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
Isatuximab

(New therapeutic indication: multiple myeloma, first-line, suitable 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 isatuximab (Sarclisa) was listed for the first time on 1 February 2021 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 18 July 2025, isatuximab received marketing authorisation for a new therapeutic indication to be 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 12 August 2025, i.e. at the latest within four weeks of informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with

Chapter 5 Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient isatuximab with the new therapeutic indication

"SARCLISA is indicated in combination with bortezomib, lenalidomide, and dexamethasone, for the induction treatment of adult patients with newly diagnosed multiple myeloma who are eligible 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 isatuximab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA 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 isatuximab.

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:

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

2.1.1 Approved therapeutic indication of Isatuximab (Sarclisa) in accordance with the product information

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

Therapeutic indication of the resolution (resolution of 19.02.2026):

See new therapeutic indication according to marketing authorisation.

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

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant; induction treatment

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

- An induction therapy consisting of:
  - Bortezomib + thalidomide + dexamethasone (VTd)

    or
  - bortezomib + cyclophosphamide + dexamethasone (VCd) [only patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy are eligible; see Annex VI to Section K of the Pharmaceuticals Directive]

    or
  - daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd)

    or
  - daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd),

- followed by a high-dose therapy with melphalan and subsequent autologous stem cell transplant

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 carmustine, cyclophosphamide, doxorubicin, melphalan and vincristine, the proteasome inhibitor bortezomib, the CD38 antibody daratumumab, 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 eligible for autologous stem cell transplant.

On 2. In principle, autologous and allogeneic stem cell transplants are considered in the present therapeutic indication.

On 3. In the therapeutic indication of newly diagnosed multiple myeloma, the following resolutions on the benefit assessment of medicinal products with new active ingredients (Section 35a SGB V) are available:
- Daratumumab in combination with bortezomib, lenalidomide and dexamethasone (resolution of 15 May 2025)
- Daratumumab in combination with bortezomib, thalidomide and dexamethasone (resolution of 20 August 2020)

Resolution of the Federal Joint Committee (G-BA) on an amendment of the Pharmaceuticals Directive (AM-RL): Annex VI (off-label use):
Bortezomib plus cyclophosphamide plus dexamethasone for the induction therapy of newly diagnosed multiple myeloma (resolution of 20 May 2021).

There is also a resolution dated 19.01.2017 on the Directive on Inpatient Treatment Methods (last revised 17 June 2021) – Annex II: Methods whose assessment procedures have been suspended (resolution of 19.01.2017):

- Autologous multiple transplants (tandem transplantation) for multiple myeloma
- Allogeneic stem cell transplant for multiple myeloma in first-line therapy

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 indication according to Section 35a paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy"). A written statement from the German Society for Haematology and Medical Oncology (DGHO) is available.

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 care.

Overall, the research revealed extensive evidence from systematic reviews and relevant guidelines on treatment options for adults with newly diagnosed multiple myeloma that are suitable for autologous stem cell transplant.

Accordingly, patients were given induction therapy as standard prior to autologous stem cell transplant. In the available evidence, the induction therapy is based on a trio or tetra combination, which should contain a proteasome inhibitor. The approved combinations of bortezomib with thalidomide and dexamethasone (VTd) and daratumumab with bortezomib and thalidomide and dexamethasone (D-VTd) are eligible for this. By resolution of 20 August 2020, the G-BA identified a non-quantifiable additional benefit of the combination therapy of daratumumab with bortezomib and thalidomide and dexamethasone, compared to bortezomib + thalidomide + dexamethasone. The two combination therapies of D-VTd and VTd are considered to be equally appropriate comparator therapies for the treatment phase of induction therapy.

The combination of bortezomib, cyclophosphamide and dexamethasone is further considered as induction therapy. The latter is only indicated for patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy in accordance with Annex VI to Section K of the Pharmaceuticals Directive.

The combination of daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd) is another approved treatment option in the present therapeutic indication. An additional benefit of daratumumab + bortezomib + lenalidomide + dexamethasone is not proven in the benefit assessment thereof (resolution of 15 May 2025). As described above, the present guidelines recommend a trio or tetra combination as induction therapy. In their written statement, the DGHO recommend the tetra combination consisting of anti-CD38 antibody (daratumumab or isatuximab) + bortezomib + lenalidomide + dexamethasone as the standard first-line therapy in the present therapeutic indication. The combination therapy VRd is included as a further treatment option for induction therapy in the appropriate comparator therapy.

