Gemeinsamer Bundesausschuss

Justification

to 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
Daratumumab (new therapeutic indication: multiple myeloma, ineligible for stem cell transplant, combination with bortezomib, lenalidomide and dexamethasone)

of 19 February 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all 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 studies the pharmaceutical company have 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 decide on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient daratumumab was listed for the first time on 1 June 2016 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

Daratumumab is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999. Within the previously approved therapeutic indications, the sales volume of daratumumab with the statutory health insurance at pharmacy sales prices, including value-added tax exceeded € 30 million. Evidence must therefore be provided for daratumumab in accordance with Section 5, paragraph 1 through 6 VerfO, and the additional benefit compared with the appropriate comparator therapy must be demonstrated.

On 30 January 2025, the pharmaceutical company submitted an application for postponement of the date for the start of the benefit assessment procedure for daratumumab in the therapeutic indication "Treatment of adult patients with newly diagnosed multiple myeloma

who are ineligible for autologous stem cell transplant" in accordance with Section 35a, paragraph 5b SGB V.

At their session on 20 March 2025, the G-BA approved the application pursuant to Section 35a paragraph 5b SGB V and postponed the relevant date for the start of the benefit assessment and the submission of a dossier for the benefit assessment for the therapeutic indication in question to four weeks after the marketing authorisation of the other therapeutic indication covered by the application, at the latest six months after the first relevant date. The marketing authorisation for the other therapeutic indication covered by the application according to Section 35a paragraph 5b SGB V was granted within the 6-month period.

On 4 April 2025, daratumumab received the marketing authorisation for the therapeutic indication "Treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant". The extension of the marketing authorisation for the therapeutic indication "Treatment of adult patients with smouldering multiple myeloma who are at high risk of developing multiple myeloma" was granted on 18 July 2025. Both extensions of the marketing authorisation are classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334 from 12.12.2008, sentence 7).

On 15 August 2025, the pharmaceutical company submitted a dossier in accordance with Section 4, paragraph 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient daratumumab with the therapeutic indication

"DARZALEX is indicated in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant."

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 17 November 2025 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 daratumumab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA have 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 daratumumab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made the following assessment:

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of Daratumumab (Darzalex) in accordance with the product information

DARZALEX is indicated in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma.

Therapeutic indication of the resolution (resolution of 19.02.2026):

DARZALEX is indicated in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with newly diagnosed multiple myeloma who are **ineligible** for autologous stem cell transplant

Appropriate comparator therapy for daratumumab in combination with bortezomib, lenalidomide and dexamethasone:

– Daratumumab in combination with lenalidomide and dexamethasone

or

– daratumumab in combination with bortezomib, melphalan and prednisone

or

– Bortezomib in combination with melphalan and prednisone

or

– Bortezomib in combination with lenalidomide and dexamethasone

or

– thalidomide in combination with melphalan and prednisone

or

– bortezomib in combination with cyclophosphamide and dexamethasone (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)

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):

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 they determine 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 terms of authorisation status, the chemotherapeutic agents bendamustine, carmustine, cyclophosphamide, doxorubicin, melphalan and vincristine, the proteasome inhibitor bortezomib, the CD38 antibody daratumumab and isatuximab, the immunomodulatory substances lenalidomide and thalidomide as well as the glucocorticoids dexamethasone, prednisolone and prednisone are available for the treatment of adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.

Some of the marketing authorisations are tied to (specific) concomitant active ingredients. In addition, the combination of bortezomib, cyclophosphamide and dexamethasone can be prescribed off-label.

On 2. According to the therapeutic indication, patients are ineligible for autologous stem cell transplant. Non-medicinal treatment is not considered as the appropriate comparator therapy for the present therapeutic indication.

