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

of 15 February 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 teclistamab on 1 September 2023 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 31 August 2023.

The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on 1 December 2023 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 teclistamab compared to 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 teclistamab.

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 Teclistamab (Tecvayli) in accordance with the product information

Tecvayli 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 15.02.2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

Appropriate comparator therapy for teclistamab:

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

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

- 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 extent and duration of the response.

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 para. 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

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:

1st 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 teclistamab, the following active ingredients are approved for the present therapeutic indication:

Belantamab mafodotin[2], 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, 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. It is assumed that high-dose chemotherapy with stem cell transplantation is not an option for patients at the time of current therapy. Therefore, a non-medicinal treatment cannot be considered in the present therapeutic indication.

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

- Belantamab mafodotin – resolution of 5 October 2023
- 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

[2] The EMA's Committee for Medicinal Products for Human Use recommended in December 2023 against extension of the conditional marketing authorisation for belantamab mafodotin. A decision by the European Commission in this regard is still pending at the time of the resolution.

- 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 at least three 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 response and tolerability of prior myeloma therapy play a key role in the choice of therapy.

With regard to the relapsed disease situation, 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 in the first relapse. 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 are generally used and combined in individual order. This is also done against the background that a therapeutic advantage of triplet therapies over doublet therapies is countered by an increased therapy toxicity, so that they are unsuitable for all patients. According to the S3 guideline, patients with 4 or more prior therapies should be examined to see whether a triplet therapy is reasonable and possible. Furthermore, there is a recommendation that a therapy with classical cytostatic agents should also be examined.

With regard to the treatment setting with at least three prior therapies, the scientific-medical societies focus on a heterogeneous patient collective. It also follows that an individual therapy has to be chosen for the treatment setting, which is determined by patient-related factors, whereby the prior therapies and the response to them also play an important role here. If the patients showed an adequate and long response to a therapy, a re-therapy can in principle also be considered according to the scientific-medical societies. Immunomodulating substances or proteasome inhibitors can also be used again in later lines of therapy, whereby another preparation of these substance classes should be used preferentially. In addition to combination therapies with novel

active ingredients, the scientific-medical societies also refer to classical cytostatic agents.

Overall, all approved active ingredients and combinations of active ingredients thereof can be considered.

For the cytostatic agent carmustine, the available evidence does not provide sufficient recommendations regarding its use as a therapy option in this therapeutic indication.

For isatuximab in combination with carfilzomib and dexamethasone, the benefit assessment of the G-BA did not show an additional benefit compared to carfilzomib in combination with dexamethasone (resolution of 4 November 2021). The same applies to carfilzomib in combination with daratumumab and dexamethasone, according to which an additional benefit compared to carfilzomib in combination with dexamethasone is not proven (resolution of the G-BA of 15 July 2021).

Belantamab mafodotin has a conditional marketing authorisation as monotherapy for the treatment of multiple myeloma in adults, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

The EMA's Committee for Medicinal Products for Human Use recommended in December 2023 against extension of the conditional marketing authorisation for belantamab mafodotin. A decision by the European Commission in this regard is still pending.

By resolution of 5 October 2023, the G-BA classifies the extent of the additional benefit of the orphan drug belantamab mafodotin as non-quantifiable solely on the basis of the additional benefit of belantamab mafodotin to be assumed from a legal perspective in accordance with Section 35a, paragraph 1, sentence 11, half-sentence 1 SGB V on the basis of the criteria in Section 5, paragraph 7 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), taking into account the severity of the disease and the therapeutic objective in the treatment of the disease.

Therefore, belantamab mafodotin is not considered as an appropriate comparator therapy.

The active ingredient selinexor is a new treatment option for the treatment setting after at least one prior therapy (combination with bortezomib and dexamethasone) and at least four prior therapies (combination with dexamethasone). Both for the combination of selinexor with bortezomib and dexamethasone and for the combination of selinexor with dexamethasone, it was determined by resolution of 16 March 2023 that an additional benefit over the appropriate comparator therapy is not proven.

For the CAR-T cell therapies idecabtagene vicleucel (resolution of 16 June 2022) and ciltacabtagene autoleucel (resolution of 17 August 2023), a hint for a non-quantifiable additional benefit was identified in each case 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.

Melphalan flufenamide is a therapy option for the treatment of patients 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.

Talquetamab is a new treatment option for the treatment setting after at least three prior therapies. The active ingredient was approved on 21.08.2023 and has only been available in Germany for a short time. Based on the generally accepted state of medical knowledge, talquetamab is not determined to be an appropriate comparator therapy.

In summary, the active ingredients or therapies involving combination of active ingredients carmustine, isatuximab in combination with carfilzomib and dexamethasone, carfilzomib in combination with daratumumab and dexamethasone, belantamab mafodotin, selinexor, idecabtagene vicleucel, ciltacabtagene autoleucel, melphalan flufenamide and talquetamab cannot be considered as an appropriate comparator therapy.