The present guidelines and the statements of the clinical experts in the written statement procedure also refer to the trio combination consisting of bortezomib,

lenalidomide and dexamethasone. As part of a completed marketing authorisation procedure by the European Medicines Agency (EMA) for lenalidomide (Revlimid) for the treatment of newly diagnosed multiple myeloma, it was however found that no conclusions regarding either superiority or non-inferiority to standard therapy can be drawn on the basis of the presented evidence for adults eligible for autologous stem cell transplant[2]. Accordingly, the combination therapy of bortezomib + lenalidomide + dexamethasone is not determined as an appropriate comparator therapy for the induction therapy phase.

Induction therapy is followed by high-dose therapy with subsequent autologous stem cell transplant. According to guidelines, melphalan is the high-dose therapy standard.

Antineoplastic consolidation therapy following autologous stem cell transplant has not yet shown any advantage in terms of overall survival and cannot be considered the standard based on the available evidence. Here, the concept of "consolidation" therapy must be distinguished from that of "maintenance treatment", which address different therapeutic goals. Only when D-VTd or D-VRd-based induction therapy is administered does consolidation therapy with 2 cycles of D-VTd or D-VRd following high-dose therapy and autologous stem cell transplant correspond to the dosage regimen according to the product information for daratumumab.

The present approved therapeutic indication for isatuximab refers exclusively to induction treatment of adults who are eligible for autologous stem cell transplant. The therapeutic concept for the treatment of patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant includes induction therapy followed by high-dose therapy with subsequent autologous stem cell transplant, as well as maintenance treatment, for which the guidelines provide clear recommendations. Maintenance treatment and consolidation therapy are not included in the appropriate comparator therapy as they are not part of the present marketing authorisation of isatuximab.

[2] European Medicines Agency (EMA). Assessment report: Revlimid. 28 March 2019 URL: https://www.ema.europa.eu/en/documents/variation-report/revlimid-h-c-717-ii-0102-g-epar-assessment-report-variation_en.pdf

Change of the appropriate comparator therapy:

In the originally determined appropriate comparator therapy, consolidation therapy and maintenance treatment were also included as part of the overall therapeutic concept, in addition to induction therapy.

The present approved therapeutic indication for isatuximab refers exclusively to induction treatment of adults who are eligible for autologous stem cell transplant. With reference to this in their statement on the benefit assessment, the pharmaceutical company raise the objection that maintenance treatment is not covered by the marketing authorisation of isatuximab, which is why maintenance treatment cannot be considered as part of the appropriate comparator therapy. In line with this objection, the G-BA do not include maintenance treatment in the appropriate comparator therapy specified for the present resolution. In this context, based on the wording of the approved therapeutic indication for isatuximab, consolidation therapy is also not defined as part of the appropriate comparator therapy.

This change of the appropriate comparator therapy has no impact on the present assessment of the additional benefit of isatuximab.

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 isatuximab is assessed as follows:

An additional benefit is not proven.

Justification:

The pharmaceutical company submitted results from the ongoing, open-label, randomised controlled trial GMMG-HD7 comparing isatuximab + bortezomib + lenalidomide + dexamethasone with bortezomib + lenalidomide + dexamethasone for the benefit assessment.

A total of 662 patients were enrolled and randomised in a 1:1 ratio. Randomisation for the induction phase was stratified by stage of the disease (stage I/II versus stage III versus unclassified; according to the International Staging System). The study has been ongoing since 18.10.2018 exclusively at study sites in Germany and is scheduled to continue until March 2027.

The study treatment is divided into two phases: Part 1 Induction and intensification, and Part 2 Maintenance. The marketing authorisation is based on Part 1. Part 2 is currently still ongoing and is not part of the marketing authorisation. Only data from Part 1 of the study are available for the present benefit assessment. The entire therapeutic concept of first-line therapy (induction, high-dose therapy with subsequent autologous stem cell transplant, consolidation and maintenance) must be taken into account for the assessment of the additional benefit in the therapeutic indication of newly diagnosed multiple myeloma in adults.