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

- Isatuximab – resolution of 7 August 2025 (combination with bortezomib, lenalidomide and dexamethasone)
- Daratumumab – resolution of 16 May 2024 (combination with bortezomib, melphalan and prednisone)
- Daratumumab – resolution of 18 March 2022 (combination with lenalidomide and dexamethasone)

Annex VI to Section K of the Pharmaceuticals Directive – Prescribability of approved medicinal products in non-approved therapeutic indications (off-label use):

- Bortezomib plus cyclophosphamide plus dexamethasone for the induction therapy of newly diagnosed multiple myeloma (resolution of 20 May 2021).

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present 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 indication according to Section 35a paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy"). No written opinions were received.

Among the approved active ingredients listed under subparagraph 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 care.

The available evidence on the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant recommends trio or tetra combination therapies based on an immunomodulator and/or proteasome inhibitor. In this regard, the combination therapies bortezomib + melphalan + prednisone, thalidomide + melphalan + prednisone, lenalidomide + melphalan + prednisone and the combination therapy bortezomib + lenalidomide + dexamethasone can be considered according to the authorisation status. No clear recommendation can be derived from the available evidence for the dual combination therapy of lenalidomide in combination with dexamethasone, which is why this therapy option is not determined as an appropriate comparator therapy.

In addition to the combination therapy of daratumumab + bortezomib + lenalidomide + dexamethasone, which is the subject of the assessment, two further combination therapies based on daratumumab are approved for patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant. By resolution

of 16 May 2024, the G-BA determined an indication of a considerable additional benefit of the combination therapy of daratumumab + bortezomib + melphalan + prednisone, compared to a combination therapy according to doctor's instructions. By resolution of 18 March 2022, the G-BA identified a hint for a considerable additional benefit of the combination therapy daratumumab + lenalidomide + dexamethasone compared to lenalidomide + dexamethasone. These two combination therapies are recommended by the current guidelines.

The evidence for the combination therapy of lenalidomide + melphalan + prednisone is inferior overall compared to the other combination therapies. In contrast to bortezomib or thalidomide + melphalan + prednisone, no advantage compared to melphalan + prednisone was shown with regard to survival. Lenalidomide + melphalan + prednisone is therefore not determined as an appropriate comparator therapy.

Furthermore, the combination therapy of bortezomib, cyclophosphamide and dexamethasone can be prescribed off-label, restricted to patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy in the therapeutic indication of newly diagnosed multiple myeloma, irrespective of the eligibility for stem cell transplant. This combination is also recommended in the available evidence.

The combination therapy of isatuximab + bortezomib + lenalidomide + dexamethasone is another, still relatively new treatment option in the present therapeutic indication (marketing authorisation granted on 20.01.2025). By resolution of 7 August 2025, a hint for a minor additional benefit of isatuximab + bortezomib + lenalidomide + dexamethasone, compared with bortezomib + lenalidomide + dexamethasone, was identified in the relevant benefit assessment. Based on the generally accepted state of medical knowledge, the combination of isatuximab + bortezomib + lenalidomide + dexamethasone is not determined as an appropriate comparator therapy.

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

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

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

Hint for a minor additional benefit

Justification:

The pharmaceutical company submitted results from the open-label, randomised phase III CEPHEUS study for the benefit assessment.

The CEPHEUS study investigated the safety and efficacy of daratumumab in combination with bortezomib, lenalidomide and dexamethasone (D-VRd) compared with bortezomib, lenalidomide and dexamethasone (VRd).

The CEPHEUS study was conducted in a total of 98 study sites in Europe, Asia, North America and South America between November 2018 and October 2025.

Adults with newly diagnosed multiple myeloma, who were ineligible for autologous stem cell transplant or who had rejected autologous stem cell transplant (N = 395), were enrolled.

Ineligibility for autologous stem cell transplant was defined according to the inclusion criteria of the CEPHEUS study as age ≥ 65 years or age < 65 years with coexisting relevant comorbidities. The medical investigators also assessed the suitability of patients younger than 70 years of age for autologous stem cell transplant.