In accordance with the recommendation of the S3 guideline, the G-BA also assumes that no further antineoplastic/ myeloma-specific therapy can be considered for some patients, best supportive care being the appropriate treatment for them. Best supportive care is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life.

Overall, a patient-individual therapy is thus determined as the appropriate comparator therapy, taking into account the prior therapies as well as the extent and duration of the response.

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.

2.1.3 Extent and probability of the additional benefit

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

An additional benefit is not proven.

Justification:

The pharmaceutical company presented results from the pivotal MajesTEC-1 study for the benefit assessment of teclistamab 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 MajesTEC-1 study is an open-label, single-arm, phase I/II study for investigating the safety and efficacy of teclistamab 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 ongoing study has been conducted in a total of 39 study sites in Europe and North America since May 2017 and consists of two study phases. In the 1st phase, the dosage of teclistamab used to treat the 165 patients enrolled in the 2nd phase was determined.

In addition to the safety and tolerability of teclistamab, the endpoints of the study include response, progression-free survival and overall survival, as well as patient-reported endpoints in phase 2 of the study. The planned end of the study is two years after the last participant has received the starting dose of teclistamab.

Due to the single-arm study design, the MajesTEC-1 study presented by the pharmaceutical company does not allow a comparison with the appropriate comparator therapy and is therefore unsuitable for the assessment of an additional benefit of teclistamab compared with the appropriate comparator therapy.

An additional benefit of teclistamab 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, is therefore not proven.

Overall assessment

The results of the single-arm MajesTEC-1 study are available for the assessment of the additional benefit of teclistamab. The results of the single-arm MajesTEC-1 study presented are unsuitable for assessment of the additional benefit as they do not allow a comparison with the appropriate comparator therapy. Therefore, an additional benefit of teclistamab 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 Limitation of the period of validity of the resolution

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

The results of the MajesTEC-1 study presented for the assessment of the additional benefit of teclistamab are unsuitable for an assessment of the additional benefit of teclistamab compared with the appropriate comparator therapy due to the single-arm study design.

The first results of the ongoing randomised controlled trial MajesTEC-9 comparing teclistamab versus a therapy according to doctor's instructions with selection of pomalidomide in combination with bortezomib and dexamathasone and carfilzomib in combination with dexamethasone are expected in August 2025.[3]

Since clinical data are expected which are relevant for the benefit assessment of the medicinal product, it is justified to limit the validity of the resolution until further scientific knowledge is available for the assessment of the additional benefit of teclistamab. The limitation enables

[3] https://clinicaltrials.gov/study/NCT05572515

the expected results from the MajesTEC-9 study to be included in the benefit assessment of the medicinal product in accordance with Section 35a SGB V.

For this purpose, the G-BA considers a limitation for the resolution until 1 January 2027 to be appropriate.

Conditions of the limitation:

For the new benefit assessment after expiry of the deadline, the MajesTEC-9 study results from the analysis of overall survival and on all other patient-relevant endpoints used for the evidence of an additional benefit are to be presented in the dossier.

A change in the limitation can generally be granted if it is justified and clearly demonstrated that the limitation is insufficient or too long.

In particular, an amendment to the time limit may be granted if an application for marketing authorisation of a new therapeutic indication for teclistamab, which includes all or part of the present therapeutic indication, is submitted to the G-BA no later than two months before the expiry of the period of validity of the resolution and an application for an extension of the time limit is submitted on this basis.

In accordance with Section 3, No. 7 AM-NutzenV in conjunction with Chapter 5 Section 1, paragraph 2, No. 7 VerfO, the procedure for the benefit assessment of the medicinal product teclistamab recommences when the deadline has expired. For this purpose, the pharmaceutical company must submit a dossier to the G-BA at the latest on the date of expiry to prove the extent of the additional benefit of teclistamab in comparison with the appropriate comparator therapy (Section 4, paragraph 3, number 5 AM-NutzenV in conjunction with Chapter 5 Section 8, paragraph 1, number 5 VerfO). If the dossier is not submitted or is incomplete, the G-BA may determine that an additional benefit has not been proven.

The possibility that a benefit assessment for the medicinal product teclistamab can be carried out at an earlier point in time due to other reasons (cf. Chapter 5 Section 1, paragraph 2, nos. 2 to 4 VerfO) remains unaffected hereof.

2.1.5 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Tecvayli with the active ingredient teclistamab.

Tecvayli received a conditional approval.

Teclistamab is approved 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.

A patient-individual therapy was determined by the G-BA to be the appropriate comparator therapy, taking into account the prior therapies as well as the extent and duration of the response.

For the benefit assessment of teclistamab, the pharmaceutical company submitted results of the single-arm MajesTEC-1 study.

The data presented are unsuitable for comparison with the appropriate comparator therapy.

An additional benefit of teclistamab as monotherapy for 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, is therefore not proven.

The period of validity of the resolution is limited to 1 January 2027.