As induction therapy, patients in the GMMG-HD7 study receive treatment with bortezomib, lenalidomide and dexamethasone for 3 cycles (1 cycle corresponds to 6 weeks) after

randomisation in both study arms. In the intervention arm, treatment was also given in combination with isatuximab. This is followed by stem cell mobilisation, high-dose therapy with melphalan and autologous stem cell transplant. Prior to maintenance treatment, all patients were randomised again to either combination therapy with lenalidomide + isatuximab or monotherapy with lenalidomide, each administered in a 28-day cycle until disease progression, the occurrence of unacceptable toxicity, or for a maximum of 3 years.

The primary endpoint of the study is minimal residual disease (MRD) negativity rate and progression-free survival (PFS). Secondary endpoints were assessed in the categories of mortality, morbidity, health-related quality of life and side effects.

Overall, two data cut-offs are available:

− 1st data cut-off from 21.04.2021

− 2nd data cut-off from 31.01.2024

The final data cut-off from 31.01.2024 is used for the present benefit assessment. This data cut-off contains the final data on PFS after the first randomisation (Part 1 of the study).

Implementation of the appropriate comparator therapy:

The induction therapy with bortezomib + lenalidomide + dexamethasone (VRd) used in the comparator arm of the GMMG-HD7 study does not correspond to any of the options for induction therapy specified in the appropriate comparator therapy.

With regard to induction therapy with VRd, as part of a completed EMA marketing authorisation procedure for lenalidomide (Revlimid) for the treatment of newly diagnosed multiple myeloma, it was found that no conclusions regarding either superiority or non-inferiority to standard therapy can be drawn on the basis of the presented evidence for adults eligible for autologous stem cell transplant[2]. The EMA have therefore not made a positive recommendation for a marketing authorisation of VRd for patients who are eligible for an autologous stem cell transplant and have limited the positive recommendation to patients who are ineligible for an autologous stem cell transplant. The corresponding European Public Assessment Report (EPAR)[2] stated in this regard that the EMA will revisit the question of marketing authorisation of VRd for patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant as soon as new suitable evidence is available for this research question. However, since this decision by the EMA on the facts presented, no suitable new studies that would allow reassessment of this research question are available. Accordingly, the combination therapy of bortezomib + lenalidomide + dexamethasone is not determined as an appropriate comparator therapy for the induction therapy phase.

In contrast, clinical experts stated in the written statement procedure that VRd is a relevant therapy option in induction therapy and that induction therapy with VRd also corresponds to the German healthcare context.

Conclusion:

Overall, the induction therapy with VRd conducted in the comparator arm of the GMMG-HD7 study does not correspond to the appropriate comparator therapy determined by the G-BA. Thus, the appropriate comparator therapy was not implemented in the GMMG-HD7 study, and the study is therefore not suitable for the assessment of the additional benefit. An additional benefit of isatuximab in combination with bortezomib, lenalidomide and

dexamethasone for the induction treatment of newly diagnosed multiple myeloma in adults, who are eligible for autologous stem cell transplant, is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient isatuximab:

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

The G-BA determined the following as appropriate comparator therapy:

- An induction therapy consisting of:
  - Bortezomib + thalidomide + dexamethasone (VTd)

    or
  - bortezomib + cyclophosphamide + dexamethasone (VCd) [only patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy are eligible; see Annex VI to Section K of the Pharmaceuticals Directive]

    or
  - daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd)

    or
  - daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd),

- followed by a high-dose therapy with melphalan and subsequent autologous stem cell transplant

The pharmaceutical company presented the ongoing, open-label, randomised GMMG-HD7 study comparing isatuximab + bortezomib + lenalidomide + dexamethasone with bortezomib + lenalidomide + dexamethasone (VRd) for the assessment of the additional benefit of isatuximab in combination with bortezomib, lenalidomide and dexamethasone.

The induction therapy with VRd used in the comparator arm of the GMMG-HD7 study does not correspond to any of the options for induction therapy specified in the appropriate comparator therapy.

With regard to induction therapy with VRd, as part of a completed EMA marketing authorisation procedure for lenalidomide (Revlimid) for the treatment of newly diagnosed multiple myeloma, it was found that no conclusions regarding either superiority or non-inferiority to standard therapy can be drawn on the basis of the presented evidence for adults eligible for autologous stem cell transplant. Accordingly, induction therapy with VRd was not determined by the G-BA as an appropriate comparator therapy for the induction therapy phase.