The pharmaceutical company presented evaluations of the post hoc sub-population of patients who are ineligible for autologous stem cell transplant. This sub-population includes patients under the age of 70, who, in the opinion of the medical investigator, were ineligible for autologous stem cell transplant, as well as patients ≥ 70 years of age. The sub-population of patients, who are ineligible for autologous stem cell transplant (n = 289), is used for the benefit assessment.

The primary endpoint of the study was the minimal residual disease (MRD) negativity rate. Secondary endpoints were overall survival and endpoints in the categories of morbidity, health-related quality of life and side effects.

With regard to subsequent therapies, some therapy options, which do not comply with current guideline recommendations, were used in the intervention and comparator arms of the CEPHEUS study.

The pharmaceutical company presented the results of the second data cut-off of the CEPHEUS study from 07.05.2024 for the benefit assessment. As part of the written statement procedure, the pharmaceutical company presented the results of the final data cut-off from 08.10.2025. The results of the final data cut-off are used for the benefit assessment.

Extent and probability of the additional benefit

Mortality

Overall survival is operationalised in the CEPHEUS study as the time from randomisation to death, lost to follow-up, withdrawal of informed consent, or end of study, whichever occurred first. For the endpoint of overall survival, there was no statistically significant difference between the treatment arms.

Morbidity

Progression-free survival (PFS)

PFS is operationalised in the CEPHEUS study as the time from randomisation to the time of first disease progression, assessed based on the criteria of the International Myeloma Working Group (IMWG), or the time to death from any cause, whichever occurs first.

For the PFS endpoint, there was a statistically significant advantage of daratumumab + bortezomib + lenalidomide + dexamethasone compared to bortezomib + lenalidomide + dexamethasone.

The present PFS endpoint is a composite endpoint consisting of endpoints from the categories "mortality" and "morbidity". The mortality endpoint component is already assessed via the overall survival endpoint as an independent endpoint. The morbidity component "disease progression" was assessed according to IMWG criteria and thus, not in a symptom-related manner but only by means of laboratory parametric, imaging, and haematological procedures.

Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient relevance of the PFS endpoint. The overall statement on the extent of the additional benefit remains unaffected.

Minimal residual disease (MRD)

The endpoint of MRD negativity rate was the primary endpoint of the CEPHEUS study and was defined as the percentage of study participants who, after randomisation, achieved MRD negativity and a complete response by means of bone marrow puncture at any time during the study, but before disease progression or subsequent myeloma therapy, or both.

The endpoint of MRD negativity rate is not used for derivation of an additional benefit. As this may be a relevant prognostic factor, the endpoint is presented additionally.

The results for the endpoint of MRD negativity rate 3 years after randomisation and at a threshold value of 10^{-5} cells show a statistically significant difference to the advantage of daratumumab + bortezomib + lenalidomide + dexamethasone compared to bortezomib + lenalidomide + dexamethasone.

Symptomatology (EORTC QLQ-C30; EORCT QLQ-MY20)

Disease symptomatology was assessed in the CEPHEUS study using the cancer-specific questionnaire EORTC QLQ-C30 and the additional module EORTC QLQ-MY20.

The pharmaceutical company submitted evaluations of the time to first deterioration with a response threshold ≥ 10 points.

Only for the symptom of constipation was there a statistically significant difference to the advantage of daratumumab + bortezomib + lenalidomide + dexamethasone compared to bortezomib + lenalidomide + dexamethasone. With regard to the other EORTC QLQ-C30 symptom scales and the EORTC QLQ-MY20, there were no statistically significant differences between the treatment arms.

Health status (EQ-5D VAS)

The health status was assessed in the CEPHEUS study using the visual analogue scale (VAS) of the EQ-5D. The time to confirmed permanent deterioration in health status by ≥ 15 points is used for the present benefit assessment. There was a statistically significant difference to the advantage of daratumumab + bortezomib + lenalidomide + dexamethasone compared to bortezomib + lenalidomide + dexamethasone.

