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 Mosunetuzumab (follicular lymphoma, after ≥ 2 prior therapies)

of 15 December 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.

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 limit 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 on the internet 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 July 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 mosunetuzumab. 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 22 June 2022.

Mosunetuzumab for the treatment of follicular lymphoma after ≥ 2 prior systemic therapies is approved as a medicinal product for the treatment of rare diseases 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 4 October 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 has adopted its resolution on the basis of the dossier of the pharmaceutical company, the dossier assessment carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G12-01) prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure.

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 mosunetuzumab.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Mosunetuzumab (Lunsumio) in accordance with the product information

Lunsumio as monotherapy is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies.

Therapeutic indication of the resolution (resolution of 15 December 2022):

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

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

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Justification:

To assess the extent of the additional benefit of mosunetuzumab as monotherapy, the pharmaceutical company submitted data from the ongoing, pivotal, single-arm phase I/II GO29781 study. The study investigated the safety, pharmacokinetics as well as the biological and clinical activity of mosunetuzumab as monotherapy or in combination with atezolizumab in adults with relapsed or refractory haematological malignancies.

After setting the recommended phase II dose (RP2D), indication-specific cohorts were formed in the dose expansion phase of the study. The sub-cohort of the GO29781 study that is relevant for the benefit assessment includes adults with relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies who were treated with the pivotal dose of mosunetuzumab monotherapy. According to the inclusion criteria, patients had to have grade 1 to 3a, relapsed or refractory follicular lymphoma and an ECOG status of 0-1, as well as have received an alkylane and an anti-CD20 therapy in the prior therapy.

The assessment-relevant sub-cohort comprises 90 patients. The median age of the patients was 60 years, and one third of them had received two, three or more prior therapies. Autologous stem cell transplant was performed in approx. 21% of the patients and CAR-T cell

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

therapy in approx. 3% of the patients in the prior therapy. About 54% of patients had bulky disease of varying degrees and about 44% had a FLIPI score of 3 or 4. Information on the symptomatology of the patients at the start of the study is not available.

Monotherapy with mosunetuzumab was administered over eight cycles of 21 days each. Continuation of therapy for up to a further nine cycles (17 cycles in total) was possible if partial remission (PR) or stable disease (SD) had been achieved during the first eight cycles. In addition, re-therapy with mosunetuzumab for eight additional cycles was also possible, provided complete remission (CR) was achieved during the initial eight cycles and disease progression occurred after completion of therapy. Re-therapy was given to 3 subjects in the GO29781 study.

The ongoing GO29781 study is being conducted in 38 study sites in the United States (US), Australia, Canada, South Korea and Europe. The recruitment of patients for the assessment-relevant sub-cohort took place from May 2019 to September 2020. The primary endpoint of the study is CR, secondary endpoints include overall survival, patient-reported morbidity and quality of life endpoints, as well as side effects.

Three data cut-offs of the GO29781 study have been performed so far. An interim analysis of 15 March 2021 and two update analyses dated 27 August 2021 and 3 January 2022. Specific rules that determine the timing of the data cut-offs á priori could not be identified from the study documents. The update analysis of 27 August 2021 was requested by the European Medicines Agency (EMA) as part of the marketing authorisation procedure. A full study report is available for this update analysis. The reason for the data cut-off of 3 January 2022 was not clear from the dossier and the written statement of the pharmaceutical company. In the oral hearing on the present benefit assessment procedure, it was clarified that the data cut-off of 3 January 2022 was neither planned á priori nor requested by the EMA. In addition, only select data outputs for the endpoint assessment in module 4 and no complete study report are available for this data cut-off. Therefore, the data cut-off of 27 August 2021 is used in the present benefit assessment.

Mortality

The overall survival is defined in the GO29781 study as the time from the first mosunetuzumab dose to death from any cause.

As of the data cut-off of 27 August 2021, a total of 8 subjects (8.9%) had died. The median overall survival had not yet been reached. Due to the single-arm study design, a comparative assessment of the results on overall survival is not possible.

Morbidity

Complete remission (CR; presented additionally)

The primary endpoint of the GO29781 study is complete remission (CR), which was assessed by an independent review committee (IRC).

The assessment was carried out according to the criteria of Cheson et al. (2007), mainly by means of imaging procedures. In addition, the patients also had to show a complete disappearance of symptomatology. A complete disappearance of the symptomatology is assessed as patient-relevant. However, for subjects who do not have disease-related symptomatology at the start of the study, the determination of CR is based solely on CT and PET investigations. If the response is assessed exclusively on the basis of imaging findings, the assessment of morbidity is not based on disease symptoms, but on asymptomatic findings that are not directly patient-relevant.

It is unclear how many of the patients included in the assessment-relevant sub-cohort were symptomatic at the start of the study and how symptoms were recorded and documented. A separate presentation of the CR results according to symptomatic and asymptomatic patients is not available. Therefore, the results on CR are only presented additionally.

As of the data cut-off of 27 August 2021, 60% of patients achieved a CR. Due to the single-arm study design, a comparative assessment of the results on CR is not possible.

Health status (EQ-5D VAS)

Health status was assessed in the GO29781 study using the visual analogue scale of the EuroQoL 5 dimensions (EQ-5D-VAS).

In the dossier, evaluations of the mean change between baseline and the first day of each even cycle are available for the data cut-off of 27 August 2021. The EQ-5D-VAS was only evaluated for study participants for whom a baseline value and at least one post-baseline value were available. In addition, only the questionnaires of patients who received therapy with mosunetuzumab when responding to the questionnaire were taken into account.

With its written statement, the pharmaceutical company submits responder analyses on the EQ-5D VAS with a relevance threshold of 15% of the scale range. These evaluations are not usable because the return rate is already below 70% for cycle 6.

In this assessment, therefore, the mean changes from baseline to cycle 4 are presented. Due to the single-arm study design, a comparative assessment of the results on EQ-5D VAS is not possible.

EORTC QLQ-C30 (symptom scales)

Disease symptomatology was assessed in the GO29781 study using the symptom scales of the EORTC-QLQ-C30 questionnaire.

In the dossier, the pharmaceutical company presents responder analyses with a threshold value of 10 points as well as evaluations of the mean change from baseline for the fatigue scale as of the data cut-off of 27 August 2021. This selective evaluation of only one symptom scale of the EORTC QLQ-C30 is not usable for the present benefit assessment.

With its written statement, the pharmaceutical company submits responder analyses for all symptom scales of the EORTC QLQ-C30 with a relevance threshold of 15% of the scale range

or 15 points. The evaluation refers to study participants for whom a baseline value and at least one post-baseline value were available and who received therapy with mosunetuzumab when responding to the questionnaire. These responder analyses cannot be used for the present benefit assessment, as the return rate is already below 70% before or at cycle 8.

Evaluations of mean change from baseline for all symptom scales of the EORTC QLQ-C30 were not submitted for the data cut-off of 27 August 2021.

Thus, the data presented on the symptom scales of the EORTC QLQ-C30 are not usable overall for the present benefit assessment. Nevertheless, a comparative assessment of the data on the EORTC QLQ-C30 is not possible due to the single-arm study design.

Quality of life

Health-related quality of life was assessed in the GO29781 study using the FACT-LymS questionnaire and the functional scales of the EORTC QLQ-C30 questionnaire.

EORTC QLQ-C30 (functional scales)

In the dossier, the pharmaceutical company presents responder analyses with a threshold value of 10 points as well as evaluations of the mean change from baseline for the physical functioning scale as of the data cut-off of 27 August 2021. This selective evaluation of only one functional scale of the EORTC QLQ-C30 is not usable for the present benefit assessment.

With its written statement, the pharmaceutical company submits responder analyses for all functional scales of the EORTC QLQ-C30 with a relevance threshold of 15% of the scale range or 15 points. The evaluation refers to study participants for whom a baseline value and at least one post-baseline value were available and who received therapy with mosunetuzumab when responding to the questionnaire. These responder analyses cannot be used for the present benefit assessment, as the return rate is already below 70% before or at cycle 8.