In summary, the GMMG-HD7 study is not suitable for the assessment of the additional benefit of isatuximab + bortezomib + lenalidomide + dexamethasone compared with the appropriate comparator therapy. Thus, no suitable data are available to enable an assessment of the additional benefit, which is why an additional benefit of isatuximab in combination with

bortezomib and lenalidomide and dexamethasone in the treatment of patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant is not proven.

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

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

The dossier submitted by the pharmaceutical company tends to underestimate the provisional baseline incidence of patients with newly diagnosed multiple myeloma, who are eligible for autologous stem cell transplant, for the year 2022.

In order to ensure a consistent determination of the patient numbers in the present therapeutic indication, the G-BA refer to the derivation of the target population used as a basis in the resolution on the benefit assessment of daratumumab (resolution of 15 May 2025). A more valid estimate of the number of patients in the SHI target population is available here; this can be used despite continuing uncertainties.

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 Sarclisa (active ingredient: isatuximab) at the following publicly accessible link (last access: 11 February 2026):

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

Treatment with isatuximab 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 European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (including patient identification card). The training material contains in particular information and warnings on how to manage the risk of isatuximab interfering with blood typing (indirect antihuman globulin test or indirect Coombs test). Isatuximab-induced interference with blood typing may persist for approximately 6 months after the last infusion of the medicinal product; therefore, healthcare professionals should advise patients to carry their patient identification card with them until 6 months after the end of 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 the maximum treatment duration, if specified in the product information.

Inpatient treatments

Some treatment options are carried out on an inpatient basis. The inpatient costs are calculated on the basis of the case flat fee revenues, which result from the valuation ratios of the respective DRG (Diagnosis Related Group) multiplied by the federal base rate value of 2025 (€ 4,394.22). Furthermore, the nursing revenue is included in the inpatient costs. This is calculated from the average length of stay of the concerned DRG multiplied by the nursing fee according to Section 15 para. 2a KHEntgG (Act on Fees for Full and Semi-inpatient Hospital Services) (from 28 March 2024: € 250) and the treatment-specific nursing revenue valuation ratio. The calculation of the costs of the inpatient treatments is standardised in the following on the basis of the DRG case flat fee catalogue 2025 and the nursing revenue catalogue 2025, the Federal base rate value of 2025 as well as the nursing fee pursuant to Section 15, paragraph 2a German Hospital Fee Act (KHEntgG), since the federal base rate value for 2026 was not yet available at the time of the cost calculation (15 December 2025).

Treatment period:

Adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant; induction treatment

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Isatuximab in combination with bortezomib, lenalidomide and dexamethasone				
Isatuximab	42-day cycle: Cycle 1: Day 1, 8, 15, 22 and 29 Cycle 2 – 3: Day 1, 15 and 29	3	5 (cycle 1) 3 (cycle 2 – 3)	11
Bortezomib	42-day cycle: Day 1, 4, 8, 11, 22, 25, 29 and 32	3	8	24
Lenalidomide	On days 1 – 14 and 22 – 35 of a 42-day cycle	3	28	84
Dexamethasone PO/ IV[3]	On the days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32 and 33 of a 42-day cycle	3	17	51
High-dose chemotherapy and subsequent autologous stem cell transplant				
Stem cell collection	once		4.2 – 5.0 (average length of stay)	4.2 – 5.0
High-dose chemotherapy + autologous stem cell transplant	once		19	19.0