In summary, an improvement, which is based on the advantage in terms of the time to confirmed permanent deterioration in health status, can be observed in the endpoint category of morbidity overall. The results for the symptom of constipation are not used for derivation of the additional benefit, taking into account the extent and clinical relevance of the observed effect.

<u>Quality of life</u>

Health-related quality of life is assessed in the CEPHEUS study using the functional scales of the EORTC-QLQ C30 and the additional module EORCT QLQ-MY20.

There were no statistically significant differences between the treatment arms in the analyses of the time to first deterioration by ≥ 10 points.

Side effects

Serious adverse events (SAEs) and severe AEs

For the endpoints of SAEs and severe AEs, there were no statistically significant differences between the treatment arms of the presented study respectively.

Discontinuation due to AEs

With regard to the endpoint of discontinuation of at least one active ingredient component due to AE, the study showed no statistically significant differences between the treatment arms.

Specific adverse events

With regard to the specific AEs of peripheral neuropathy, there were no statistically significant differences between the treatment arms.

Overall assessment

Results on mortality, morbidity, quality of life and side effects are available from the CEPHEUS study for the assessment of the additional benefit of daratumumab in combination with bortezomib, lenalidomide and dexamethasone, compared to the combination therapy of bortezomib + lenalidomide + dexamethasone, for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant. The results for the sub-population of patients who are ineligible for autologous stem cell transplant are used for the benefit assessment.

With regard to overall survival, there was no statistically significant difference between the study arms.

In terms of symptomatology, assessed using EORTC QLQ-C30 and EORTC QLQ-MY20, there was only a statistically significant advantage of daratumumab + bortezomib + lenalidomide + dexamethasone in the symptom of constipation, which, considering the extent and clinical relevance of the observed effect, is not used for derivation of the additional benefit.

Based on the EQ-5D VAS results, an advantage of daratumumab + bortezomib + lenalidomide + dexamethasone can be found in terms of health status for the time to confirmed permanent deterioration.

For the health-related quality of life, assessed using EORTC QLQ-C30 and EORTC QLQ-MY20, and with regard to the endpoint category of side effects, there were no statistically significant differences between the treatment arms.

An overall assessment of the results for the patient-relevant endpoints showed an advantage for health status in the endpoint category of morbidity. For the other endpoints of morbidity, health-related quality of life and side effects, neither an advantage nor a disadvantage of daratumumab in combination with bortezomib, lenalidomide and dexamethasone could be identified.

As a consequence, the G-BA identified a minor additional benefit of daratumumab in combination with bortezomib, lenalidomide and dexamethasone compared with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.

Reliability of data (probability of additional benefit)

The present assessment is based on the results of the randomised, open-label, controlled phase III CEPHEUS study. At the study level, the risk of bias is rated as low.

Significant uncertainties arise due to the lack of blinding, which leads to a high risk of bias in patient-reported endpoints due to the subjective nature of endpoint assessment.

Taking into account the uncertainties mentioned above, an overall hint for the identified additional benefit can be derived.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient daratumumab.

The therapeutic indication assessed here is as follows:

"Daratumumab (Darzalex) is indicated in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant."

As the appropriate comparator therapy, the G-BA determined various combination therapies as alternative comparator therapies, including bortezomib in combination with lenalidomide and dexamethasone. For the benefit assessment, the pharmaceutical company presented the results of the open-label, randomised CEPHEUS study, in which bortezomib in combination with lenalidomide and dexamethasone was used in the comparator arm.

There was no significant difference between the study arms in terms of overall survival.

In terms of morbidity, an advantage of daratumumab + bortezomib + lenalidomide + dexamethasone can be identified for the endpoint of health status.

For the health-related quality of life and side effects, there were no significant differences between the study arms.

In the overall assessment, the G-BA identified a minor additional benefit of daratumumab in combination with bortezomib, lenalidomide and dexamethasone compared with bortezomib, lenalidomide and dexamethasone.

The reliability of data is classified as a "hint" due to the uncertainty arising from the risk of bias in the endpoint of health status.