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 dossier of the pharmaceutical company. These are based on the information in the G-BA resolution on the benefit assessment of ciltacabtagene autoleucel (resolution of 17 August 2023) and idecabtagene vicleucel (resolution of 16 June 2022) in the same therapeutic indication. Since the target population is the same, the pharmaceutical company's approach is considered plausible.

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 about 1,210 to 1,310 subjects in the SHI target population.

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 Tecvayli (active ingredient: teclistamab) at the following publicly accessible link (last access: 10 January 2024):

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

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

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

In accordance with the requirements of the European Medicines Agency (EMA) regarding additional risk minimisation measures, the pharmaceutical company must ensure that all patients and caregivers who are expected to come into contact with the use of teclistamab have access to a patient card or receive a patient card that informs and clarifies patients about the risks of CRS. The patient card also contains a warning for healthcare professionals that the patient is receiving teclistamab.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 January 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.

The maximum cumulative total dose of doxorubicin is 450 - 550 mg/m^2 BSA. On this basis, an approximate treatment duration of 6 to 9 cycles is assumed for doxorubicin monotherapy (at a dosage of 60 to 75 mg/m^2) and an approximate treatment duration of 7 to 18 cycles for combination therapy with doxorubicin (at a dosage of 30 to 60 mg/m^2).

In combination with other antineoplastic medicinal products, the treatment regimen and dosages of vincristine, carmustine, melphalan, cyclophosphamide and prednisone are based on the ECOG study (1997)[10].

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

The cost representation of the combination of dexamethasone with other antineoplastic medicinal products is adequately covered by the therapy options[4] already addressed.

4 Pomalidomide in combination with dexamethasone
Pomalidomide in combination with bortezomib and dexamethasone
Panobinostat in combination with bortezomib and dexamethasone
Lenalidomide in combination with dexamethasone
Ixazomib in combination with lenalidomide and dexamethasone
Isatuximab in combination with pomalidomide and dexamethasone
Elotuzumab + pomalidomide + dexamethasone
Elotuzumab in combination with lenalidomide and dexamethasone
Daratumumab in combination with bortezomib and dexamethasone
Daratumumab in combination with lenalidomide and dexamethasone
Carfilzomib in combination with dexamethasone

For the "doxorubicin in combination with other antineoplastic medicinal products" combination which was defined as the appropriate comparator therapy, no study could be identified that would allow cost representation. The costs can therefore not be quantified.

The treatment costs for best supportive care are different from patient to patient. Because best supportive care has been determined as the appropriate comparator as part of a patient-individual therapy, best supportive care is also reflected in the medicinal product to be assessed. The type and scope of best supportive care can vary depending on the medicinal product to be assessed and the comparator 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				
Teclistamab				
Teclistamab	Step-up dosage regimen: Day 1, 3, 5 Maintenance dosage regimen: 1 x every 7 days Maintenance dosage regimen for complete or improved response: 1 x every 14 days	3.0 25.0 13.0	1 1 1	1st year: 3.0 25.0 13.0
Appropriate comparator therapy				
Bortezomib monotherapy				
Bortezomib	Day 1, 4, 8, 11: 21-day cycle	8.0	4	32.0
Bortezomib in combination with pegylated liposomal doxorubicin				
Bortezomib	Day 1, 4, 8, 11: 21-day cycle	8.0	4	32.0
Doxorubicin (pegylated, lysosomal)	Day 4: 21-day cycle	8.0	1	8.0
Bortezomib in combination with dexamethasone				
Bortezomib	Day 1, 4, 8, 11:	4.0 – 8.0	4	16.0 – 32.0

Carfilzomib in combination with lenalidomide and dexamethasone
Bortezomib in combination with dexamethasone

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	21-day cycle			
Dexamethasone	Day 1, 2, 4, 5, 8, 9, 11, 12: 21-day cycle	4.0 - 8.0	8	32.0 – 64.0
Carfilzomib in combination with lenalidomide and dexamethasone				
Carfilzomib	1st -12. 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	1st year: 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	1st year: 23.0	1	1st year: 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	1st year: 0 (Cycle 1 - 2) 2 (Cycle 3 - 6)	1st year: 29.0[5]

[5] 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

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
			3 (From cycle 7)	
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	1st year: 23.0	1	1st year: 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	1st year: 0 (Cycle 1 - 2) 2 (Cycle 3 - 6) 3 (From cycle 7)	1st year: 29.0[6]
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	1st year: 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 of the bortezomib cycles	8.0	6 (cycle 1 - 3) 7 (cycle 4 - 8)	53.0[6]
Daratumumab monotherapy				
Daratumumab	Week 1 - 8: 1 x every 7 days Week 9 - 24:	1st year: 23.0	1	1st year: 23.0