[3] On the days of isatuximab administration, 20 mg of the dexamethasone dose is intravenously administered as premedication.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
			(average length of stay)	
Appropriate comparator therapy				
Bortezomib + thalidomide + dexamethasone (VTd)				
Induction				
Bortezomib	On the days 1, 4, 8 and 11 of a 28-day cycle	4 – 6	4	16 – 24
Thalidomide	Day 1 – 28 of a 28-day cycle	4 – 6	28	112 – 168
Dexamethasone PO	On the days 1, 2, 3, 4, 8, 9, 10 and 11 of a 28-day cycle	4 – 6	8	32 – 48
High-dose therapy with melphalan and subsequent autologous stem cell transplant				
Stem cell collection	once		4.2 – 5.0 (average length of stay)	4.2 – 5.0
High-dose chemotherapy + autologous stem cell transplant	once		19.0 (average length of stay)	19.0
Bortezomib + cyclophosphamide + dexamethasone (VCd) (only patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy are eligible; see Annex VI to Section K of the Pharmaceuticals Directive)				
Induction				
Bortezomib	Day 1, 4, 8, 11 of a 21-day cycle	3 – 4	4	12 – 16
Cyclophosphamide	Day 1 of a 21-day cycle	3 – 4	1	3 – 4
Dexamethasone	On the days 1, 2, 4, 5, 8, 9, 11, 12 of a 21-day cycle	3 – 4	8	24 – 32
High-dose therapy with melphalan and subsequent autologous stem cell transplant				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Stem cell collection	once		4.2 – 5.0 (average length of stay)	4.2 – 5.0
High-dose chemotherapy + autologous stem cell transplant	once		19.0 (average length of stay)	19.0
daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd)				
Induction				
Daratumumab	28-day cycle: Cycle 1 – 2 1 x every 7 days Cycle 3 – 4 1 x every 14 days	4	Cycle 1 - 2: 4 Cycle 3 – 4: 2	12
Bortezomib	Day 1, 4, 8 and 11 of a 28-day cycle	4	4	16
Thalidomide	Day 1 – 28 of a 28-day cycle	4	28	112
Dexamethasone[4]	Cycle 1 – 2: Day 1, 2, 8, 9, 15, 16, 22 and 23 Cycle 3 – 4: Day 1, 2, 8, 9, 15 and 16 of a 28-day cycle	4	4	16
High-dose therapy with melphalan and subsequent autologous stem cell transplant				
Stem cell collection	once		4.2 – 5.0 (average length of stay)	4.2 – 5.0

[4] On the days of daratumumab injection, 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
High-dose chemotherapy + autologous stem cell transplant	once		19.0 (average length of stay)	19.0
Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd)				
Induction				
Daratumumab	Cycle 1 – 2 Day 1, 8, 15 and 22 Cycle 3 – 4 Day 1 and 15 of a 28-day cycle	4	Cycle 1 - 2: 4 Cycle 3 – 4: 2	12
Bortezomib	Day 1, 4, 8 and 11 of a 28-day cycle	4	4	16
Lenalidomide	Day 1 – 21 of a 28-day cycle	4	21	84
Dexamethasone[5]	On the days 1 – 4 and 9 – 12 of a 28-day cycle	4	7	28
High-dose chemotherapy and subsequent autologous stem cell transplant				
Stem cell collection	once		4.2 – 5.0 (average length of stay)	4.2 – 5.0
High-dose chemotherapy + autologous stem cell transplant	once		19.0 (average length of stay)	19.0

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

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)[6].

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.

Adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant; induction 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
Medicinal product to be assessed					
Isatuximab in combination with bortezomib, lenalidomide and dexamethasone					
Induction					
Isatuximab	10 mg/kg	777 mg	1 x 500 mg + 3 x 100 mg	11	11 x 500 mg + 33 x 100 mg
Bortezomib	1.3 mg/m² = 2.5 mg	2.5 mg	1 x 2.5 mg	24	24 x 2.5 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	84	84 x 25 mg
Dexamethasone PO	20 mg	20 mg	1 x 20 mg	40	40 x 20 mg
Dexamethasone IV	20 mg	20 mg	5 x 4 mg	11	55 x 4 mg
High-dose therapy with melphalan and subsequent autologous stem cell transplant					
	once				
Appropriate comparator therapy					
Bortezomib + thalidomide + dexamethasone (VTd)					
Induction					
Bortezomib	1.3 mg/m² = 2.5 mg	2.5 mg	1 x 2.5 mg	16 – 24	16 x 2.5 mg – 24 x 2.5 mg
Thalidomide	Cycle 1 Day 1 – 14:	Cycle 1 Day 1 – 14:	Cycle 1 Day 1 - 14	112 – 168	112 x 50 mg –

