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) Elranatamab (multiple myeloma, at least 3 prior therapies)

of 4 July 2024

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 relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient elranatamab on 15 January 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. 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 15 January 2024.

The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on 15 April 2024 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

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

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 Elranatamab (Elrexfio) in accordance with the product information

Elrexfio is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Therapeutic indication of the resolution (resolution of 04.07.2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Appropriate comparator therapy for elranatamab as monotherapy:

A patient-individual therapy under selection of:

- carfilzomib in combination with lenalidomide and dexamethasone
- elotuzumab in combination with lenalidomide and dexamethasone
- elotuzumab in combination with pomalidomide and dexamethasone

1 General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

- daratumumab in combination with bortezomib and dexamethasone
- daratumumab in combination with lenalidomide and dexamethasone
- daratumumab in combination with carfilzomib and dexamethasone
- daratumumab in combination with pomalidomide and dexamethasone (only for subjects who are refractory to lenalidomide)
- isatuximab in combination with carfilzomib and dexamethasone
- isatuximab in combination with pomalidomide and dexamethasone
- pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)
- ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)
- carfilzomib in combination with dexamethasone

taking into account the active ingredients and combinations of active ingredients used in the prior therapies as well as the type and duration of the response to the respective prior therapies

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Appropriate comparator therapy for elranatamab as monotherapy:

A patient-individual therapy under selection of:

- carfilzomib in combination with lenalidomide and dexamethasone
- elotuzumab in combination with lenalidomide and dexamethasone
- elotuzumab in combination with pomalidomide and dexamethasone
- daratumumab in combination with bortezomib and dexamethasone
- daratumumab in combination with lenalidomide and dexamethasone
- daratumumab in combination with carfilzomib and dexamethasone
- daratumumab in combination with pomalidomide and dexamethasone
- isatuximab in combination with carfilzomib and dexamethasone
- isatuximab in combination with pomalidomide and dexamethasone
- pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)

- ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)
- panobinostat in combination with bortezomib and dexamethasone
- carfilzomib in combination with dexamethasone
- pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)
- lenalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)
- bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)
- bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)
- daratumumab monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)
- cyclophosphamide as monotherapy or in combination with dexamethasone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)
- melphalan as monotherapy or in combination with prednisolone or prednisone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)

taking into account the general condition, the active ingredients and combinations of active ingredients used in the prior therapies and the type and duration of the response to the respective prior therapies

<u>Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):</u>

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.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

<u>Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:</u>

on 1. In addition to elranatamab, the following active ingredients are approved in the present therapeutic indication:

bortezomib, carfilzomib, carmustine, ciltacabtagene autoleucel, cyclophosphamide, daratumumab, dexamethasone, doxorubicin, doxorubicin (pegylated liposomal), elotuzumab, idecabtagene vicleucel, isatuximab, ixazomib, lenalidomide, melphalan, melphalan flufenamide, panobinostat, pomalidomide, prednisolone, prednisone, selinexor, teclistamab, talquetamab and vincristine.

The marketing authorisations are in part linked to (specified) concomitant active ingredients and to the type of the prior therapies.

on 2. A non-medicinal treatment is unsuitable as a comparator therapy in this therapeutic indication.

on 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Talquetamab – resolution of 7 March 2024
- Teclistamab – resolution of 15 February 2024
- Ciltacabtagene autoleucel – resolution of 17 August 2023
- Selinexor – resolutions of 16 March 2023
- Melphalan flufenamide – resolution of 16 March 2023
- Idecabtagene vicleucel – resolution of 16 June 2022
- Carfilzomib – resolutions of 15 February 2018 and 15 July 2021
- Daratumumab – resolutions of 15 February 2018, 3 February 2022 and 15 September 2022
- Elotuzumab – resolutions of 1 December 2016 and 16 December 2021
- Isatuximab – resolutions of 4 November 2021
- Ixazomib – resolution of 21 April 2022
- Panobinostat – resolution of 17 March 2016
- Pomalidomide – resolutions of 17 March 2016 and 5 December 2019

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

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

Among the approved active ingredients listed under 1.), only certain active ingredients named below will be included in the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of health care provision.

The evidence is limited for patients who have received three or at least four lines of prior therapy. A uniform treatment standard cannot be derived from the available evidence. National and international guidelines generally refer to patient-individual therapy which is influenced by various factors. According to the S3 guideline, the active

ingredients and combinations of active ingredients used in prior therapies as well as the type and duration of the response to the respective prior therapies and the general condition of the patients play a key role in the choice of therapy.

One criterion for patient-individual therapy is the duration of the response to the prior therapy. If the disease progresses under the respective prior therapy or if the duration of response after completion of the respective prior therapy is less than 12 months, it will not be considered again in the further course of treatment in accordance with the generally recognised state of medical knowledge. Accordingly, this therapy using the specific active ingredients or combinations of active ingredients in the further course of treatment may again be a suitable treatment option for relapsed patients in whom a response in the form of a complete remission (CR), a very good partial response (VGPR) and a partial response (PR) of more than 12 months after the end of therapy was achieved with a specific previous therapy.

The therapy recommendations of the S3 guideline differentiate between the treatment setting of the first to third recurrence and from the fourth recurrence onwards. This is due to the very heterogeneous patient population in the advanced lines of therapy, for whom the substances used in the earlier lines of therapy are increasingly no longer an option and who therefore have a poorer prognosis. Accordingly, in the present therapeutic indication of relapsed/refractory multiple myeloma, a distinction between two distinct patient populations depending on the number of prior therapies is considered appropriate despite the overlap of certain therapy options.

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

With regard to the relapsed/refractory disease situation after three prior therapies, the S3 guideline initially states that a triplet therapy with two new substances (monoclonal antibody, immunomodulatory agent, proteasome inhibitor) and a steroid should be used for patients. Furthermore, with reference to the respective approved therapeutic indications of the active ingredients, the guideline on the therapy of the 1st to 3rd relapse states that regarding each combination therapy all product classes can be generally used and combined in individual order. This is also done against the background that the therapeutic benefit of triplet therapies over doublet therapies is offset by increased therapy toxicity, meaning that they are unsuitable for all patients.

Overall, all approved therapies and preferably all approved triplet therapies with two new substances and a steroid are therefore initially considered. With regard to the individual therapy options, the following limitations apply to the respective active ingredients and combinations of active ingredients in the present therapeutic indication:

The therapy options pomalidomide in combination with bortezomib and dexamethasone (PVd) and ixazomib in combination with lenalidomide and dexamethasone (IRd) are restricted to patients with a specific refractoriness to the active ingredients or combinations of active ingredients used in the previous treatments. The suitability of patients for the use of PVd and IRd as part of patient-individual therapy must be demonstrated based on the type and duration of response to the respective prior therapies in accordance with the specified limitations.

In addition to the triplet therapies, the dual combination of carfilzomib and dexamethasone is also determined as an appropriate comparator therapy as part of patient-individual therapy. By G-BA resolution of 15 February 2018, a hint for a considerable additional benefit of this combination therapy compared to bortezomib in combination with dexamethasone was identified in the benefit assessment for adults after at least one prior therapy.

Overall, the appropriate comparator therapy is thus determined as a patient-individual therapy taking into account the 12 active ingredient combinations specified in the resolution, taking into account the active ingredients and combination of active ingredients used in the prior therapies as well as the type and duration of the response to the respective prior therapies.

Concerning the approved active ingredients that have not been determined as appropriate comparator therapy as part of patient-individual therapy in the present determination of the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, guideline recommendations and the reality of care:

the CAR-T cell therapies idecabtagene vicleucel and ciltacabtagene autoleucel are approved for the treatment of patients who have undergone at least three prior therapies. For idecabtagene vicleucel (resolution of 16 June 2022) as well as ciltacabtagene autoleucel (resolution of 17 August 2023), a hint for a non-quantifiable additional benefit was identified since the scientific data basis did not allow quantification. This was done against the background that no statement could be made about the extent of the additional benefit on the basis of the indirect comparisons presented for both therapy options.