[6] 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

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	1 x every 14 days From week 25: 1 x every 28 days			
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	1st year 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: 1	1st year: 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	1st year: 28.0
Pomalidomide	Day 1 - 21: 28-day cycle	13.0	21	273.0
Dexamethasone	1st cycle: Day 1, 8, 15, 22	13.0	1st cycle: 4	1st year: 28.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	From 2nd cycle: Day 1, 15 28-day cycle		From 2nd cycle: 2	
Ixazomib in combination with lenalidomide and dexamethasone				
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				
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	1st year: 84.0
Panobinostat in combination with bortezomib and dexamethasone				
Panobinostat	1st - 16th cycle: Day 1, 3, 5, 8, 10, 12 21-day cycle	8.0 – 16.0	6	48.0 – 96.0
Bortezomib	1st - 8th cycle: Day 1, 4, 8, 11 9th - 16th cycle: Day 1, 8 21-day cycle	8.0 – 16.0	1st - 8th cycle: 4 9th - 16th cycle: 2	32.0 – 48.0
Dexamethasone	1st - 8th cycle: Day 1, 2, 4, 5, 8, 9, 11, 12 9th - 16th cycle: Day 1, 2, 8, 9 21-day cycle	8.0 – 16.0	1st - 8th cycle: 8 9th - 16th cycle:	64.0 – 96.0

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
			4	
Pomalidomide in combination with bortezomib and dexamethasone				
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
Pomalidomide in combination with dexamethasone				
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 (in combination with other antineoplastic medicinal products) [10]				
Cyclophosphamide	Day 1 of a 35-day cycle	10.4	1	10.4
Melphalan	Day 1 – 4 of a 35-day cycle	10.4	4	41.6
Carmustine	Day 1 of a 35-day cycle	10.4	1	10.4
Vincristine[7]	Day 1 of a 35-day cycle	10.4	1	10.4
Prednisone	1st - 3rd cycle: Day 1 - 7, 8 - 14 From 4th cycle: Day 1 - 7	10.4	1st - 3rd cycle: 14	1st year: 93.8

[7] The single dose of vincristine should not exceed 2 mg according to the product information.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
			From 4th cycle: 7	
Melphalan				
Melphalan	Continuously, 1 x every 28 days	13.0	1	13.0
Melphalan in combination with prednisolone or prednisone				
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
Doxorubicin monotherapy				
Doxorubicin	Day 1 21-day cycle	6.0 – 9.0	1	6.0 – 9.0
Doxorubicin (in combination with other antineoplastic medicinal products)				
No data available.				
Vincristine (in combination with other antineoplastic medicinal products) [10]				
Cyclophosphamide	Day 1 of a 35-day cycle	10.4	1	10.4
Melphalan	Day 1 - 4 35-day cycle	10.4	4	41.6
Carmustine	Day 1 35-day cycle	10.4	1	10.4
Vincristine[7]	Day 1 35-day cycle	10.4	1	10.4
Prednisone	1st - 3rd cycle: Day 1 - 7, 8 - 14 From 4th cycle: Day 1 - 7	10.4	1st - 3rd cycle: 14 From 4th cycle: 7	1st year: 93.8
Prednisone (in combination with other antineoplastic medicinal products)[10]				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Cyclophosphamide	Day 1 of a 35-day cycle	10.4	1	10.4
Melphalan	Day 1 - 4 35-day cycle	10.4	4	41.6
Carmustine	Day 1 35-day cycle	10.4	1	10.4
Vincristine[7]	Day 1 35-day cycle	10.4	1	10.4
Prednisone	1st - 3rd cycle: Day 1 - 7, 8 - 14 From 4th cycle: Day 1 - 7	10.4	1st - 3rd cycle: 14 From 4th cycle: 7	1st year: 93.8
Prednisolone (in combination with other antineoplastic medicinal products)[10]				
Cyclophosphamide	Day 1 of a 35-day cycle	10.4	1	10.4
Melphalan	Day 1 - 4 35-day cycle	10.4	4	41.6
Carmustine	Day 1 35-day cycle	10.4	1	10.4
Vincristine[7]	Day 1 35-day cycle	10.4	1	10.4
Prednisone	1st - 3rd cycle: Day 1 - 7, 8 - 14 From 4th cycle: Day 1 - 7	10.4	1st - 3rd cycle: 14 From 4th cycle: 7	1st year: 93.8
Best supportive care				
Best supportive care[8]	Different from patient to patient			

Consumption:

8 When comparing teclistamab versus best supportive care, the costs of best supportive care must also be additionally considered for the medicinal product to be assessed.

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)[9].