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	50 mg <u>Day 15 – 28</u> 50 mg – 100 mg <u>Cycle 2 – 6</u> 50 mg – 200 mg	50 mg <u>Day 15 – 28</u> 50 mg – 100 mg <u>Cycle 2 – 6</u> 50 mg – 200 mg	1 x 50 mg <u>Day 15 – 28</u> 1 x 50 mg – 1 x 100 mg <u>Cycle 2 – 6</u> 1 x 50 mg – 2 x 100 mg		14 x 50 mg + 294 x 100 mg
Dexamethasone PO	40 mg	40 mg	1 x 40 mg	32 – 48	32 x 40 mg – 48 x 40 mg
High-dose therapy with melphalan and subsequent autologous stem cell transplant					
	once				
Bortezomib + cyclophosphamide + dexamethasone (VCd) (only patients with peripheral polyneuropathy or an increased risk of developing peripheral polyneuropathy are eligible; 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	12 – 16	12 x 2.5 mg – 16 x 2.5 mg
Cyclophosphamide	900 mg/m^2 = 1,719 mg	1,719 mg	2 x 1,000 mg	3 – 4	6 x 1,000 mg – 8 x 1,000 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	24 – 32	24 x 40 mg – 32 x 40 mg
High-dose therapy with melphalan and subsequent autologous stem cell transplant					
	once				
daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd)					
Induction					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	12	12 x 1,800 mg
Bortezomib	1.3 mg/m^2 = 2.5 mg	2.5 mg	1 x 2.5 mg	16	16 x 2.5 mg
Thalidomide	100 mg	100 mg	1 x 100 mg	112	112 x 100 mg
Dexamethasone4	<u>Cycle 1 – 2</u> Day 1, 2, 8, 9, 15, 16, 22 and 23 <u>and cycle 3 – 4</u> Day 1 and 2: 40 mg	40 mg	1 x 40 mg	10	10 x 40 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Dexamethasone4	Cycle 3 – 4 Day 8, 9, 15 and 16: 20 mg	20 mg	1 x 20 mg	6	6 x 20 mg
High-dose therapy with melphalan and subsequent autologous stem cell transplant					
	once				
Daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd)					
Induction					
Daratumumab	1,800 mg	1,800 mg	1 x 1,800 mg	12	12 x 1,800 mg
Bortezomib	1.3 mg/m^2 = 2.5 mg	2.5 mg	1 x 2.5 mg	16	16 x 2.5 mg
Lenalidomide	25 mg	25 mg	1 x 25 mg	84	84 x 25 mg
Dexamethasone	40 mg	40 mg	1 x 40 mg	28	28 x 40 mg
High-dose therapy with melphalan and subsequent autologous stem cell transplant					
	once				

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 reference prices shown in the cost representation may not represent the cheapest available alternative.

Inpatient treatments:

Calculation year:	DRG	Average length of stay [d]	DRG valuation ratio (main department)	Federal base case value	Nursing revenue valuation ratio	Nursing fee	Case flat fee revenue	Nursing revenue	Total case flat fee revenue and nursing revenue
Medicinal product to be assessed									
High-dose chemotherapy with autologous stem cell transplant									
Stem cell collection									
2025	A42C	4.2	0.809	€ 4,394.22	0.843	€ 250	€ 3,554.92	€ 885.15	€ 4,440.07
or									
2025	R61H	5.0	0.609	€ 4,394.22	0.8204	€ 250	€ 2,676.08	€ 1,025.50	€ 3,701.58
Stem cell transplant									
2025	A15D	19	3.823	€ 4,394.22	1.0538	€ 250	€ 16,799.10	€ 5,005.55	€ 21,804.65
Appropriate comparator therapy									
High-dose chemotherapy with autologous stem cell transplant									
Stem cell collection									
2025	A42C	4.2	0.809	€ 4,394.22	0.843	€ 250	€ 3,554.92	€ 885.15	€ 4,440.07
or									
2025	R61H	5.0	0.609	€ 4,394.22	0.8204	€ 250	€ 2,676.08	€ 1,025.50	€ 3,701.58
Stem cell transplant									
2025	A15D	19	3.823	€ 4,394.22	1.0538	€ 250	€ 16,799.10	€ 5,005.55	€ 21,804.65

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					
Isatuximab 100 mg	1 CIS	€ 333.96	€ 1.77	€ 17.86	€ 314.33
Isatuximab 500 mg	1 CIS	€ 1,621.58	€ 1.77	€ 89.32	€ 1,530.49
Bortezomib 2.5 mg	1 PSI	€ 185.37	€ 1.77	€ 8.26	€ 175.34
Dexamethasone 20 mg[7]	20 TAB	€ 54.09	€ 1.77	€ 0.00	€ 52.32
Dexamethasone 4 mg[7]	10 SFI	€ 16.92	€ 1.77	€ 0.44	€ 14.71
Lenalidomide 25 mg[7]	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Lenalidomide 25 mg[7]	21 HC	€ 79.08	€ 1.77	€ 5.36	€ 71.95
Appropriate comparator therapy					
Daratumumab 1,800 mg	1 SFI	€ 5,809.87	€ 1.77	€ 0.00	€ 5,808.10
Dexamethasone 20 mg[7]	10 TAB	€ 32.42	€ 1.77	€ 0.00	€ 30.65
Dexamethasone 40 mg[7]	10 TAB	€ 46.29	€ 1.77	€ 0.00	€ 44.52