The active ingredient selinexor is approved for the treatment setting after at least one prior therapy in combination with bortezomib and dexamethasone. For this combination therapy, it was determined by resolution of 16 March 2023 that an additional benefit compared to the appropriate comparator therapy is not proven.

Melphalan flufenamide is a therapy option for the treatment of subjects with at least three prior therapies. For melphalan flufenamide, the G-BA determined by resolution of 16 March 2023 that an additional benefit is not proven, as no suitable data were available to enable an assessment of the additional benefit.

Teclistamab is a therapy option for the treatment of subjects with at least three prior therapies. By resolution of 15 February 2024, it was determined that an additional benefit of teclistamab is not proven, as no data were available to enable the assessment of an additional benefit.

Talquetamab is another therapy option for the treatment of subjects who have undergone at least three prior therapies. As part of a benefit assessment for medicinal products for the treatment of a rare disease, the G-BA resolution of 7 March 2024 identified a hint for a non-quantifiable additional benefit of talquetamab since the scientific data did not allow quantification.

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

In accordance with the S3 guideline, patients who have undergone at least four prior therapies should also first be assessed to determine whether triplet therapy is appropriate and possible based on the status of the prior therapies.

In addition, the S3 guideline also refers to doublet therapies, classic cytostatic agents, bispecific antibodies and CAR-T cell therapies.

Initially, therefore, all therapy options suitable for the treatment of patients who have undergone three prior therapies can also be considered for patients who have undergone at least four prior therapies (see patient group a). In addition, patient-individual criteria are also decisive for the treatment decision here, which is why a patient-individual therapy was determined as an appropriate comparator therapy. In addition to the active ingredients and combinations of active ingredients used in the prior therapies and the type and duration of the response to the respective prior therapies, the general condition is another relevant criterion for the selection of the patient-individual therapy for the extensively pretreated patients in this patient population.

In addition to the treatment options listed for patient group a), the treatment options listed below are considered suitable comparators as part of patient-individual therapy:

Dual combinations can also be considered for at least double-refractory subjects who are ineligible for triplet therapy.

For at least triple refractory subjects who are ineligible for triplet or doublet therapy, daratumumab, cyclophosphamide and melphalan, each as monotherapy, as well as cyclophosphamide in combination with dexamethasone and melphalan in combination with prednisone or prednisolone, are also suitable comparators as part of patient-individual therapy. Ineligibility for triplet or doublet therapy should be justified on the basis of the patients' refractoriness and comorbidity and taking into account the toxicity of the respective therapy.

In the benefit assessment of the resolution of 16 March 2023, it was identified that an additional benefit of the combination of active ingredients selinexor in combination with dexamethasone compared to the appropriate comparator therapy is not proven. Selinexor in combination with dexamethasone is therefore not considered to be a suitable comparator as part of patient-individual therapy.

For patients who have undergone at least four prior therapies, it is assumed that this patient group will generally continue to receive antineoplastic treatment in the present therapeutic indication. Best supportive care is therefore not considered an appropriate comparator therapy.

Overall, the appropriate comparator therapy is thus determined as a patient-individual therapy by selecting the above-mentioned active ingredients and combinations of active ingredients and taking into account the general condition, the active ingredients and combinations of active ingredients used in the prior therapies and the type and duration of the response to the respective prior therapies.

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

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

Change of the appropriate comparator therapy

Originally, the appropriate comparator therapy was determined as follows:

Adults with relapsed or refractory multiple myeloma who have received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and a monoclonal anti-CD38 antibody, and who have demonstrated disease progression on the last therapy

Appropriate comparator therapy for elranatamab as monotherapy:

A patient-individual therapy under selection of:

- bortezomib monotherapy
- bortezomib + pegylated liposomal doxorubicin
- bortezomib + dexamethasone
- carfilzomib + lenalidomide and dexamethasone
- carfilzomib + dexamethasone
- daratumumab + lenalidomide + dexamethasone
- daratumumab + bortezomib + dexamethasone

- daratumumab monotherapy
- daratumumab + pomalidomide + dexamethasone
- elotuzumab + lenalidomide + dexamethasone
- Elotuzumab + pomalidomide + dexamethasone
- isatuximab + pomalidomide + dexamethasone
- ixazomib + lenalidomide + dexamethasone
- lenalidomide + dexamethasone
- panobinostat + bortezomib and dexamethasone
- pomalidomide + bortezomib and dexamethasone
- pomalidomide + dexamethasone
- cyclophosphamide in combination with other antineoplastic medicinal products
- melphalan as monotherapy or in combination with prednisolone or prednisone
- doxorubicin as monotherapy or in combination with other antineoplastic medicinal products
- vincristine in combination with other antineoplastic medicinal products
- dexamethasone in combination with other antineoplastic medicinal products
- prednisolone in combination with other antineoplastic medicinal products
- prednisone in combination with other antineoplastic medicinal products
- best supportive care

taking into account prior therapies as well as the manifestation and duration of the response.

The present amendment to the appropriate comparator therapy was necessary against the background of a further development of the generally recognised state of medical knowledge. The treatment options and their significance in the present therapeutic indication are subject to dynamic developments, in particular due to the establishment of numerous new treatment options, including in the previous lines of therapy, which also affects the significance of treatment options in the present treatment setting. In this regard, new active ingredients are already being used in earlier lines of therapy, which has an impact on the significance of these active ingredients or therapeutic alternatives in later lines of therapy, taking into account any refractoriness that may occur. As a result, several treatment options originally considered suitable as part of patient-individual therapy are no longer considered appropriate comparator therapies due to the determination of the appropriate comparator therapy for the present resolution. On the other hand, several treatment options or further triplet

therapies are added to the appropriate comparator therapy or as part of the patient-individual therapy.

In addition, a distinction between two distinct patient populations depending on the number of prior therapies is considered appropriate (see above under "on 4.").

This change to the appropriate comparator therapy has no effects on the present assessment of the additional benefit, nor does it require the benefit assessment to be carried out again.

2.1.3 Extent and probability of the additional benefit

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

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

An additional benefit is not proven.

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

An additional benefit is not proven.

Justification:

The pharmaceutical company presented results from the pivotal MagnetisMM-3 study for the benefit assessment of elranatamab for the treatment of adults with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulator, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

The MagnetisMM-3 study is an open-label, single-arm, phase II study for investigating the safety and efficacy of elranatamab for the treatment of adults with relapsed or refractory multiple myeloma whose previous lines of therapy included an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody.

The study that has been ongoing since February 2021 with 187 patients enrolled in a total of 53 study sites in Europe, North America, Australia and Japan investigates two sub-populations. In cohort A, patients were naive to therapy directed against the B-cell maturation antigen [BCMA], while patients in cohort B had already received therapy directed against BCMA.

In addition to the safety and tolerability of elranatamab, the endpoints of the study include response, progression-free survival and overall survival, as well as patient-reported endpoints.

Furthermore, the pharmaceutical company examined the possibility of an indirect comparison between cohort A of the MagnetisMM-3 study and an external control arm from the TM-MM

database (Therapy Monitor Multiple Myeloma). According to the information provided by the pharmaceutical company, however, it was not possible to achieve sufficient balance between the two groups to be compared in the relevant confounders, which is why the pharmaceutical company concluded that the initially planned indirect comparison of the two cohorts could not be carried out completely.

Due to the single-arm study design, the MagnetisMM-3 study presented by the pharmaceutical company does not allow a comparison with the appropriate comparator therapy overall and is therefore unsuitable for the assessment of an additional benefit of elranatamab compared with the appropriate comparator therapy.