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

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					
Teclistamab					
Teclistamab	Step-up dosing: Day 1: 0.06 mg/kg Day 3: 0.3 mg/kg Day 5: 1.5 mg/kg Maintenance dosing: 1.5 mg/kg	Step-up dosing: Day 1: 4.66 mg Day 3: 23.31 mg Day 5: 116.55 mg Maintenance dosing: 116.55 mg	Step-up dosing: Day 1: 1 x 30 mg Day 3: 1 x 30 mg Day 5: 1 x 153 mg Maintenance dosing: 1 x 153 mg	1.0 1.0 1.0 38.0 (25.0 + 13.0)	1st year: 2.0 x 30 mg 39.0 x 153 mg
Appropriate comparator therapy					
Bortezomib monotherapy					
Bortezomib	1.3 mg/m²	2.48 mg	1 x 2.5 mg	32.0	32 x 2.5 mg
Bortezomib in combination with pegylated liposomal doxorubicin					
Bortezomib	1.3 mg/m²	2.48 mg	1 x 2.5 mg	32.0	32 x 2.5 mg
Doxorubicin (pegylated, lysosomal)	30 mg/m²	57.3 mg	1 x 20 mg 1 x 50 mg	8.0	8 x 20 mg 8 x 50 mg
Bortezomib in combination with dexamethasone					
Bortezomib	1.3 mg/m²	2.48 mg	1 x 2.5 mg	16.0 – 32.0	16 - 32 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	32.0 – 64.0	32 – 64 x 20 mg

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

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 51.57 mg	1st cycle Day 1, 2 1 x 10 mg + 1 x 30 mg Thereafter 1 x 60 mg	1st year 76.0	1st year 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 106.96 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	1st year 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	1st year: 23.0	1st year: 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	1st year: 29.0	1st year: 29 x 40 mg
Daratumumab in combination with pomalidomide and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	1st year: 23.0	1st year: 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	1st year: 29.0	1st year: 29 x 40 mg
Daratumumab in combination with bortezomib and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	1st year: 21.0	1st year: 21 x 1,800 mg
Bortezomib	1.3 mg/m²	2.48 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 monotherapy					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	1st year: 23.0	1st year: 23 x 1,800 mg
Elotuzumab in combination with lenalidomide and dexamethasone					

Elotuzumab	10 mg/kg	777 mg	2 x 400 mg	1st year: 30.0	1st year: 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	1st year: 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: 1554 mg	1st - 2nd cycle Day 1, 8, 15, 22: 2 x 400 mg From 3rd cycle Day 1: 4 x 400 mg	1st year: 19.0	1st year: 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	1st year: 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 +	28.0	1st year:

			3 x 100 mg		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	28.0	28 x 40 mg
Ixazomib in combination with lenalidomide and dexamethasone					
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					
Lenalidomide	25 mg	25 mg	1 x 25 mg	273.0	273 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	1st year: 84.0	1st year: 84 x 40 mg
Panobinostat in combination with bortezomib and dexamethasone					
Panobinostat	20 mg	20 mg	1 x 20 mg	48.0 – 96.0	48 x 20 mg – 96 x 20 mg
Bortezomib	1.3 mg/m^2	2.48 mg	1 x 2.5 mg	32.0 – 48.0	32 x 2.5 mg – 48 x 2.5 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	64.0 – 96.0	64 x 20 mg – 96 x 20 mg
Pomalidomide in combination with bortezomib and dexamethasone					
Pomalidomide	4 mg	4 mg	1 x 4 mg	243.6	243.6 x 4 mg
Bortezomib	1.3 mg/m^2	2.48 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					
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 (in combination with other antineoplastic medicinal products)[10]					
Cyclophosphamide	400 mg/m^2	764 mg	1 x 1,000 mg	10.4	10.4 x 1,000 mg
Melphalan	8 mg/m^2	15.28 mg	8 x 2 mg	41.6	332.8 x 2 mg
Carmustine	20 mg/m^2	38.2 mg	1 x 100 mg	10.4	10.4 x 100 mg
Vincristine[7]	1.2 mg/m^2	2 mg	1 x 2 mg	10.4	10.4 x 2 mg
Prednisone	1st - 3rd cycle Day 1 - 7	1st - 3rd cycle Day 1 - 7 76.4 mg	1 x 50 mg 1 x 20 mg 1 x 10 mg	93.8	1st year 72.8 x 50 mg

10 Oken MM, Harrington DP, Abramson N et al, Comparison of melphalan and prednisone with vincristine, carmustine, melphalan, cyclophosphamide, and prednisone in the treatment of multiple myeloma. Cancer 1997; 79(8): 1561-1567. https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/%28SICI%291097-0142%2819970415%2979%3A8%3C1561%3A%3AAID-CNCR18%3E3.0.CO%3B2-W