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 resolution on the benefit assessment of isatuximab in combination with bortezomib, lenalidomide and dexamethasone (resolution of 7 August 2025) and daratumumab in combination with bortezomib, melphalan and prednisone (resolution of 16 May 2024).

The patient numbers presented by the pharmaceutical company are an underestimate due to the method used to calculate the change rates in sample sizes. This is therefore no better estimate than the patient numbers, which are used in the aforementioned resolutions and can be relied upon despite the continuing uncertainty.

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 Darzalex (active ingredient: daratumumab) at the following publicly accessible link (last access: 2 December 2025):

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

Treatment with daratumumab 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 training material and a patient identification card. The training material for medical professionals and blood banks contains instructions on how to manage the risk of daratumumab interfering with blood typing (indirect antihuman globulin test or Coombs test). Interference with blood typing induced by daratumumab may persist for up to six months after the last infusion of the medicinal product; therefore, medical professionals should advise patients to carry their patient identification card with them for up to six months after the end of the treatment.

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 December 2025). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

The annual treatment costs shown refer to the first year of treatment.

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

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.

Treatment period:

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Daratumumab in combination with bortezomib, lenalidomide and dexamethasone				
Daratumumab	Cycle 1 - 2: 3 x per 21-day cycle Cycle 3 – 8: 1 x per 21-day cycle From cycle 9 1 x per 28-day cycle	15.0	3 (cycle 1 – 2) 1 (cycle 3 – 8) 1 (from cycle 9)	19.0
Bortezomib	On days 1, 4, 8 and 11 of a 21-day cycle	8	4	32
Lenalidomide	Cycle 1 – 8 Day 1 - 14 of a 21-day cycle From cycle 9 Day 1 – 21 of a 28-day cycle	15.0	14 (cycle 1 – 8) 21 (from cycle 9)	259.0
Dexamethasone	Cycle 1 – 8 Day 1, 2, 4, 5, 8, 9, 11 and	15.0	6 (cycle 1 – 2) 7 (cycle 3 – 8)	75.0[2]

[2] On the days of daratumumab administration, the dexamethasone dose is administered as premedication.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	12 of a 21-day cycle From cycle 9 On days 1, 8, 15 and 22 of a 28-day cycle		3 (from cycle 9)	
Appropriate comparator therapy				
Daratumumab in combination with lenalidomide and dexamethasone				
Daratumumab	28-day cycle: Cycle 1 - 2: Day 1, 8, 15, 22 Cycle 3 – 6: Day 1 and 15 From cycle 7 Day 1	13.0	4 (cycle 1 – 2) 2 (cycle 3 – 6) 1 (from cycle 7)	23.0
Lenalidomide	Day 1 – 21 28-day cycle	13.0	21	273.0
Dexamethasone PO	Day 1, 8, 15, 22 28-day cycle	13.0	0 (cycle 1 – 2) 2 (cycle 3 – 6) 3 (from cycle 7)	29.0[3]
daratumumab in combination with bortezomib, melphalan and prednisone				
Daratumumab	Cycle 1	8.7	6 (cycle 1)	21.4

[3] On the days of daratumumab administration, 40 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
	6 x per 42-day cycle <u>From cycle 2:</u> 2 x per 42-day cycle		2 (from cycle 2)	
Bortezomib	<u>Cycle 1</u> 8 x per 42-day cycle <u>From cycle 2:</u> 4 x per 42-day cycle	8.7	8 (cycle 1) 4 (from cycle 2)	38.8
Melphalan PO	Day 1 – 4 of the 42-day cycles	8.7	4	34.8
Prednisone PO	Day 2 – 4 of the 42-day cycles	8.7	3	26.1
Bortezomib in combination with melphalan and prednisone				
Bortezomib	<u>Cycle 1 – 4</u> 8 x per 42-day cycle <u>From cycle 5:</u> 4 x per 42-day cycle	8.7	8 (cycle 1 – 4) 4 (from cycle 5)	50.8
Melphalan	Day 1 – 4 of the 42-day cycles	8.7	4	34.8