An additional benefit of elranatamab for the treatment of adults with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy is therefore not proven.

Conclusion

The results of the single-arm MagnetisMM-3 study are available for the assessment of the additional benefit of elranatamab. These are unsuitable for the assessment of the additional benefit, as they do not allow a comparison with the appropriate comparator therapy. Therefore, an additional benefit of elranatamab as monotherapy for the treatment of adults with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy is not proven.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Elrexfio with the active ingredient elranatamab. Elrexfio received a conditional marketing authorisation.

Elranatamab is indicated for the treatment of adults with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

In the therapeutic indication to be considered, two patient groups were distinguished by the number of prior therapies.

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

The G-BA determined a patient-individual therapy as an appropriate comparator therapy, taking into account the active ingredients and combinations of active ingredients used in the

prior therapies as well as the type and duration of the response to the respective prior therapies.

For the benefit assessment of elranatamab, the pharmaceutical company submitted results of the single-arm MagnetisMM-3 study.

This study does not allow a comparison with the appropriate comparator therapy, which is why an additional benefit of elranatamab for the treatment of adults in this patient group is not proven.

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

The G-BA determined a patient-individual therapy as an appropriate comparator therapy, taking into account the general condition, the active ingredients and combinations of active ingredients used in the prior therapies as well as the type and duration of the response to the respective prior therapies.

For the benefit assessment of elranatamab, the pharmaceutical company submitted results of the single-arm MagnetisMM-3 study.

This study does not allow a comparison with the appropriate comparator therapy, which is why an additional benefit of elranatamab for the treatment of adults in this patient group is not proven.

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 resolution is based on the information from the IQWiG[2] addendum.

The pharmaceutical company calculated the number of patients in the SHI target population using five derivation steps. In doing so, the procedure for idecabtagene vicleucel (multiple myeloma after at least 3 prior therapies, resolution of 16 June 2021) and the uncertainties identified therein were taken into account. IQWIG bases its calculations for sub-populations a) and b) on the patient number determined by the pharmaceutical company. For the calculation of the sub-populations, the percentage of patients with 3 prior therapies or with at least 4 prior therapies from the MagnetisMM-3 study was related to the number of the total population determined by the pharmaceutical company.

[2] IQWIG addendum to project A24-12 – Elranatamab (multiple myeloma)

The number of patients in the SHI target population is subject to uncertainty due to the following aspects:

- The determination of the target population solely on the basis of incidence reports leads to uncertainties, since the percentages of newly ill subjects are transferred to subjects ill in previous years. This uncertainty also applies to the determination of the percentage values for subjects with smouldering multiple myeloma (SMM) and disease progression from an incident population.
- When calculating the percentage of people with multiple myeloma and at least three prior therapies including an immunomodulatory agent, proteasome inhibitor and anti-CD38 antibody, only subjects who were receiving causal therapy at the time of observation are considered. On the basis of the submitted calculation, it cannot be checked whether a complete and correct coverage of all active ingredients approved for the therapeutic indication was carried out. The calculated percentage value does not take into account all subjects with a prior therapy who received a fourth line of therapy in the same year.
- The transfer of the percentage values from the MagnetisMM-3 study to the total population is subject to the uncertainty that there are further inclusion and exclusion criteria for the study population compared to the healthcare context, which can make transferability more difficult.

Due to the uncertainties described above, the following percentage values are assumed for the best possible estimate of the target population:

- Current 10-year prevalence of multiple myeloma: 33,853
- Percentage of subjects with multiple myeloma in diagnosis group ICD-10 C90.-: 94.9%
- Number of subjects with multiple myeloma requiring therapy by exclusion of SMM: 27,489 – 29,553
- Percentage of subjects with at least 3 prior therapies: 5.2%
- Percentage of SHI-insured subjects: 87.3%
- Number of SHI-insured subjects in the total population: 1,249 – 1,342
- Percentage of patients with 3 prior therapies in the MagnetisMM-3 study: 12.1%
- Percentage of patients with at least 4 prior therapies in the MagnetisMM-3 study: 87.9%

The result of the total population is in the same order of magnitude as the patient number decided by resolution on talquetamab (multiple myeloma after at least 3 prior therapies, resolution of 7 March 2024). The result of sub-population b) is within the range of the assumed true value of the patient number in the resolution on belantamab mafodotin (multiple myeloma after at least 4 prior therapies, resolution of 5 October 2023).

The uncertainties identified in connection with the benefit assessments for the active ingredients mentioned continue to exist. Nevertheless, the information provided is the best possible estimate based on the data currently available.

This results in around 150 to 160 subjects for sub-population a) (3 prior therapies) and around 1,100 - 1,180 subjects for sub-population b) (at least 4 prior therapies).

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 Elrexfio (active ingredient: elranatamab) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 21 June 2024):

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

Treatment with elranatamab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with multiple myeloma.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide a patient card.

The patient card is intended to explain the risks of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome and when patients should seek urgent medical treatment in the event of signs and symptoms. In addition, the patient card reminds patients that they should stay close to a medical facility and be monitored daily for signs and symptoms for 48 hours after being administered the step-up doses.

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The EMA will assess new information on this medicinal product at least annually and update the product information as necessary.

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: 15 June 2024).

The costs for the first year of treatment are shown for the cost representation in the resolution.

Treatment period:

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

For bortezomib monotherapy and in combination with pegylated liposomal doxorubicin, a treatment duration of eight cycles is assumed, even if the actual treatment duration may differ from patient to patient.

Treatment with ixazomib in combination with lenalidomide and dexamethasone for more than 24 cycles should be based on an individual risk-benefit assessment, as data on tolerability and toxicity beyond 24 cycles are limited.

Treatment with carfilzomib in combination with lenalidomide and dexamethasone spanning beyond 18 cycles should be based on an individual risk-benefit assessment, as data on the tolerability and toxicity of carfilzomib beyond 18 cycles are limited.

When combining melphalan with prednisone or prednisolone, the treatment regimens and dosages follow the underlying product information for melphalan, prednisone or prednisolone.

For the cyclophosphamide + dexamethasone combination which was defined as the appropriate comparator therapy, no study that would allow cost representation could be identified. The costs can therefore not be quantified.

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Elranatamab				
Elranatamab	Step-up dosage regimen: Day 1, 4 Maintenance dosage regimen from week 2:	2	1	2

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	Day 1 1 x every 7 days Maintenance dosage regimen in case of response from week 25: 1 x every 14 days	51.1 37.1	1 1	51.1 37.1
Appropriate comparator therapy				
A patient-individual therapy under selection of:				
carfilzomib in combination with lenalidomide and dexamethasone				
Carfilzomib	1st -12th cycle: Day 1, 2, 8, 9, 15, 16 From 13th cycle: Day 1, 2, 15, 16 28-day cycle	13.0	1st - 12th cycle: 6	76.0
Lenalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52.0
Carfilzomib in combination with dexamethasone				
Carfilzomib	Day 1, 2, 8, 9, 15, 16: 28-day cycle	13.0	6	78.0
Dexamethasone	Day 1, 2, 8, 9, 15, 16, 22, 23: 28-day cycle	13.0	8	104.0
Daratumumab in combination with lenalidomide and dexamethasone				
Daratumumab	Week 1 - 8: 1 x every 7 days Week 9 - 24: 1 x every 14 days From week 25: 1 x every 28 days	23.0	1	23.0
Lenalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	Cycle 1 – 2: 0 Cycle 3 – 6: 2 From cycle 7 onwards: 3	29.0[3]
Daratumumab in combination with pomalidomide and dexamethasone (only for subjects who are refractory to lenalidomide)				
Daratumumab	Week 1 - 8: 1 x every 7 days Week 9 - 24: 1 x every 14 days From week 25: 1 x every 28 days	23.0	1	23.0
Pomalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	Cycle 1 - 2: 0 Cycle 3 - 6: 2 From cycle 7 onwards: 3	29.0[3]
Daratumumab in combination with bortezomib and dexamethasone				
Daratumumab	Week 1 - 9: 1 x every 7 days Week 10 - 24: 1 x every 21 days From week 25: 1 x every 28 days	1st year: 21.0	1	21.0
Bortezomib	Day 1, 4, 8 and 11: 21-day cycle	8.0	4	32.0
Dexamethasone	Day 1, 2, 4, 5, 8, 9, 11, 12	8.0	Cycle 1 - 3: 6 Cycle 4 - 8:	53.0[4]