	40 mg/m² Day 8 - 14 20 mg/m² From 4th cycle Day 1 - 7 40 mg/m²	Day 8 - 14 38.2 mg From 4th cycle Day 1 - 7 76.4 mg	or 2 x 20 mg		114.8 x 20 mg 72.8 x 10 mg
Melphalan monotherapy					
Melphalan	0.4 mg/kg	31.08 mg	1 x 50 mg	13.0	13.0 x 50 mg
Melphalan in combination with prednisone or prednisolone[10]					
Melphalan	Day 1: 15 mg/m²	Day 1: 28.65 mg	1 x 50 mg	8.7	8.7 x 50 mg
Melphalan	Day 1: 15 mg/m²	Day 1: 28.65 mg	1 x 50 mg	13.0	13.0 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	104.4 x 50 mg + 34.8 x 5 mg
Prednisone	Day 1 – 4: 2 mg/kg	Day 1 – 4: 155.4 mg	3 x 50 mg + 1 x 5 mg	52.0	156.0 x 50 mg + 52.0 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	104.4 x 50 mg + 34.8 x 5 mg
Prednisolone	Day 1 – 4: 2 mg/kg	Day 1 – 4: 155.4 mg	3 x 50 mg + 1 x 5 mg	52.0	156.0 x 50 mg + 52.0 x 5 mg
Doxorubicin					
Doxorubicin[11]	60 mg/m² - 75 mg/m²	114.6 mg – 143.25 mg	1 x 150 mg	6.0 – 9.0	6.0 x 150 mg - 9.0 x 150 mg
Doxorubicin (in combination with other antineoplastic medicinal products					
No data available.					
Vincristine (in combination with other antineoplastic medicinal products)[10]					
Cyclophosphamide	400 mg/m²	764 mg	1 x 1,000 mg	10.4	10.4 x 1,000 mg
Melphalan	8 mg/m²	15.28 mg	8 x 2 mg	41.6	332.8 x 2 mg
Carmustine	20 mg/m²	38.2 mg	1 x 100 mg	10.4	10.4 x 100 mg
Vincristine[7]	1.2 mg/m²	2 mg	1 x 2 mg	10.4	10.4 x 2 mg
Prednisone	1st - 3rd cycle Day 1 - 7	1st - 3rd cycle Day 1 - 7 76.4 mg	1 x 50 mg 1 x 20 mg 1 x 10 mg	93.8	1st year 72.8 x 50 mg

[11] Maximum cumulative dose according to the product information: 450 - 550 mg/m² BSA.

	40 mg/m² Day 8 - 14 20 mg/m² From 4th cycle Day 1 - 7 40 mg/m²	Day 8 - 14 38.2 mg From 4th cycle Day 1 - 7 76.4 mg	or 2 x 20 mg		114.8 x 20 mg 72.8 x 10 mg
Prednisolone (in combination with other antineoplastic medicinal products)[10]					
Cyclophosphamide	400 mg/m²	764 mg	1 x 1,000 mg	10.4	10.4 x 1,000 mg
Melphalan	8 mg/m²	15.28 mg	8 x 2 mg	41.6	332.8 x 2 mg
Carmustine	20 mg/m²	38.2 mg	1 x 100 mg	10.4	10.4 x 100 mg
Vincristine[7]	1.2 mg/m²	2 mg	1 x 2 mg	10.4	10.4 x 2 mg
Prednisolone	1st - 3rd cycle Day 1 - 7 40 mg/m² Day 8 - 14 20 mg/m² From 4th cycle Day 1 - 7 40 mg/m²	1st - 3rd cycle Day 1 - 7 76.4 mg Day 8 - 14 38.2 mg From 4th cycle Day 1 - 7 76.4 mg	1 x 50 mg 1 x 20 mg 1 x 10 mg or 2 x 20 mg	93.8	1st year 72.8 x 50 mg 114.8 x 20 mg 72.8 x 10 mg
Prednisone (in combination with other antineoplastic medicinal products)[10]					
Cyclophosphamide	400 mg/m²	764 mg	1 x 1,000 mg	10.4	10.4 x 1,000 mg
Melphalan	8 mg/m²	15.28 mg	8 x 2 mg	41.6	332.8 x 2 mg
Carmustine	20 mg/m²	38.2 mg	1 x 100 mg	10.4	10.4 x 100 mg
Vincristine[7]	1.2 mg/m²	2 mg	1 x 2 mg	10.4	10.4 x 2 mg
Prednisone	1st - 3rd cycle Day 1 - 7 40 mg/m² Day 8 - 14 20 mg/m²	1st - 3rd cycle Day 1 - 7 76.4 mg Day 8 - 14 38.2 mg	1 x 50 mg 1 x 20 mg 1 x 10 mg or 2 x 20 mg	93.8	1st year 72.8 x 50 mg 114.8 x 20 mg 72.8 x 10 mg

	From 4th cycle Day 1 - 7 40 mg/m^2	From 4th cycle Day 1 - 7 76.4 mg			
Best supportive care					
Best supportive care	Different from patient to patient				

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					
Teclistamab 30 mg	1 SFI	€ 1,311.51	€ 2.00	€ 71.99	€ 1,237.52
Teclistamab 153 mg	1 SFI	€ 6,486.15	€ 2.00	€ 367.13	€ 6,117.02
Appropriate comparator therapy					
Bortezomib 2.5 mg	1 PSI	€ 185.37	€ 2.00	€ 8.26	€ 175.11
Carfilzomib 10 mg	1 PIS	€ 197.03	€ 2.00	€ 10.28	€ 184.75
Carfilzomib 30 mg	1 PIS	€ 568.43	€ 2.00	€ 30.84	€ 535.59
Carfilzomib 60 mg	1 PIS	€ 1,125.54	€ 2.00	€ 61.69	€ 1,061.85
Carmustine 100 mg	1 PSS	€ 3,842.62	€ 2.00	€ 185.28	€ 3,655.34
Cyclophosphamide 1000 mg	6 PSI	€ 127.45	€ 2.00	€ 6.43	€ 119.02
Daratumumab 1,800 mg	1 SFI	€ 5,937.34	€ 2.00	€ 0.00	€ 5,935.34
Dexamethasone 8 mg[12]	100 TAB	€ 123.41	€ 2.00	€ 8.87	€ 112.54
Dexamethasone	10 TAB	€ 32.42	€ 2.00	€ 0.00	€ 30.42

[12] 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
20 mg[12]					
Dexamethasone 20 mg[12]	20 TAB	€ 54.09	€ 2.00	€ 0.00	€ 52.09
Dexamethasone 20 mg[12]	50 TAB	€ 118.88	€ 2.00	€ 0.00	€ 116.88
Dexamethasone 40 mg[12]	50 TAB	€ 188.03	€ 2.00	€ 0.00	€ 186.03
Doxorubicin 150 mg[12]	1 SFI	€ 418.36	€ 2.00	€ 0.00	€ 416.36
Doxorubicin 100 mg[12]	1 CIS	€ 285.79	€ 2.00	€ 0.00	€ 283.79
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 5 mg[12]	63 HC	€ 117.32	€ 2.00	€ 8.38	€ 106.94
Melphalan 2 mg	50 FCT	€ 56.24	€ 2.00	€ 2.49	€ 51.75
Melphalan 50 mg	1 DSS	€ 52.34	€ 2.00	€ 2.27	€ 48.07
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[12]	100 TAB	€ 15.43	€ 2.00	€ 0.33	€ 13.10
Prednisolone 10 mg[12]	100 TAB	€ 17.81	€ 2.00	€ 0.51	€ 15.30
Prednisolone 20 mg[12]	100 TAB	€ 21.62	€ 2.00	€ 0.81	€ 18.81
Prednisolone 50 mg[12]	50 TAB	€ 31.44	€ 2.00	€ 1.59	€ 27.85
Prednisone 5 mg[12]	100 TAB	€ 16.74	€ 2.00	€ 0.43	€ 14.31
Prednisone 10 mg[12]	100 TAB	€ 21.23	€ 2.00	€ 0.00	€ 19.23
Prednisone 20 mg[12]	100 TAB	€ 29.29	€ 2.00	€ 1.42	€ 25.87
Prednisone 50 mg[12]	50 TAB	€ 68.06	€ 2.00	€ 4.49	€ 61.57
Vincristine 2 mg	1 VIA	€ 37.66	€ 2.00	€ 1.25	€ 34.41
Abbreviations: VIA = vial; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PSI = powder for solution for injection; PIC = powder for the preparation of an infusion solution concentrate; TAB = tablets; PIF = powder for the preparation of an infusion solution; PIS = powder and solvent for the preparation of an infusion solution, PII = powder and solvent for solution for injection or infusion; FCT = film-coated tablets,					

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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 teclistamab, pomalidomide, daratumumab and lenalidomide should be tested for the presence of HBV infection before initiating the respective treatment. For the diagnosis of suspected chronic hepatitis B, sensibly coordinated steps are required[13]. 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. If HBs antigen is positive, an active HBV infection is detected.

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.

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							
Teclistamab							
HBV diagnostics							
HBs antigen (GOP 32781)	-	-	-	-	€ 5.50	1.0	€ 5.50
Anti-HBs antibody (GOP 32617)	-	-	-	-	€ 5.50	1.0	€ 5.50
Anti-HBc antibody (GOP 32614)	-	-	-	-	€ 5.90	1.0	€ 5.90
HBV DNA (GOP 32823)	-	-	-	-	€ 89.50	1.0	€ 89.50
Premedication before each step-up dose							
Dexamethasone 16 mg, IV [12]	10 AMP x 8 mg	€ 20.38	€ 2.00	€ 0.72	€ 17.66	3.0	€ 17.66
Paracetamol 500 - 1,000 mg, oral[12]	10 TAB x 500 mg	€ 2.96	€ 0.15	€ 0.13	€ 2.68	3.0	€ 2.68 - € 3.01