Evaluations of mean change from baseline for all functional scales of the EORTC QLQ-C30 were not submitted for the data cut-off of 27 August 2021.

Thus, the data presented on the functional scales of the EORTC QLQ-C30 are not usable overall for the present benefit assessment. Nevertheless, a comparative assessment of the data on the EORTC QLQ-C30 is not possible due to the single-arm study design.

FACT-LymS

Disease-specific quality of life was assessed using the validated Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) questionnaire. Only questionnaires completed on the first day of every second therapy cycle were used for the evaluations. The evaluation was carried out for study participants for whom a baseline value and at least one post-baseline value were available. Data collected after the end of mosunetuzumab therapy were not included in the evaluation.

In the dossier, the pharmaceutical company submits evaluations of the mean change from baseline and a responder analysis with a relevance threshold of 3 points for the data cut-off of 27 August 2021. This relevance threshold is below a scale range of 15%. With its written statement, the pharmaceutical company submits a responder analysis with a relevance threshold of 15% of the scale range or 9 points. However, since the return rates are already below 70% for cycle 8, the responder analyses cannot be used for the present benefit assessment.

In this assessment, therefore, the mean changes from baseline to cycle 6 are presented. Due to the single-arm study design, a comparative assessment of the results on FACT-LymS is not possible.

Side effects

Adverse events occurred in all patients in the assessment-relevant sub-cohort.

Severe adverse events (AEs) of CTCAE grade ≥ 3 occurred in 70% of the patients. An incidence of ≥ 5% was found in the system organ classes (SOC) blood and lymphatic system disorders, metabolism and nutrition disorders, infections and infestations, and investigations.

Serious AEs occurred in 46.7% of the patients. An incidence of ≥ 5% was found in SOC immune system disorders, metabolism and nutrition disorders, and infections and infestations.

The study medication was discontinued by 4 patients due to AEs.

AEs of special interest included cytokine release syndrome (CRS; grading according to Lee et al. (2014)), flare reactions, hepatic events, infections as well as nervous system disorders and psychiatric disorders. The most common were nervous system disorders and psychiatric disorders (about 69%), followed by infections (about 51%) and CRS (about 46%). CRS was assessed as serious in about 23% of the patients.

Due to the single-arm study design, a comparative assessment of the results on the endpoint category of side effects is not possible.

Overall assessment

The data from the single-arm phase I/II GO29781 study are available for the present benefit assessment. The assessment-relevant sub-population includes patients with relapsed or refractory FL who have received at least two prior systemic therapies and have been treated with a pivotal dose of mosunetuzumab monotherapy. Data on mortality, morbidity, health-related quality of life and side effects are available.

The median overall survival had not yet been reached at the data cut-off of 27 August 2021.

The evaluations presented for the EORTC QLQ-C30 for the endpoint category of morbidity and quality of life are not usable.

Severe adverse events (AEs) of CTCAE grade ≥ 3 occurred in 70% of the patients and serious AEs in 46.7% of the patients.

A comparative assessment in all endpoint categories is not possible due to the single-arm study design.

In the overall assessment, the extent of the additional benefit is classified as non-quantifiable since the scientific data does not allow quantification.

Significance of the evidence

The benefit assessment is based on data from the single-arm phase I/II GO29781 study. There is no adequate comparison.

Since only single-arm data are available and a comparative assessment is not possible, the reliability of data is assessed with a hint.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Lunsumio® with the active ingredient mosunetuzumab. Mosunetuzumab was approved as an orphan drug under special conditions for the treatment of adults with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic treatments.

For the benefit assessment, the pharmaceutical company presents the data from the single-arm phase I/II GO29781 study on mortality, morbidity, health-related quality of life and side effects.

A comparative assessment in all endpoint categories is not possible due to the single-arm study design.

In the overall assessment, a hint for a non-quantifiable additional benefit is identified since the scientific data does not allow quantification.

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 based the resolution on the patient numbers from the resolution on the benefit assessment of tisagenlecleucel for the treatment of follicular lymphoma after two or more lines of systemic therapy (resolution of 1 December 2022).

The derivation of the patient numbers in the resolution on tisagenlecleucel is based on data from the InGef database, which contains anonymised, longitudinal insurance data of approx. 9 million statutorily insured persons in Germany. Uncertainties arise in the extrapolation to the relevant SHI population, since it is unclear whether all relevant ICD-10-GM codes were taken into account on the one hand. On the other, there may be uncertainty and a tendency to underestimate the identification of the percentage of patients who have ≥ 2 prior therapies and require treatment anew. For this purpose, the pharmaceutical company examined the

patients who received a specific therapy in 2020 and had received at least two lines of systemic therapy in the previous 6 years. This neglected patients who had already received at least one therapy before this period. This step is also fraught with uncertainties in the selection and search for therapies that are considered specific. Furthermore, there are uncertainties in the extrapolation to the SHI population.

The derivation of patient numbers in the present procedure on mosunetuzumab is based on the incidence rates reported by the RKI and the Society of Epidemiological Cancer Registries in Germany (GEKID) for the period from 1999 to 2018 for the diagnosis code C82 (FL). The extrapolation to the relevant SHI population is mainly based on data from the publication by Kanas et al. (2021). These data were collected in France, Germany, Italy, Spain and the United Kingdom. In addition, the data is historical and based on surveys of doctors, so that it is unclear whether any changes in therapy recommendations are taken into account. Overall, the representativeness and transferability of the data to the German healthcare context is not entirely guaranteed.

In the opinion of the G-BA, the patient numbers available in the present benefit assessment procedure do not represent a clearly better estimate compared to the patient numbers from the resolution on tisagenlecleucel, which are based solely on the slightly more up-to-date German data.

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 Lunsumio (active ingredient: mosunetuzumab) at the following publicly accessible link (last access: 2 November 2022):

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

Treatment with mosunetuzumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with follicular lymphoma. In addition, mosunetuzumab must only be administered in a setting that is sufficiently medically equipped to treat severe reactions such as cytokine release syndrome (CRS).

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

In accordance with the requirements of the European Medicines Agency (EMA) regarding additional measures to minimise risks, the pharmaceutical company must ensure that each

subject treated with mosunetuzumab receives a patient pass which informs and clarifies the risks of CRS and includes a warning for the healthcare professionals treating the subjects.

Patients with grade 3b follicular lymphoma were not investigated in the dose expansion phase of the GO29781 study.

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 December 2022).

Treatment with mosunetuzumab takes place over 8 cycles. If necessary, it may be administered for a maximum of 17 cycles. The annual treatment costs are thus presented as a range.

Treatment period:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration 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.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Mosunetuzumab	21-day cycle Cycle 1: 1 x on day 1, 8, 15 Cycle 2 - 8 or 17: 1 x on day 1	8 – 17	1 - 3	10 – 19

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 co-morbidities) are not taken into account when calculating the annual treatment costs.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Mosunetuzumab	Cycle 1: 1 mg/ 2 mg/ 60 mg Cycle 2: 60 mg Cycle 3 – 8 or 17: 30 mg	Cycle 1: 63 mg Cycle 2: 60 mg Cycle 3 - 8 or 17: 30 mg	Cycle 1: 3 x 1 mg + 2 x 30 mg Cycle 2: 2 x 30 mg Cycle 3 - 8 or 17: 1 x 30 mg	10 (8 cycles) 19 (17 cycles)	3 x 1 mg + 10 x 30 mg 3 x 1 mg + 19 x 30 mg

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					
Mosunetuzumab 1 mg	1 CIS	€ 320.05	€ 1.77	€ 17.10	€ 301.18
Mosunetuzumab 30 mg	1 CIS	€ 9,037.82	€ 1.77	€ 512.86	€ 8,523.19
Abbreviations: IFC = concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 01 December 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.

Premedication

As premedication, intravenous corticosteroids (20 mg dexamethasone or 80 mg methylprednisolone), an antihistamine (e.g. 50 - 100 mg diphenhydramine orally or intravenously), and an antipyretic (e.g. 500 - 1,000 mg paracetamol) must be administered prior to each infusion with mosunetuzumab before cycles 1 and 2, according to the product information of the medicinal product to be assessed. For the present procedure, dexamethasone IV is presented as the corticosteroid and dimetindene IV as the antihistamine. Premedication may also be required from cycle 3 onwards if affected subjects develop cytokine release syndrome during therapy with the medicinal product to be assessed. The additional SHI costs are therefore presented as a range.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I to the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129, paragraph 5a SGB V, when a non-prescription medicinal product is dispensed invoiced according Section 300, a medicinal product sale price applies to the insured person in the amount of the sale price of the pharmaceutical company plus the surcharges according to Sections 2 and 3 of the Pharmaceutical Price Ordinance in the valid version of 31 December 2003.

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)[2].

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

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days / year	Costs/ patient/ year
Premedication							
Paracetamol 500 - 1,000 mg	Cycle 1 - 2 (regular)[3]						
	10 TAB each 500 mg	€ 1.06[4]	€ 0.05	€ 0.04	€ 0.97	4	€ 0.39
	10 TAB each 1,000 mg	€ 1.06[4]	€ 0.05	€ 0.04	€ 0.97	4	€ 0.39
	Cycle 1 - 17 (in case of need)[3]						
	20 TAB each 500 mg	€ 1.50[4]	€ 0.08	€ 0.06	€ 1.36	19	€ 1.29
	10 TAB each 1,000 mg	€ 1.06[4]	€ 0.05	€ 0.04	€ 0.97	19	€ 1.84
Dexamethasone IV 20 mg	Cycle 1 - 2 (regular)[3]						
	10 AMP each 8 mg	€ 20.35[4]	€ 1.77	€ 0.72	€ 17.86	4	€ 14.29
	10 AMP each 4 mg	€ 16.89[4]	€ 1.77	€ 0.44	€ 14.68	4	€ 5.87
	Cycle 1 - 17 (in case of need)[3]						
	10 AMP each 8 mg	€ 20.35[4]	€ 1.77	€ 0.72	€ 17.86	19	€ 67.87
	10 AMP each 4 mg	€ 16.89[4]	€ 1.77	€ 0.44	€ 14.68	19	€ 27.89
Dimetindene IV 1 mg/10 kg = 7.7 mg	Cycle 1 - 2 (regular)[3]						
	5 SFI each 4 mg	€ 23.67	€ 1.77	€ 5.58	€ 16.32	4	€ 26.11
	Cycle 1 - 17 (in case of need)[3]						
	5 SFI each 4 mg	€ 23.67	€ 1.77	€ 5.58	€ 16.32	19	€ 124.03
Abbreviations: TAB = tablets; AMP = ampoules; SFI = solution for injection							

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

[3] Premedication is required for all patients in cycles 1 and 2, and for cycles 3 and beyond, premedication is given to patients in whom CRS of any grade has occurred at the previous dose.

[4] Fixed reimbursement rate

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 do not add to the pharmacy sales price but follow the rules for calculation in the special agreement on contractual unit costs of retail pharmacist services (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 Mosunetuzumab

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

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

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

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

On 22 June 2022, the pharmaceutical company submitted a dossier for the benefit assessment of mosunetuzumab 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 4 October 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 25 October 2022.

The oral hearing was held on 7 November 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 6 December 2022, and the proposed resolution was approved.

At its session on 15 December 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	27 September 2022	Information of the benefit assessment of the G-BA
Working group Section 35a	1 November 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	7 November 2022	Conduct of the oral hearing
Working group Section 35a	15 November 2022 29 November 2022	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	6 December 2022	Concluding discussion of the draft resolution
Plenum	15 December 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 15 December 2022

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

Prof. Hecken