[7] 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
Dexamethasone 40 mg[7]	20 TAB	€ 81.59	€ 1.77	€ 0.00	€ 79.82
Dexamethasone 40 mg[7]	50 TAB	€ 188.03	€ 1.77	€ 0.00	€ 186.26
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
Cyclophosphamide 1,000 mg	1 PSI	€ 33.69	€ 1.77	€ 1.24	€ 30.68
Lenalidomide 25 mg[7]	63 HC	€ 117.32	€ 1.77	€ 8.38	€ 107.17
Lenalidomide 25 mg[7]	21 HC	€ 79.08	€ 1.77	€ 5.36	€ 71.95
Thalidomide 50 mg	28 HC	€ 633.82	€ 1.77	€ 78.78	€ 553.27
Thalidomide 100 mg	30 CTA	€ 706.69	€ 1.77	€ 88.00	€ 616.92
Abbreviations: HC = hard capsules; 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).

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

[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

evaluated and the appropriate comparator therapy and are consequently considered as additionally required SHI services in the resolution.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5aSGB V, when a non-prescription medicinal product 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
Appropriate comparator therapy							
Daratumumab *+ bortezomib + thalidomide + dexamethasone (D-VTd) (induction)*							
Premedication							
Dexamethasone 40 mg, PO[7]	10 TAB x 40 mg	€ 46.29	€ 1.77	€ 0.00	€ 44.52	10	€ 44.52
Dexamethasone 20 mg, PO[7]	10 TAB x 20 mg	€ 32.42	€ 1.77	€ 0.00	€ 30.65	2	€ 30.65
Paracetamol 500 - 1,000 mg, PO[7,9]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	12	€ 3.15 – € 6.02
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	€ 26.24	€ 1.77	€ 6.92	€ 17.55	12	€ 87.75
Daratumumab *in combination with bortezomib, lenalidomide and dexamethasone (D-VRd) (induction)*							
Premedication							
Dexamethasone 40 mg, PO[7]	10 TAB x 40 mg	€ 46.29	€ 1.77	€ 0.00	€ 44.52	4	€ 44.52
Dexamethasone 20 mg, PO[7]	10 TAB x 20 mg	€ 32.42	€ 1.77	€ 0.00	€ 30.65	8	€ 30.65
Paracetamol 500 - 1,000 mg, PO[7,9]	20 TAB x 500 mg 10 TAB x 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	12	€ 3.15 – € 6.02
Dimetindene 1 mg/10 kg = 7.8 mg, IV	5 SFI x 4 mg	€ 26.24	€ 1.77	€ 6.92	€ 17.55	12	€ 87.75
Daratumumab							

[9] 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
Lenalidomide Thalidomide							
HBV screening							
HBV test Hepatitis B surface antigen status (FSI 32781)	–	–	–	–	€ 5.06	1.0	€ 5.06
Anti-HBc antibody (FSI 32614)	–	–	–	–	€ 5.43	1.0	€ 5.43
Abbreviations: SFI = solution for injection; TAB = tablets							

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 eligible for autologous stem cell transplant; induction treatment

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.

References:
Product information for isatuximab (Sarclisa); SARCLISA 20 mg/ml concentrate for the preparation of an infusion solution; last revised: July 2025

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 29 October 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. The Subcommittee on Medicinal Products newly determined the appropriate comparator therapy at their session on 12 August 2025.

On 12 August 2025, the pharmaceutical company submitted a dossier for the benefit assessment of isatuximab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 13 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 isatuximab.

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.

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	29 October 2024	Determination of the appropriate comparator therapy
If applicable: Subcommittee on Medicinal Products	12 August 2025	New determination of the appropriate comparator therapy
Working group Section 35a	17 December 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	12 January 2026	Conduct of the oral hearing
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