[13] 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

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
	10 TAB x 1000 mg	€ 3.32	€ 0.17	€ 0.14	€ 3.01		
Dimetindene 1 mg/10 kg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	3.0	€ 32.86
Appropriate comparator therapy							
Daratumumab *in combination with lenalidomide and dexamethasone*							
Premedication							
Dexamethasone 40 mg, oral [12]	50 TAB x 40 mg	€ 188.03	€ 2.00	€ 0.00	€ 186.03	23	€ 85.57
Paracetamol 500 - 1,000 mg, oral [12]	20 TAB x 500 mg 10 TAB x 1000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	23	€ 3.62 - € 6.92
Dimetindene 1 mg/10 kg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	23	€ 151.16
Daratumumab *in combination with bortezomib and dexamethasone*							
Premedication							
Dexamethasone 20 mg, oral [12]	50 TAB x 40 mg	€ 118.88	€ 2.00	€ 0.00	€ 116.88	21	€ 49.09
Paracetamol 500 - 1,000 mg, oral [12]	20 TAB x 500 mg 10 TAB x 1000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	21	€ 3.31 - € 6.32
Dimetindene 1 mg/10 kg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	21	€ 138.01
Daratumumab *in combination with pomalidomide and dexamethasone*							
Premedication							
Dexamethasone 40 mg, oral [12]	50 TAB x 40 mg	€ 188.03	€ 2.00	€ 0.00	€ 186.03	23	€ 85.57
Paracetamol 500 - 1,000 mg, oral [12]	20 TAB x 500 mg 10 TAB x 1000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	23	€ 3.62 - € 6.92
Dimetindene 1 mg/10 kg, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	23	€ 151.16
Daratumumab *monotherapy*							
Premedication							
Methyl prednisolone	3 PII x 32 mg	€ 25.32	€ 2.00	€ 6.36	€ 16.96	23	€ 260.05 - € 520.11

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	Treatment days/ year	Costs/ patient/ year
60 mg - 100 mg, IV							
Postmedication							
Methyl prednisolone 20 mg, oral	100 TAB x 4 mg 100 TAB x 16 mg	€ 29.35 € 73.84	€ 2.00 € 2.00	€ 1.43 € 4.19	€ 25.92 € 67.65	46 46	€ 42.69
***Elotuzumab** in combination with lenalidomide and dexamethasone*							
Premedication in combination with lenalidomide and dexamethasone							
Dexamethasone 8 mg, IV [12]	100 SFI x 8 mg	€ 94.43	€ 2.00	€ 3.94	€ 88.49	30	€ 26.55
Dimetindene 1 mg/10 kg BW, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	30	€ 197.16
Famotidine 20 mg, oral [12]	100 TAB x 20 mg	€ 20.18	€ 2.00	€ 0.70	€ 17.48	30	€ 5.24
Paracetamol 500 – 1,000 mg, oral [12]	20 TAB x 500 mg 10 TAB x 1000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	30	€ 4.73 - € 9.03
***Elotuzumab** in combination with pomalidomide and dexamethasone*							
Premedication in combination with pomalidomide and dexamethasone							
Dexamethasone 8 mg, IV[12]	100 SFI x 8 mg	€ 94.43	€ 2.00	€ 3.94	€ 88.49	19	€ 16.81
Dimetindene 1 mg/10 kg BW, IV	5 SFI x 4 mg	23.72	€ 2.00	€ 5.29	€ 16.43	19	€ 124.87
Famotidine 20 mg, oral[12]	100 TAB x 20 mg	€ 20.18	€ 2.00	€ 0.70	€ 17.48	19	€ 3.32
Paracetamol 500 – 1,000 mg, oral[12]	20 TAB x 500 mg 10 TAB x 1000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	19	€ 2.99 - € 5.72
Daratumumab ***Lenalidomide*** ***Pomalidomide***							
HBV diagnostics							
HBs antigen (GOP 32781)	-	-	-	-	€ 5.50	1.0	€ 5.50
Anti-HBs antibody (GOP 32617)	-	-	-	-	€ 5.50	1.0	€ 5.50

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
Anti-HBc antibody (GOP 32614)	-	-	-	-	€ 5.90	1.0	€ 5.90
HBV DNA (GOP 32823)	-	-	-	-	€ 89.50	1.0	€ 89.50
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 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131, paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic drugs a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs do not add to the pharmacy sales price but follow the rules for calculation in the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe). The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the special agreement on contractual unit costs of retail pharmacist services (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.

<u>Concomitant active ingredient:</u>

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:

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

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 teclistamab (Tecvayli); Tecvayli solution for injection; last revised: August 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 09 June 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at its session on 12 September 2023.

On 31 August 2023, the pharmaceutical company submitted a dossier for the benefit assessment of teclistamab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 1 September 2023 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 teclistamab.

The dossier assessment by the IQWiG was submitted to the G-BA on 21 November 2023, and the written statement procedure was initiated with publication on the G-BA website on 1 December 2023. The deadline for submitting statements was 22 December 2023.

The oral hearing was held on 8 January 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 6 February 2024, and the proposed resolution was approved.

At its session on 15 February 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	9 June 2020	Determination of the appropriate comparator therapy

Subcommittee Medicinal products	12 September 2023	New implementation of the appropriate comparator therapy
Subcommittee Medicinal products	8 January 2024	Information on written statements received, conduct of the oral hearing
Working group Section 35a	17 January 2024 31 January 2024	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal products	6 February 2024	Concluding discussion of the draft resolution
Plenum	15 February 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 15 February 2024

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

Prof. Hecken