[3] On the days of daratumumab administration, 20 mg of the dexamethasone dose is used as premedication and 20 mg on the day after daratumumab administration

[4] On the days of daratumumab administration, 20 mg of the dexamethasone dose is used as premedication.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	of the bortezomib cycles		7	
Daratumumab in combination with carfilzomib and dexamethasone				
Daratumumab	Cycle 1–2: Day 1, 8, 15, 22 Cycle 3–6: Day 1, 15 From cycle 7 onwards: Day 1 28-day cycle	13.0	Cycle 1–2: 4 Cycle: 3-6: 2 From cycle 7 onwards: 1	23.0
Carfilzomib	Day 1, 2, 8, 9, 15 16 28-day cycle	13.0	6	78.0
Dexamethasone	Day 1, 2, 8, 9, 15.16, 22: 28-day cycle	13.0	Cycle 1-2: 3 Cycle 3-6: 5 From cycle 7 onwards: 6	68.0[5]
Elotuzumab in combination with lenalidomide and dexamethasone				
Elotuzumab	1st - 2nd cycle: Day 1, 8, 15, 22 From 3rd cycle: Day 1, 15 28-day cycle	13.0	1st - 2nd cycle 4 From 3rd cycle 2	30.0
Lenalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52.0
Elotuzumab + pomalidomide + dexamethasone				
Elotuzumab	1st - 2nd cycle: Day 1, 8, 15, 22 From 3rd cycle: Day 1 28-day cycle	13.0	1st - 2nd cycle: 4 From 3rd cycle:	19.0

[5] On the days of daratumumab administration, the treatment dose of dexamethasone is used as premedication.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
			1	
Pomalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52.0
Isatuximab in combination with pomalidomide and dexamethasone				
Isatuximab	1st cycle: Day 1, 8, 15, 22 From 2nd cycle: Day 1, 15 28-day cycle	13.0	1st cycle: 4 From 2nd cycle: 2	28.0
Pomalidomide	Day 1 - 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52
Isatuximab in combination with carfilzomib and dexamethasone				
Isatuximab	1st cycle: Day 1, 8, 15, 22 From 2nd cycle: Day 1, 15 28-day cycle	13.0	1st cycle: 4 From 2nd cycle: 2	28.0
Carfilzomib	Day 1, 2, 8, 9, 15, 16: 28-day cycle	13.0	6	78.0
Dexamethasone PO / IV	Day 1, 2, 8, 9, 15, 16, 22, 23: 28-day cycle	13.0	8	104.0[6]
Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)				
Ixazomib	Day 1, 8, 15 of a 28-day cycle	13.0	3	39.0
Lenalidomide	Day 1 – 21 of a 28-day cycle	13.0	21	273.0

[6] On the days of isatuximab and/or carfilzomib administration, 20 mg of the dexamethasone dose is administered intravenously and on the other days orally.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Dexamethasone	Day 1, 8, 15, 22 of a 28-day cycle	13.0	4	52.0
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)				
Pomalidomide	Day 1 – 14: 21-day cycle	17.4	14	243.6
Bortezomib	1st - 8th cycle: Day 1, 4, 8, 11 From 9th cycle: Day 1, 8 21-day cycle	17.4	1st - 8th cycle: 4 From 9th cycle: 2	1st year: 50.8
Dexamethasone	1st - 8th cycle: Day 1, 2, 4, 5, 8, 9, 11, 12 From 9th cycle: Day 1, 2, 8, 9 21-day cycle	17.4	1st - 8th cycle: 8 From 9th cycle: 4	1st year: 101.6

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Elranatamab				
Elranatamab	Step-up dosage regimen: Day 1, 4 Maintenance dosage regimen from week 2: Day 1 1 x every 7 days	2 51.1	1 1	2 51.1

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	Maintenance dosage regimen in case of response from week 25: 1 x every 14 days	37.1	1	37.1
Appropriate comparator therapy				
A patient-individual therapy under selection of:				
Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)				
Bortezomib	Day 1, 4, 8, 11: 21-day cycle	8	4	32
Doxorubicin (pegylated, liposomal)	Day 4: 21-day cycle	8	1	8
Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)				
Bortezomib	Day 1, 4, 8, 11: 21-day cycle	4 – 8	4	16 – 32
Dexamethasone	Day 1, 2, 4, 5, 8, 9, 11, 12: 21-day cycle	4 - 8	8	32 – 64
Carfilzomib in combination with lenalidomide and dexamethasone				
Carfilzomib	1st -12th cycle: Day 1, 2, 8, 9, 15, 16 From 13th cycle: Day 1, 2, 15, 16 28-day cycle	13.0	1st - 12th cycle: 6 From 13th cycle: 4	76.0
Lenalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52.0
Carfilzomib in combination with dexamethasone				
Carfilzomib	Day 1, 2, 8, 9, 15, 16: 28-day cycle	13.0	6	78.0
Dexamethasone	Day 1, 2, 8, 9, 15, 16, 22, 23: 28-day cycle	13.0	8	104.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Daratumumab in combination with lenalidomide and dexamethasone				
Daratumumab	Week 1 - 8: 1 x every 7 days Week 9 - 24: 1 x every 14 days From week 25: 1 x every 28 days	23.0	1	23.0
Lenalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	Cycle 1 – 2: 0 Cycle 3 – 6: 2 From cycle 7 onwards: 3	29.0[3]
Daratumumab in combination with pomalidomide and dexamethasone				
Daratumumab	Week 1 - 8: 1 x every 7 days Week 9 - 24: 1 x every 14 days From week 25: 1 x every 28 days	23.0	1	23.0
Pomalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	Cycle 1 – 2: 0 Cycle 3 – 6: 2 From cycle 7 onwards: 3	29.0[3]
Daratumumab in combination with bortezomib and dexamethasone				
Daratumumab	Week 1 - 9: 1 x every 7 days Week 10 - 24: 1 x every 21 days	21.0	1	21.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	From week 25: 1 x every 28 days			
Bortezomib	Day 1, 4, 8 and 11: 21-day cycle	8	4	32
Dexamethasone	Day 1, 2, 4, 5, 8, 9, 11, 12 of the bortezomib cycles	8	Cycle 1 - 3: 6 Cycle 4 - 8: 7	53[4]
Daratumumab in combination with carfilzomib and dexamethasone				
Daratumumab	Cycle 1–2: Day 1, 8, 15, 22 Cycle 3–6: Day 1, 15 From cycle 7 onwards: Day 1 28-day cycle	13.0	Cycle 1–2: 4 cycle: 3-6: 2 From cycle 7 onwards: 1	23.0
Carfilzomib	Day 1, 2, 8, 9, 15 16 28-day cycle	13.0	6	78.0
Dexamethasone	Day 1, 2, 8, 9, 15.16, 22: 28-day cycle	13.0	Cycle 1–2: 3 cycle: 3-6: 5 From cycle 7 onwards: 6	68.0[5]
Daratumumab monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)				
Daratumumab	Week 1 - 8: 1 x every 7 days Week 9 - 24: 1 x every 14 days From week 25: 1 x every 28 days	23.0	1	23.0
Elotuzumab in combination with lenalidomide and dexamethasone				
Elotuzumab	1st - 2nd cycle: Day 1, 8, 15, 22	13.0	1st - 2nd cycle	30.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	From 3rd cycle: Day 1, 15 28-day cycle		4 From 3rd cycle 2	
Lenalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52.0
Elotuzumab + pomalidomide + dexamethasone				
Elotuzumab	1st - 2nd cycle: Day 1, 8, 15, 22 From 3rd cycle: Day 1 28-day cycle	13.0	1st - 2nd cycle: 4 From 3rd cycle: 1	19.0
Pomalidomide	Day 1 – 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52.0
Isatuximab in combination with pomalidomide and dexamethasone				
Isatuximab	1st cycle: Day 1, 8, 15, 22 From 2nd cycle: Day 1, 15 28-day cycle	13.0	1st cycle: 4 From 2nd cycle: 2	28.0
Pomalidomide	Day 1 - 21: 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22: 28-day cycle	13.0	4	52
Isatuximab in combination with carfilzomib and dexamethasone				
Isatuximab	1st cycle: Day 1, 8, 15, 22 From 2nd cycle: Day 1, 15 28-day cycle	13.0	1st cycle: 4 From 2nd cycle: 2	28.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Carfilzomib	Day 1, 2, 8, 9, 15, 16: 28-day cycle	13.0	6	78.0
Dexamethasone PO / IV	Day 1, 2, 8, 9, 15, 16, 22, 23: 28-day cycle	13.0	8	104.0[6]
Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)				
Ixazomib	Day 1, 8, 15 of a 28-day cycle	13.0	3	39.0
Lenalidomide	Day 1 – 21 of a 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22 of a 28-day cycle	13.0	4	52.0
Lenalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)				
Lenalidomide	Day 1 - 21 of a 28-day cycle	13.0	21	273.0
Dexamethasone	1st - 4th cycle: Day 1 - 4, 9 - 12, 17 - 20 From 5th cycle: Day 1 - 4 28-day cycle	13.0	1st - 4th cycle: 12 From 5th cycle: 4	84.0
Panobinostat in combination with bortezomib and dexamethasone				
Panobinostat	1st - 16th cycle: Day 1, 3, 5, 8, 10, 12 21-day cycle	8 – 16	6	48 – 96
Bortezomib	1st - 8th cycle: Day 1, 4, 8, 11 9th - 16th cycle: Day 1, 8 21-day cycle	8 – 16	1st – 8th cycle: 4 9th - 16th cycle: 2	32 – 48
Dexamethasone	1st - 8th cycle: Day 1, 2, 4, 5, 8, 9, 11, 12	8 – 16	1st – 8th cycle: 8	64 – 96

