VAS). In addition, there is a statistically significant, clinically relevant benefit for the morbidity endpoint "MG-ADL AUC", which takes into account the chronic fluctuating course of the disease over 20 weeks.

For health-related quality of life, there is an advantage of efgartigimod alfa based on MG-QoL15r.

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observation period would have been necessary to be able to map the sustainability of the effects.

Furthermore, there are uncertainties as to whether and to what extent refractory patients are included in the study population. It is thus unclear whether the effects observed in the ADAPT study can be unconditionally transferred to this patient group.

In the overall assessment, there is a hint for a considerable additional benefit of efgartigimod alfa as an add-on to standard therapy.

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

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

The G-BA bases its resolution on the patient numbers from the dossier submitted by the pharmaceutical company. However, the data are subject to uncertainties arising from the determination of the prevalence rate of generalised myasthenia from routine data analysis.

In the case of rare diseases, it is questionable whether an age and gender-adjusted extrapolation of data from the company health insurance funds to the SHI system is sufficient to achieve representativeness for all SHI-insured persons. In addition, there is uncertainty about the extent to which subjects with ocular manifestations alone were enrolled in the study.

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 Vyvgart (active ingredient: efgartigimod alfa) at the following publicly accessible link (last access: 25 November 2022):

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

Treatment with efgartigimod alfa should only be initiated and monitored by doctors experienced in the therapy of neuromuscular diseases.

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 February 2023).

Treatment period:

The dosage recommended in the product information was used as the calculation basis. One treatment cycle of efgartigimod alfa lasts 4 weeks. Further treatment cycles are administered

on a patient-individual basis according to clinical assessment and at the earliest 7 weeks after the first infusion.

The AChE inhibitor neostigmine is applied several times a day in different ways in a patient-individual manner.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Efgartigimod alfa	1 x every 7 days per 4 week cycle	1 – 7.4	4	4 - 29.6
Patient-individual standard therapy[2]				
Azathioprine	Continuously, 1 x daily	365	1	365
Prednisolone	Continuously, 1 x daily	365	1	365
Prednisone	Continuously, 1 x daily	365	1	365
Pyridostigmine	Continuously, 2 – 4 x daily	365	1	365
Neostigmine	Different from patient to patient			
Distigmine	Continuously, 1 x daily	365	1	365
Mycophenolate mofetil[3]	Continuously, 0.5 – 2.5 mg daily	365	1	365

Consumption:

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements were applied (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)[4].

[2] As an alternative to azathioprine and mycophenolate mofetil, patients may be treated with other non-steroidal immunosuppressants such as methotrexate, cyclosporine and tacrolimus. These are not approved in the therapeutic indication and are therefore not included in the costs.

[3] Mycophenolate mofetil is not approved in the therapeutic indication under consideration, but is reimbursable within the framework of off-label use (AM-RL Annex VI) in the case of resistance to treatment with the approved substances or in the case of azathioprine intolerance.

4 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
Medicinal product to be assessed					
Efgartigimod alfa	10 mg/ kg BW	770 mg	2 x 400 mg	4 – 29.6	8 – 59.2 x 400 mg
Patient-individual standard therapy[2]					
Azathioprine	2 mg/ kg BW = 154 mg – 3 mg/kg BW = 231 mg	154 mg – 231 mg	1 x 100 mg + 1 x 50 mg – 2 x 100 mg + 1 x 25 mg	365	365 x 100 mg + 365 x 50 mg 730 x 100 mg + 365 x 25 mg
Prednisolone	5 mg – 15 mg	5 mg – 15 mg	1 x 5 mg 1 x 5 mg 1 x 10 mg	365	365 x 5 mg 365 x 5 mg + 365 x 10 mg
Prednisone	5 mg – 15 mg	5 mg – 15 mg	1 x 5 mg 1 x 5 mg 1 x 10 mg	365	365 x 5 mg 365 x 5 mg + 365 x 10 mg
Pyridostigmine	10 mg – 540 mg	30 mg – 1080 mg	3 x 10 mg – 6 x 180 mg	365	1095 x 10 mg 2190 x 180 mg
Neostigmine	Different from patient to patient				
Distigmine	10 mg	10 mg	2 x 5 mg	365	730 x 5 mg
Mycophenolate mofetil	500 mg – 2500 g	500 mg – 2500 g	1 x 500 mg – 5 x 500 mg	365	365 x 500 mg – 1825 x 500 mg

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Costs:

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					
Efgartigimod alfa 400 mg	1 CIS	€ 9,522.39	€ 2.00	€ 926.63	€ 8,593.76
Patient-individual standard therapy[2]					
Azathioprine[5] 100 mg	100 FCT	€ 57.98	€ 2.00	€ 3.69	€ 52.29
Azathioprine[5] 50 mg	100 TAB	€ 40.64	€ 2.00	€ 2.32	€ 36.32
Azathioprine[5] 25 mg	100 FCT	€ 29.74	€ 2.00	€ 1.46	€ 26.28
Prednisolone[5] 5 mg	100 TAB	€ 15.40	€ 2.00	€ 0.33	€ 13.07
Prednisolone[5] 10 mg	100 TAB	€ 17.78	€ 2.00	€ 0.51	€ 15.27
Prednisone[5] 5 mg	100 TAB	€ 16.71	€ 2.00	€ 0.43	€ 14.28
Prednisone[5] 10 mg	100 TAB	€ 21.19	€ 2.00	€ 0.78	€ 18.41
Pyridostigmine bromide 10 mg	100 FCT	€ 21.02	€ 2.00	€ 1.23	€ 17.79
Pyridostigmine bromide 180 mg	100 RET	€ 264.08	€ 2.00	€ 32.00	€ 230.08
Neostigmine methylsulfate	Different from patient to patient				
Distigmine bromide 5 mg	50 TAB	€ 90.43	€ 2.00	€ 7.51	€ 80.92
Mycophenolate mofetil[5] 500 mg	250 FCT	€ 409.91	€ 2.00	€ 31.53	€ 376.38
Abbreviations: CIS = concentrate for the preparation of an infusion solution; TAB = tablets; RET = retard tablets; FCT = film-coated tablets					

LAUER-TAXE® last revised: 1 February 2023

[5] 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.

No additionally required SHI services are taken into account for the cost representation.

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.

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 Efgartigimod alfa

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.

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

On 31 August 2022, the pharmaceutical company submitted a dossier for the benefit assessment of efgartigimod alfa to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 1 December 2022 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 22 December 2022.

The oral hearing was held on 9 January 2023.

An amendment to the benefit assessment with a supplementary assessment was submitted on 25 January 2023.

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 7 February 2023, and the proposed resolution was approved.

At its session on 16 February 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	22 November 2022	Information of the benefit assessment of the G-BA
Working group Section 35a	3 January 2023	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	9 January 2023	Conduct of the oral hearing
Working group Section 35a	18 January 2023 1 February 2023	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal products	7 February 2023	Concluding discussion of the draft resolution
Plenum	16 February 2023	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 16 February 2023

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

Prof. Hecken