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Prednisone	Day 1 – 4 of the 42-day cycles	8.7	4	34.8
Bortezomib in combination with lenalidomide and dexamethasone				
Induction				
Bortezomib	On days 1, 4, 8 and 11 of a 21-day cycle	8	4	32
Lenalidomide	Day 1 – 14 of a 21-day cycle	8	14	112
Dexamethasone	On days 1, 2, 4, 5, 8, 9, 11 and 12 of a 21-day cycle	8	8	64
Follow-up treatment				
Lenalidomide	Day 1 – 21 of a 28-day cycle	7.0	21	147.0
Dexamethasone	On days 1, 8, 15 and 22 of a 28-day cycle	7.0	4	28.0
thalidomide in combination with melphalan and prednisone				
Thalidomide	Day 1 – 42 of a 42-day cycle	8.7	42	365.0
Melphalan	Day 1 – 4 of a 42-day cycle	8.7	4	34.8

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Prednisone	Day 1 – 4 of a 42-day cycle	8.7	4	34.8
Bortezomib in combination with cyclophosphamide and dexamethasone (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)				
Bortezomib	Day 1, 4, 8 and 11 of a 21-day cycle	17.4	4	69.6
Cyclophosphamide IV	Day 1 of a 21-day cycle	17.4	1	17.4
Dexamethasone PO	Day 1, 2, 4, 5, 8, 9, 11, 12 of a 21-day cycle	17.4	8	139.2

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) [4].

As it is not always possible to achieve the exact calculated dose per day with the commercially available dosage strengths, in these cases rounding up or down to the next higher or lower available dose that can be achieved with the commercially available dose potencies as well as the scalability of the respective dosage form.

[4] Federal health reporting. Average body measurements of the population (2021, both sexes, 18 years and older), www.gbe-bund.de

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

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					
Daratumumab in combination with bortezomib, lenalidomide and dexamethasone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	19.0	19 x 1,800 mg
Bortezomib	1.3 mg/m^2	2.5 mg	1 x 2.5 mg	32	32 x 2.5 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	259.0	259 x 25 mg
Dexamethasone	20 mg	20 mg	1 x 20 mg	54.0	54 x 20 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	21.0	21 x 40 mg
Appropriate comparator therapy					
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	40 mg	29.0	29 x 40 mg
Daratumumab in combination with bortezomib, melphalan and prednisone					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	21.4	21.4 x 1,800 mg
Bortezomib	1.3 mg/m^2 = 2.5 mg	2.5 mg	1 x 2.5 mg	38.8	38.8 x 2.5 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 PO	9 mg/m² = 17.2 mg	17.2 mg	9 x 2 mg	34.8	313.2 x 2 mg
Prednisone PO	60 mg/m² = 114.6 mg	114.6 mg	2 x 50 mg + 1 x 10 mg + 1 x 5 mg	26.1	52.2 x 50 mg + 26.1 x 10 mg + 26.1 x 5 mg
Bortezomib in combination with melphalan and prednisone					
Bortezomib	1.3 mg/m² = 2.5 mg	2.5 mg	1 x 2.5 mg	50.8	50.8 x 2.5 mg
Melphalan	9 mg/m² = 17.2 mg	17.2 mg	9 x 2 mg	34.8	313.2 x 2 mg
Prednisone	60 mg/m² = 114.6 mg	114.6 mg	2 x 50 mg + 1 x 10 mg + 1 x 5 mg	34.8	69.6 x 50 mg + 34.8 x 10 mg + 34.8 x 5 mg
Bortezomib in combination with lenalidomide and dexamethasone					
Induction					
Bortezomib	1.3 mg/m² = 2.5 mg	2.5 mg	1 x 2.5 mg	32	32 x 2.5 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	112	112 x 25 mg
Dexamethasone PO	20 mg	20 mg	1 x 20 mg	64	64 x 20 mg
Follow-up treatment					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Lenalidomide	25 mg	25 mg	1 x 25 mg	147.0	147 x 25 mg
Dexamethasone PO	40 mg	40 mg	1 x 40 mg	28.0	28 x 40 mg
thalidomide in combination with melphalan and prednisone					
Thalidomide	200 mg	200 mg	2 x 100 mg	365.0	730 x 100 mg
Melphalan	0.25 mg/kg = 19.4 mg	19.4 mg	10 x 2 mg	34.8	348 x 2 mg
Prednisone	2 mg/kg = 155.4 mg	155.4 mg	3 x 50 mg + 1 x 5 mg	34.8	104.4 x 50 mg + 34.8 x 5 mg
Bortezomib in combination with cyclophosphamide and dexamethasone (only for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy; see Annex VI to Section K of the Pharmaceuticals Directive)					
Bortezomib	1.3 mg/m^2 = 2.5 mg	2.5 mg	1 x 2.5 mg	69.6	69.6 x 2.5 mg
Cyclophosphamide IV	900 mg/m^2 = 1,719 mg	1,719 mg	2 x 1,000 mg[5]	17.4	34.8 x 1,000 mg
Dexamethasone PO	40 mg	40 mg	1 x 40 mg	139.2	139.2 x 40 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