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	9th - 16th cycle: Day 1, 2, 8, 9 21-day cycle		9th - 16th cycle: 4	
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)				
Pomalidomide	Day 1 – 14: 21-day cycle	17.4	14	243.6
Bortezomib	1st - 8th cycle: Day 1, 4, 8, 11 From 9th cycle: Day 1, 8 21-day cycle	17.4	1st - 8th cycle: 4 From 9th cycle: 2	50.8
Dexamethasone	1st - 8th cycle: Day 1, 2, 4, 5, 8, 9, 11, 12 From 9th cycle: Day 1, 2, 8, 9 21-day cycle	17.4	1st - 8th cycle: 8 From 9th cycle: 4	101.6
Pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)				
Pomalidomide	Day 1 – 21 of a 28-day cycle	13.0	21	273.0
Dexamethasone	Day 1, 8, 15, 22 of a 28-day cycle	13.0	4	52.0
Cyclophosphamide monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)				
Cyclophosphamide	Continuously, 1 x daily or Continuously, 1 x every 21-28 days or Continuously, every 2-5 days	13.0 – 365.0	1	13.0 – 365.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Cyclophosphamide in combination with dexamethasone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)				
No specification possible				
Melphalan monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)				
Melphalan	Continuously, 1 x every 28 days	13.0	1	13.0
Melphalan in combination with prednisolone or prednisone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)				
Melphalan	Day 1 of a 28 – 42-day cycle	8.7 – 13.0	1	8.7 – 13.0
Prednisolone	Day 1 – 4 of a 28 – 42-day cycle	8.7 – 13.0	4	34.8 – 52.0
Melphalan	Day 1 of a 28 – 42-day cycle	8.7 – 13.0	1	8.7 – 13.0
Prednisone	Day 1 – 4 of a 28 – 42-day cycle	8.7 – 13.0	4	34.8 – 52.0

Consumption:

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg). This results in a body surface area of 1.91 m² (calculated according to Du Bois 1916)[7].

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.

[7] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

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					
Elranatamab					
Elranatamab	Step-up dosing: Week 1: Day 1: 12 mg	Step-up dosing: Week 1: Day 1: 12 mg	Step-up dosing: Week 1: Day 1: 1 x 12 mg	1	1 x 12 mg
	Step-up dosing: Week 1: Day 4: 32 mg	Step-up dosing: Week 1: Day 4: 32 mg	Step-up dosing: Week 1: Day 4: 1 x 32 mg	1	1 x 32 mg
	Maintenance dosing: 76 mg	Maintenance dosing: 76 mg	Maintenance dosing: 1 x 76 mg	37.1 – 51.1	37.1 x 76 mg – 51.1 x 76 mg
Appropriate comparator therapy					
A patient-individual therapy under selection of:					
carfilzomib in combination with lenalidomide and dexamethasone					
Carfilzomib	1st cycle day 1, 2 20 mg/m² Thereafter 27 mg/m²	1st cycle day 1, 2 38.2 mg Thereafter 51.6 mg	1st cycle Day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 1 x 60 mg	76.0	2 x 10 mg + 2 x 30 mg + 74 x 60 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52 x 40 mg
Carfilzomib in combination with dexamethasone					
Carfilzomib	1st cycle day 1, 2 20 mg/m² Thereafter 56 mg/m²	1st cycle day 1, 2 38.2 mg Thereafter 107 mg	1st cycle day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 2 x 10 mg + 1 x 30 mg +	78.0	154 x 10 mg + 78 x 30 mg + 76 x 60 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
			1 x 60 mg		
Dexamethasone	20 mg	20 mg	1 x 20 mg	104.0	104 x 20 mg
Daratumumab in combination with lenalidomide and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	29.0	29 x 40 mg
Daratumumab in combination with pomalidomide and dexamethasone (only for subjects who are refractory to lenalidomide)					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	29.0	29 x 40 mg
Daratumumab in combination with carfilzomib and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Carfilzomib	1st cycle day 1, 2 20 mg/m² Thereafter 56 mg/m²	1st cycle day 1, 2 38.2 mg Thereafter 107 mg	1st cycle day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 2 x 10 mg + 1 x 30 mg + 1 x 60 mg	78.0	154 x 10 mg + 78 x 30 mg + 76 x 60 mg
Dexamethasone	Day 1.2, 8, 9, 15, 16 20 mg Day 22 40 mg	Day 1.2, 8, 9, 15, 16 20 mg Day 22 40 mg	Day 1.2, 8, 9, 15, 16 1 x 20 mg Day 22 1 x 40 mg	68.0	57 x 20 mg + 11 x 40 mg
Daratumumab in combination with bortezomib and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	21.0	21 x 1,800 mg
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	32.0	32 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	53.0	53 x 20 mg
Elotuzumab in combination with lenalidomide and dexamethasone					
Elotuzumab	10 mg/kg	777 mg	2 x 400 mg	30.0	60 x 400 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	1st - 2nd cycle	1st - 2nd cycle Day 1, 8, 15, 22:	1 x 8 mg + 1 x 20 mg	52.0	30 x 8 mg + 30 x 20 mg + 22 x 40 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	Day 1, 8, 15, 22: 28 mg From 3rd cycle Day 1, 15: 28 mg Day 8, 22: 40 mg	28 mg From 3rd cycle Day 1, 15: 28 mg Day 8, 22: 40 mg	or 1 x 40 mg		
Elotuzumab + pomalidomide + dexamethasone					
Elotuzumab	1st - 2nd cycle Day 1, 8, 15, 22: 10 mg/kg From 3rd cycle Day 1: 20 mg/kg	1st - 2nd cycle Day 1, 8, 15, 22: 777 mg From 3rd cycle Day 1: 1,554 mg	1st - 2nd cycle Day 1, 8, 15, 22: 2 x 400 mg From 3rd cycle Day 1: 4 x 400 mg	19.0	60 x 400 mg
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	1st - 2nd cycle Day 1, 8, 15, 22: 28 mg From 3rd cycle Day 1: 28 mg Day 8, 15, 22: 40 mg	1st - 2nd cycle Day 1, 8, 15, 22: 28 mg From 3rd cycle Day 1 28 mg Day 8, 15, 22: 40 mg	1 x 8 mg + 1 x 20 mg or 1 x 40 mg	52.0	19 x 8 mg + 19 x 20 mg + 33 x 40 mg
Isatuximab in combination with pomalidomide and dexamethasone					
Isatuximab	10 mg/kg	777 mg	1 x 500 mg + 3 x 100 mg	28.0	28 x 500 mg + 84 x 100 mg
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52.0 x 40 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Isatuximab in combination with carfilzomib and dexamethasone					
Isatuximab	10 mg/kg	777 mg	1 x 500 mg + 3 x 100 mg	28.0	28 x 500 mg + 84 x 100 mg
Carfilzomib	1st cycle day 1, 2: 20 mg/m² Thereafter 56 mg/m²	1st cycle day 1, 2: 38.2 mg Thereafter 107 mg	1st cycle Day 1, 2: 1 x 10 mg + 1 x 30 mg Thereafter 2 x 10 mg + 1 x 30 mg + 1 x 60 mg	78.0	154 x 10 mg + 78 x 30 mg + 76 x 60 mg
Dexamethasone PO	20 mg	20 mg	1 x 20 mg	25.0	25 x 20 mg
Dexamethasone IV	20 mg	20 mg	5 x 4 mg	79.0	395 x 4 mg
Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)					
Ixazomib	4 mg	4 mg	1 x 4 mg	39.0	39 x 4 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52 x 40 mg
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)					
Pomalidomide	4 mg	4 mg	1 x 4 mg	243.6	243.6 x 4 mg
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	50.8	50.8 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	101.6	101.6 x 20 mg

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

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					
Elranatamab					
Elranatamab	Step-up dosing: Week 1: Day 1: 12 mg	Step-up dosing: Week 1: Day 1: 12 mg	Step-up dosing: Week 1: Day 1: 1 x 12 mg	1	1 x 12 mg
	Step-up dosing: Week 1: Day 4: 32 mg	Step-up dosing: Week 1: Day 4: 32 mg	Step-up dosing: Week 1: Day 4: 1 x 32 mg	1	1 x 32 mg
	Maintenance dosing: 76 mg	Maintenance dosing: 76 mg	Maintenance dosing: 1 x 76 mg	37.1 – 51.1	37.1 x 76 mg – 51.1 x 76 mg
Appropriate comparator therapy					
A patient-individual therapy under selection of:					
Bortezomib in combination with pegylated liposomal doxorubicin (only for at least double-refractory subjects who are ineligible for triplet therapy)					
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	32	32 x 2.5 mg
Doxorubicin (pegylated, liposomal)	30 mg/m²	57.3 mg	1 x 20 mg 1 x 50 mg	8	8 x 20 mg 8 x 50 mg
Bortezomib in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)					
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	16 – 32	16 - 32 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	32 – 64	32 – 64 x 20 mg
Carfilzomib in combination with lenalidomide and dexamethasone					
Carfilzomib	1st cycle day 1, 2 20 mg/m²	1st cycle day 1, 2 38.2 mg	1st cycle Day 1, 2 1 x 10 mg + 1 x 30 mg	76.0	2 x 10 mg + 2 x 30 mg + 74 x 60 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	Thereafter 27 mg/m²	Thereafter 51.57 mg	Thereafter 1 x 60 mg		
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52 x 40 mg
Carfilzomib in combination with dexamethasone					
Carfilzomib	1st cycle day 1, 2 20 mg/m² Thereafter 56 mg/m²	1st cycle day 1, 2 38.2 mg Thereafter 107 mg	1st cycle day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 2 x 10 mg + 1 x 30 mg + 1 x 60 mg	78.0	154 x 10 mg + 78 x 30 mg + 76 x 60 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	104.0	104 x 20 mg
Daratumumab in combination with lenalidomide and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	29.0	29 x 40 mg
Daratumumab in combination with pomalidomide and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	29.0	29 x 40 mg
Daratumumab in combination with bortezomib and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	21.0	21 x 1,800 mg
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	32.0	32 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	53.0	53 x 20 mg
Daratumumab in combination with carfilzomib and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Carfilzomib	1st cycle day 1, 2 20 mg/m² Thereafter 56 mg/m²	1st cycle day 1, 2 38.2 mg Thereafter 107 mg	1st cycle day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 2 x 10 mg + 1 x 30 mg + 1 x 60 mg	78.0	154 x 10 mg + 78 x 30 mg + 76 x 60 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Dexamethasone	Day 1.2, 8, 9, 15, 16 20 mg Day 22 40 mg	Day 1.2, 8, 9, 15, 16 20 mg Day 22 40 mg	Day 1.2, 8, 9, 15, 16 1 x 20 mg Day 22 1 x 40 mg	68.0	57 x 20 mg + 11 x 40 mg
Daratumumab monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	23.0	23 x 1,800 mg
Elotuzumab in combination with lenalidomide and dexamethasone					
Elotuzumab	10 mg/kg	777 mg	2 x 400 mg	30.0	60 x 400 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	1st - 2nd cycle Day 1, 8, 15, 22: 28 mg From 3rd cycle Day 1, 15: 28 mg Day 8, 22: 40 mg	1st - 2nd cycle Day 1, 8, 15, 22: 28 mg From 3rd cycle Day 1, 15: 28 mg Day 8, 22: 40 mg	1 x 8 mg + 1 x 20 mg or 1 x 40 mg	52.0	30 x 8 mg + 30 x 20 mg + 22 x 40 mg
Elotuzumab + pomalidomide + dexamethasone					
Elotuzumab	1st - 2nd cycle Day 1, 8, 15, 22: 10 mg/kg From 3rd cycle Day 1: 20 mg/kg	1st - 2nd cycle Day 1, 8, 15, 22: 777 mg From 3rd cycle Day 1: 1,554 mg	1st - 2nd cycle Day 1, 8, 15, 22: 2 x 400 mg From 3rd cycle Day 1: 4 x 400 mg	19.0	60 x 400 mg
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	1st - 2nd cycle Day 1, 8, 15, 22:	1st - 2nd cycle Day 1, 8, 15, 22:	1 x 8 mg + 1 x 20 mg or	52.0	19 x 8 mg + 19 x 20 mg + 33 x 40 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	28 mg From 3rd cycle Day 1: 28 mg Day 8, 15, 22: 40 mg	28 mg From 3rd cycle Day 1 28 mg Day 8, 15, 22: 40 mg	1 x 40 mg		
Isatuximab in combination with pomalidomide and dexamethasone					
Isatuximab	10 mg/kg	777 mg	1 x 500 mg + 3 x 100 mg	28.0	28 x 500 mg + 84 x 100 mg
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52.0 x 40 mg
Isatuximab in combination with carfilzomib and dexamethasone					
Isatuximab	10 mg/kg	777 mg	1 x 500 mg + 3 x 100 mg	28.0	28 x 500 mg + 84 x 100 mg
Carfilzomib	1st cycle day 1, 2 20 mg/m² Thereafter 56 mg/m²	1st cycle day 1, 2 38.2 mg Thereafter 107 mg	1st cycle day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 2 x 10 mg + 1 x 30 mg + 1 x 60 mg	78.0	154 x 10 mg + 78 x 30 mg + 76 x 60 mg
Dexamethasone PO	20 mg	20 mg	1 x 20 mg	25.0	25 x 20 mg
Dexamethasone IV	20 mg	20 mg	5 x 4 mg	79.0	395 x 4 mg
Ixazomib in combination with lenalidomide and dexamethasone (only for subjects who are refractory to bortezomib, carfilzomib and an anti-CD38 antibody)					
Ixazomib	4 mg	4 mg	1 x 4 mg	39.0	39 x 4 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52 x 40 mg
Lenalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)					
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	84.0	84 x 40 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Panobinostat in combination with bortezomib and dexamethasone					
Panobinostat	20 mg	20 mg	1 x 20 mg	48 – 96	48 x 20 mg – 96 x 20 mg
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	32 – 48	32 x 2.5 mg – 48 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	64 – 96	64 x 20 mg – 96 x 20 mg
Pomalidomide in combination with bortezomib and dexamethasone (only for subjects who are refractory to an anti-CD38 antibody and lenalidomide)					
Pomalidomide	4 mg	4 mg	1 x 4 mg	243.6	243.6 x 4 mg
Bortezomib	1.3 mg/m²	2.5 mg	1 x 2.5 mg	50.8	50.8 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	101.6	101.6 x 20 mg
Pomalidomide in combination with dexamethasone (only for at least double-refractory subjects who are ineligible for triplet therapy)					
Pomalidomide	4 mg	4 mg	1 x 4 mg	273.0	273 x 4 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	52.0	52 x 40 mg
Cyclophosphamide monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
Cyclophosphamide	120 mg/m² – 240 mg/m²	229.2 mg – 458.4 mg	2 x 200 mg – 1 x 500 mg	365.0	730 x 200 mg – 365 x 500 mg
	400 mg/m² – 600 mg/m²	764 mg – 1,146 mg	1 x 1,000 mg – 1 x 1,000 mg + 1 x 200 mg	73.0 – 182.5	73 x 1,000 mg – 182.5 x 1,000 mg + 182.5 x 200 mg +
	800 mg/m² - 1,600 mg/m²	1,528 mg – 3,506 mg	2 x 1,000 mg – 4 x 1,000 mg	13.0 - 17.4	26 x 1,000 mg – 69.6 x 1,000 mg
Cyclophosphamide in combination with dexamethasone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
No specification possible					
Melphalan monotherapy (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
Melphalan	0.4 mg/kg	31.1 mg	1 x 50 mg	13.0	13 x 50 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Melphalan in combination with prednisone or prednisolone (only for at least triple refractory subjects who are ineligible for triplet or doublet therapy)					
Melphalan	Day 1: 15 mg/m²	Day 1: 28.7 mg	1 x 50 mg	8.7 – 13.0	8.7 x 50 mg – 13 x 50 mg
Prednisone	Day 1 – 4: 2 mg/kg	Day 1 – 4: 155.4 mg	3 x 50 mg + 1 x 5 mg	34.8 – 52.0	104.4 x 50 mg + 34.8 x 5 mg – 156 x 50 mg + 52 x 5 mg
Prednisolone	Day 1 – 4: 2 mg/kg	Day 1 – 4: 155.4 mg	3 x 50 mg + 1 x 5 mg	34.8 – 52.0	104.4 x 50 mg + 34.8 x 5 mg – 156 x 50 mg + 52 x 5 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. Any fixed reimbursement rates shown in the cost representation may not represent the cheapest available alternative.

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					
Elranatamab 44 mg	1.1 ml SFI	€ 4,607.79	€ 2.00	€ 259.86	€ 4,345.93
Elranatamab 76 mg	1.9 ml SFI	€ 7,916.99	€ 2.00	€ 448.85	€ 7,466.14
Appropriate comparator therapy					
Bortezomib 2.5 mg	1 PSI	€ 185.37	€ 2.00	€ 8.26	€ 175.11

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
Carfilzomib 10 mg	1 PIF	€ 197.03	€ 2.00	€ 10.28	€ 184.75
Carfilzomib 30 mg	1 PIF	€ 568.43	€ 2.00	€ 30.84	€ 535.59
Carfilzomib 60 mg	1 PIF	€ 1,125.54	€ 2.00	€ 61.69	€ 1,061.85
Cyclophosphamide 1,000 mg	6 PSI	€ 127.45	€ 2.00	€ 6.43	€ 119.02
Cyclophosphamide 500 mg	6 PSI	€ 84.44	€ 2.00	€ 9.25	€ 73.19
Cyclophosphamide 200 mg	10 PSI	€ 62.80	€ 2.00	€ 2.85	€ 57.95
Daratumumab 1,800 mg	1 SFI	€ 5,809.87	€ 2.00	€ 0.00	€ 5,807.87
Dexamethasone 4 mg[8]	10 SFI	€ 16.92	€ 2.00	€ 0.44	€ 14.48
Dexamethasone 8 mg[8]	100 TAB	€ 123.41	€ 2.00	€ 8.87	€ 112.54
Dexamethasone 20 mg[8]	10 TAB	€ 32.42	€ 2.00	€ 0.00	€ 30.42
Dexamethasone 20 mg[8]	20 TAB	€ 54.09	€ 2.00	€ 0.00	€ 52.09
Dexamethasone 20 mg[8]	50 TAB	€ 118.88	€ 2.00	€ 0.00	€ 116.88
Dexamethasone 40 mg[8]	50 TAB	€ 188.03	€ 2.00	€ 0.00	€ 186.03
Pegylated liposomal doxorubicin 20 mg	1 CIS	€ 721.49	€ 2.00	€ 89.87	€ 629.62
Pegylated liposomal doxorubicin 50 mg	1 CIS	€ 1,778.90	€ 2.00	€ 224.69	€ 1,552.21
Elotuzumab 400 mg	1 PIC	€ 1,557.91	€ 2.00	€ 85.68	€ 1,470.23
Isatuximab 100 mg	1 CIS	€ 333.96	€ 2.00	€ 17.86	€ 314.10
Isatuximab 500 mg	1 CIS	€ 1,621.58	€ 2.00	€ 89.32	€ 1,530.26
Ixazomib 4 mg	3 HC	€ 6,431.30	€ 2.00	€ 364.00	€ 6,065.30
Lenalidomide 25 mg[8]	63 HC	€ 117.32	€ 2.00	€ 8.38	€ 106.94
Melphalan 50 mg	1 DSS	€ 50.49	€ 2.00	€ 2.17	€ 46.32
Panobinostat 20 mg	6 HC	€ 4,656.41	€ 2.00	€ 262.64	€ 4,391.77
Pomalidomide 4 mg	21 HC	€ 9,061.45	€ 2.00	€ 516.91	€ 8,542.54
Prednisolone 5 mg[8]	100 TAB	€ 15.43	€ 2.00	€ 0.33	€ 13.10
Prednisolone 50 mg[8]	50 TAB	€ 31.44	€ 2.00	€ 1.59	€ 27.85
Prednisone 5 mg[8]	100 TAB	€ 16.74	€ 2.00	€ 0.43	€ 14.31
Prednisone 50 mg[8]	50 TAB	€ 68.06	€ 2.00	€ 4.49	€ 61.57

[8] Fixed reimbursement rate

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
Abbreviations: HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PSI = powder for solution for injection; PIF = powder for the preparation of an infusion solution; PIC = powder for the preparation of an infusion solution concentrate; TAB = tablets; DSS = dry substance with solvent					

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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.

Patients receiving therapy with pomalidomide, daratumumab and lenalidomide should be tested for the presence of HBV infection before initiating the respective treatment.

Diagnostics to rule out chronic hepatitis B requires sensibly coordinated steps[9]. A step-by-step serological diagnosis initially consists of the examination of HBs antigen and anti-HBc antibodies. If both are negative, a past HBV infection can be excluded. In certain case constellations, further steps may be necessary in accordance with current guideline recommendations.

In deviation from this, additional required SHI services are required for the diagnosis of suspected chronic hepatitis B, which usually differ between the medicinal product to be evaluated and the appropriate comparator therapy and are consequently considered as additionally required SHI services in the resolution.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of 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 5aSGB V, when a non-prescription medicinal product

[9] S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011" https://register.awmf.org/assets/guidelines/021-011l_S3_Prophylaxe-Diagnostik-Therapie-der-Hepatitis-B-Virusinfektion_2021-07.pdf

is dispensed and invoiced in accordance with Section 300, a medicinal product dispensing price in the amount of the dispensing price of the pharmaceutical company plus the surcharges in accordance with Sections 2 and 3 of the Pharmaceutical Price Ordinance in the version valid on 31 December 2003 applies to the insured.

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Medicinal product to be assessed							
Elranatamab							
Premedication before the first 3 doses elranatamab							
Dexamethasone 20 mg, IV[8]	10 AMP x 8 mg 3 AMP x 4 mg	€ 20.38 € 13.20	€ 2.00 € 2.00	€ 0.72 € 0.15	€ 17.66 € 11.05	3	€ 28.71
Paracetamol 500 mg, PO[8]	10 TAB x 500 mg	€ 2.96	€ 0.15	€ 0.13	€ 2.68	3	€ 2.68
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	3	€ 32.86
Appropriate comparator therapy							
Daratumumab *in combination with lenalidomide and dexamethasone*							
Premedication							
Dexamethasone 40 mg, PO[8]	50 TAB x 40 mg	€ 188.03	€ 2.00	€ 0.00	€ 186.03	23.0	€ 85.57
Paracetamol 500 - 1,000 mg, PO[8,10]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	23.0	€ 3.62 - € 6.92
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	23.0	€ 151.16
Daratumumab *in combination with bortezomib and dexamethasone*							
Premedication							
Dexamethasone 20 mg, PO[8]	50 TAB x 20 mg	€ 118.88	€ 2.00	€ 0.00	€ 116.88	21.0	€ 49.09
Paracetamol 500 - 1,000 mg, PO[10,8]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	21.0	€ 3.31 - € 6.32

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

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
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	21.0	€ 138.01
Daratumumab *in combination with pomalidomide and dexamethasone*							
Premedication							
Dexamethasone 40 mg, PO[8]	50 TAB x 40 mg	€ 188.03	€ 2.00	€ 0.00	€ 186.03	23.0	€ 85.57
Paracetamol 500 - 1,000 mg, PO [10,8]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	23.0	€ 3.62 - € 6.92
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	23.0	€ 151.16
Daratumumab *in combination with carfilzomib and dexamethasone*							
Dexamethasone 20 mg, PO[8]	50 TAB x 20 mg	€ 118.88	€ 2.00	€ 0.00	€ 116.88	21.0	€ 49.09
Dexamethasone 40 mg, PO[8]	50 TAB x 40 mg	€ 188.03	€ 2.00	€ 0.00	€ 186.03	2.0	€ 7.44
Paracetamol 500 - 1,000 mg, PO [10,8]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	23.0	€ 3.62 - € 6.92
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	23.0	€ 151.16
Daratumumab *monotherapy*							
Premedication							
Methyl prednisolone 60 mg - 100 mg, IV	3 PII x 32 mg	€ 25.32	€ 2.00	€ 6.36	€ 16.96	23.0	€ 260.05 - € 520.11
Postmedication							
Methyl prednisolone 20 mg, PO[8]	100 TAB x 4 mg 100 TAB x 16 mg	€ 29.35 € 73.84	€ 2.00 € 2.00	€ 1.43 € 4.95	€ 25.92 € 66.89	46.0 46.0	€ 42.69

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
Elotuzumab *in combination with lenalidomide and dexamethasone*							
Premedication in combination with lenalidomide and dexamethasone							
Dexamethasone 8 mg, IV [8]	10 SFI x 8 mg	€ 20.38	€ 2.00	€ 0.72	€ 17.66	30.0	€ 52.98
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	30.0	€ 197.16
Famotidine 20 mg, PO [8]	100 TAB x 20 mg	€ 20.18	€ 2.00	€ 0.70	€ 17.48	30.0	€ 5.24
Paracetamol 500 – 1,000 mg, PO[8]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	30.0	€ 4.73 - € 9.03
Elotuzumab *in combination with pomalidomide and dexamethasone*							
Premedication in combination with pomalidomide and dexamethasone							
Dexamethasone 8 mg, IV[8]	10 SFI x 8 mg	€ 20.38	€ 2.00	€ 0.72	€ 17.66	19.0	€ 33.55
Dimetindene 1 mg/10 kg BW, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	19.0	€ 124.87
Famotidine 20 mg, PO[8]	100 TAB x 20 mg	€ 20.18	€ 2.00	€ 0.70	€ 17.48	19.0	€ 3.32
Paracetamol 500 – 1,000 mg, PO[8]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	19.0	€ 2.99 - € 5.72
Daratumumab Lenalidomide Pomalidomide							
HBV screening							
HBV test Hepatitis B surface antigen status (GOP 32781)	-	-	-	-	€ 5.50	1.0	€ 5.50
Anti-HBc antibody (GOP 32614)	-	-	-	-	€ 5.90	1.0	€ 5.90
Abbreviations: SFI = solution for injection; TAB = tablets, PII = powder and solvent for solution for injection or infusion							

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 1.10.2009 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 agents 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 Designation of 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 the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates 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.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c,

sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the

assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding information in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

a) Adults with relapsed and refractory multiple myeloma, who have received three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

   – No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

b) Adults with relapsed and refractory multiple myeloma, who have received at least 4 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

References:

Product information for elranatamab (Elrexfio); Elrexfio 40 mg/ml solution for injection; last revised: December 2023

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 13 April 2023, the Subcommittee on Medicinal Products determined the original appropriate comparator therapy.

On 15 January 2024, the pharmaceutical company submitted a dossier for the benefit assessment of elranatamab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 15 January 2024 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient elranatamab.

The dossier assessment by the IQWiG was submitted to the G-BA on 11 April 2024, and the written statement procedure was initiated with publication on the G-BA website on 15 April 2024. The deadline for submitting statements was 6 May 2024.

The oral hearing was held on 27 May 2024.

By letter dated 28 May 2024, IQWiG was commissioned with a supplementary determination of the patient number in the SHI target population. The addendum prepared by IQWiG was submitted to the G-BA on 13 June 2024.

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 25 June 2024, and the proposed resolution was approved.

At its session on 4 July 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	13 April 2023	Implementation of the appropriate comparator therapy
Working group Section 35a	15 May 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	27 May 2024	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary determination of patient numbers
Working group Section 35a	5 June 2024 19 June 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	25 June 2024	Concluding discussion of the draft resolution
Plenum	4 July 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 4 July 2024

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

Prof. Hecken