[5] The administration form must be intravenous according to Annex VI of the Pharmaceuticals Directive.

the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

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					
Daratumumab 1,800 mg	1 SFI	€ 5,809.87	€ 1.77	€ 0.00	€ 5,808.10
Lenalidomide 25 mg[6]	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Bortezomib 2.5 mg	1 PSI	€ 185.37	€ 1.77	€ 8.26	€ 175.34
Dexamethasone 20 mg[6]	50 TAB	€ 118.88	€ 1.77	€ 0.00	€ 117.11
Dexamethasone 20 mg[6]	10 TAB	€ 32.42	€ 1.77	€ 0.00	€ 30.65
Dexamethasone 40 mg[6]	50 TAB	€ 188.03	€ 1.77	€ 0.00	€ 186.26
Appropriate comparator therapy					
Bortezomib 2.5 mg	1 PSI	€ 185.37	€ 1.77	€ 8.26	€ 175.34
Cyclophosphamide 1,000 mg	6 PSI	€ 145.55	€ 1.77	€ 7.43	€ 136.35
Daratumumab 1,800 mg	1 SFI	€ 5,809.87	€ 1.77	€ 0.00	€ 5,808.10
Dexamethasone 40 mg[6]	50 TAB	€ 188.03	€ 1.77	€ 0.00	€ 186.26
Dexamethasone 20 mg[6]	50 TAB	€ 118.88	€ 1.77	€ 0.00	€ 117.11
Dexamethasone 20 mg[6]	20 TAB	€ 54.09	€ 1.77	€ 0.00	€ 52.32
Lenalidomide 25 mg[6]	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Melphalan 2 mg	50 FCT	€ 54.22	€ 1.77	€ 2.38	€ 50.07
Prednisone 50 mg[6]	50 TAB	€ 68.06	€ 1.77	€ 4.49	€ 61.80

[6] 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
Prednisone 10 mg[6]	100 TAB	€ 21.23	€ 1.77	€ 0.78	€ 18.68
Prednisone 5 mg[6]	100 TAB	€ 16.74	€ 1.77	€ 0.43	€ 14.54
Thalidomide 100 mg	30 CTA	€ 706.69	€ 1.77	€ 88.00	€ 616.92
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PSI = powder for solution for injection; TAB = tablets; CTA = coated tablets					

LAUER-TAXE® last revised: 15 December 2025

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.

The calculation of the additionally required SHI services is based on packs in distribution with the LAUER-TAXE® last revised on 15 September 2025 and fee structure items (FSI) - last revised in the 3rd quarter of 2025 of the uniform value scale (UVS 2025/Q3).

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 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							
Daratumumab (in combination with bortezomib, lenalidomide and dexamethasone)							
Dexamethasone 20 mg, PO[6]	20 TAB x 20 mg	€ 54.09	€ 1.77	€ 0.00	€ 52.32	12	€ 52.32
Dexamethasone 40 mg, PO[6]	50 TAB x 40 mg	€ 188.03	€ 1.77	€ 0.00	€ 186.26	7.0	€ 26.08
Paracetamol 500 – 1,000 mg, PO[6,7]	20 TAB x 500 mg	€ 3.47	€ 0.17	€ 0.15	€ 3.15	19.0	€ 2.99
	10 TAB x 1,000 mg	€ 3.32	€ 0.17	€ 0.14	€ 3.01		€ 5.72
Dimetindene IV 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	€ 26.24	€ 1.77	€ 6.92	€ 17.55	19.0	€ 133.38
Appropriate comparator therapy							
Daratumumab (in combination with lenalidomide and dexamethasone)							
Dexamethasone 40 mg, PO[6]	50 TAB x 40 mg	€ 188.03	€ 1.77	€ 0.00	€ 186.26	23	€ 85.68
Paracetamol 500 – 1,000 mg, PO[7,7]	20 TAB x 500 mg	€ 3.47	€ 0.17	€ 0.15	€ 3.15	23	€ 3.62
	10 TAB x 1,000 mg	€ 3.32	€ 0.17	€ 0.14	€ 3.01		€ 6.92
Dimetindene IV 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	€ 26.24	€ 1.77	€ 6.92	€ 17.55	23	€ 161.46
Daratumumab (in combination with bortezomib, melphalan and prednisone)							

[7] 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
Dexamethasone 20 mg[6]	50 TAB x 20 mg	€ 118.88	€ 1.77	€ 0.00	€ 117.11	21.4	€ 50.12
Paracetamol 500 – 1,000 mg[7,7]	20 TAB (500 mg)	€ 3.47	€ 0.17	€ 0.15	€ 3.15	21.4	€ 3.37
	10 TAB (1,000 mg)	€ 3.32	€ 0.17	€ 0.14	€ 3.01		€ 6.44
Dimetindene IV 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	€ 26.24	€ 1.77	€ 6.92	€ 17.55	21.4	€ 150.23
Abbreviations: SFI = solution for injection; TAB = tablets							

Screening for hepatitis B virus (HBV)

Patients receiving therapy with daratumumab, thalidomide 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[8]. 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.

[8] 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	Designation of the service	Number	Costs per unit	Costs/ patient/ year
Medicinal product to be assessed				
Daratumumab Lenalidomide	HBs antigen (FSI 32781)	1	€ 5.06	€ 5.06
	Anti-HBc antibody (FSI 32614)	1	€ 5.43	€ 5.43
Appropriate comparator therapy				
Daratumumab Lenalidomide Thalidomide	HBs antigen (FSI 32781)	1	€ 5.06	€ 5.06
	Anti-HBc antibody (FSI 32614)	1	€ 5.43	€ 5.43

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 October 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 designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

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 have 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 have 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 requirements 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 have 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 newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

No medicinal product with new active ingredients that can be used in a combination therapy, for which the requirements of Section 35a, paragraph 3, sentence 4 SGB V are fulfilled.

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 their session on 23 April 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 15 August 2025, the pharmaceutical company submitted a dossier for the benefit assessment of daratumumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 18 August 2025 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 daratumumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 November 2025, and the written statement procedure was initiated with publication on the G-BA website on 17 November 2025. The deadline for submitting written statements was 8 December 2025.

The oral hearing was held on 12 January 2026.

By letter dated 13 January 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 29 January 2026.

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 subcommittee session on 10 February 2026, and the draft resolution was approved.

At their session on 19 February 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	23 April 2025	Determination of the appropriate comparator therapy
Working group Section 35a	7 January 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	12 January 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	21 January 2026 4 February 2026	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	10 February 2026	Concluding discussion of the draft resolution
Plenum	19 February 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 19 February 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken