Linvoseltamab (multiple myeloma)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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[1] Translation of Sections I 1 to I 6 of the dossier assessment *Linvoseltamab (multiples Myelom) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Siegburger Str. 237
50679 Köln
Germany

Phone:+49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

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Keywords

Linvoseltamab, Multiple Myeloma, Benefit Assessment

Medical and scientific advice

- Ingo Schmidt-Wolf, University Hospital Bonn

IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Hans Josef van Lier.

IQWiG thanks the respondent and the patient organization 'Plasmozytom / Multiples Myelom Selbsthilfegruppe NRW e. V.' for participating in the written exchange and for their support. The respondent and the patient organization 'Plasmozytom / Multiples Myelom Selbsthilfegruppe NRW e. V.' were not involved in the actual preparation of the dossier assessment.

IQWiG employees involved in the dossier assessment

- Michael Hort
- Annalena Dunkel
- Reza Fathollah-Nejad
- Katharina Frangen
- Philip Kranz
- Prateek Mishra
- Regine Potthast
- Anke Schulz
- Carolin Weigel

Part I: Benefit assessment

I Table of contents

Page

I List of tables[2]

Page

[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
CD	cluster of differentiation
ECOG PS	Eastern Cooperative Oncology Group Performance Status
EMA	European Medicines Agency
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IMWG	International Myeloma Working Group
IPTW	inverse probability of treatment weighting
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MAIC	matching-adjusted indirect comparison
POEMS	polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
SmPC	summary of product characteristics

I 1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug linvoseltamab. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the 'company'). The dossier was sent to IQWiG on 1 October 2025.

Research question

The aim of this report is to assess the added benefit of linvoseltamab as monotherapy compared with individualized treatment as the appropriate comparator therapy (ACT) in adult patients with relapsed and refractory multiple myeloma who have received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-cluster of differentiation (CD)38 monoclonal antibody, and have demonstrated disease progression on the last therapy.

The research questions presented in Table 2 were defined in accordance with the ACT specified by the Federal Joint Committee (G-BA).

Table 2: Research questions for the benefit assessment of linvoseltamab (multipage table)

Research question	Therapeutic indication	ACT[a]
1	Adults with relapsed or refractory multiple myeloma who have received 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, e] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ carfilzomib in combination with dexamethasone

Table 2: Research questions for the benefit assessment of linvoseltamab (multipage table)

Research question	Therapeutic indication	ACT[a]
2	Adults with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, h, i] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ panobinostat in combination with bortezomib and dexamethasone ▪ carfilzomib in combination with dexamethasone ▪ pomalidomide in combination with dexamethasone[j] ▪ lenalidomide in combination with dexamethasone[j] ▪ bortezomib in combination with pegylated liposomal doxorubicin[j] ▪ bortezomib in combination with dexamethasone[j] ▪ daratumumab monotherapy[k] ▪ cyclophosphamide as monotherapy or in combination with dexamethasone[k] ▪ melphalan as monotherapy or in combination with prednisolone or prednisone[k]

a. Presented is the respective ACT specified by the G-BA.
b. The term 'individualized treatment' is used instead of previously used terms such as 'patient-specific therapy' or 'treatment of physician's choice'. This ensures consistency with the terms used in European health technology assessments (EU HTAs).
c. According to the G-BA, for the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study). The decision on individualized treatment with regard to the comparator therapy was to be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment.
d. One criterion for individualized treatment is the duration of response to previous treatment. In this regard, in accordance with generally accepted medical knowledge, the unsuitability of retreatment with the drugs or combinations of drugs used in the prior therapy is defined as disease progression during that therapy, or a duration of response of less than 12 months following the completion of that therapy. Accordingly, for patients with relapsed disease who show a response in the form of CR, VGPR and PR of more than 12 months after completion of the prior therapy, treatment using the drugs or drug combinations used in the prior therapy may also be a suitable treatment option.
e. According to the G-BA, the decision on treatment should be made taking particular account of the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments.
f. Only for patients whose tumour is refractory to a CD38 antibody and lenalidomide.
g. Only for patients whose tumour is refractory to bortezomib, carfilzomib and a CD38 antibody.

Table 2: Research questions for the benefit assessment of linvoseltamab (multipage table)

Research question	Therapeutic indication	ACT[a]
h. According to the G-BA, the decision on treatment should be made taking particular account of the patient's general condition, the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments. According to the G-BA, the unsuitability of triplet or doublet therapy should be justified on the basis of the patients' refractoriness and comorbidity, and also taking into account the toxicity of the respective therapy. i. It is assumed that patients in the given therapeutic indication generally continue antineoplastic treatment. Best supportive care is therefore not considered an ACT. j. Only for patients whose tumour is at least double-refractory and for whom triplet therapy is not suitable. k. Only for patients whose tumour is at least triple-refractory and for whom triplet or doublet therapy are not suitable. ACT: appropriate comparator therapy; CD: cluster of differentiation; CR: complete remission; EU: European Union; GB-A: Federal Joint Committee; HTA: health technology assessment; PR: partial response; VGPR: very good partial response		

The G-BA adjusted the ACT on 27 May 2025. The company deviated from the current ACT specified by the G-BA. Whilst the company also regarded individualized treatment as an ACT, taking into account prior treatments as well as the nature and duration of the response to those treatments, it listed further treatment options at the same time. The company considered the following additional treatment options to be ACTs for both research questions:

- elranatamab
- teclistamab
- talquetamab
- idecabtagene vicleucel
- ciltacabtagene autoleucel

The fact that the company deviated from the G-BA's ACT had no bearing on this benefit assessment, as the company did not provide suitable data versus the G-BA's recommended treatment options or versus the treatment options specified by the company.

The assessment of the added benefit was conducted in comparison with the G-BA's current ACT as shown in Table 2. The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Results

A review of the completeness of the study pool for both research questions failed to identify any randomized controlled trials (RCTs) that would allow a direct comparison or an adjusted indirect comparison via a common comparator of linvoseltamab versus the ACT specified by the G-BA.

It should be noted that in Module 4 A, the company excluded the RCT LINKER-MM3 from its study pool, on the grounds that it is an ongoing study currently recruiting participants for which no results are yet available. LINKER-MM3 is an open-label RCT that is potentially relevant to both research questions; it compares linvoseltamab versus elotuzumab in combination with pomalidomide and dexamethasone in adults with relapsed or refractory multiple myeloma who have previously received 1 to 4 prior treatments, including a proteasome inhibitor and lenalidomide (with or without prior treatment with an anti-CD38 antibody), and who have shown disease progression during their last treatment. The study may therefore include subpopulations that are potentially relevant to the research questions addressed in this benefit assessment. However, results were not available at the time of the benefit assessment.

As the company did not identify any studies for a direct comparison, it conducted an information retrieval for further investigations on linvoseltamab. In doing so, it identified the pivotal, non-comparative study LINKER-MM1 regarding treatment with linvoseltamab and used this to perform the derivation of the added benefit.

The company did not conduct an information retrieval for further investigations with the ACT. Notwithstanding the lack of information retrieval for the ACT, the company nevertheless presented the cohort study R5458-ONC-21101 as a non-randomized comparison versus LINKER-MM1. The company also presented this comparison in the description of the results from further investigations.

In addition, in the summary description of the added benefit , the company also presented the results of non-randomized comparisons of linvoseltamab with the bispecific antibodies teclistamab, talquetamab and elranatamab using matching-adjusted indirect comparison (MAIC) analysis. No systematic information retrieval was carried out regarding the comparators selected by the company for these analyses either. For these comparisons, the company drew on individual patient data from LINKER-MM1 for linvoseltamab and aggregate data from the MajesTEC-1 (teclistamab), MonumenTAL-1 (talquetamab) and MagnetisMM-3 (elranatamab) studies for the comparator side. Notwithstanding the fact that the data presented by the company for comparing individual arms from different studies were not adequately analysed, these analyses were not suitable for the assessment of the added benefit of linvoseltamab. Firstly, the drugs used for comparison with linvoseltamab – teclistamab, talquetamab and elranatamab – were not included in the comparator therapy specified by the G-BA. Secondly, MAIC analyses without a common comparator are generally not an adequate option for confounder adjustment. This benefit assessment therefore does not include a further examination or description of the MAIC analyses.

No review was carried out to verify the completeness of the study pool submitted by the company for further investigations, as the data submitted by the company for further investigations were in general unsuitable for the benefit assessment. This is explained below.

Evidence provided by the company

LINKER-MM1

LINKER-MM1 is an ongoing non-comparative, open-label, multicentre phase 1/2 study investigating treatment with linvoseltamab. The study enrolled adult patients with relapsed or refractory multiple myeloma who had received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory drug and an anti-CD38 antibody, and who had demonstrated disease progression on the last therapy.

Phase 1 of LINKER-MM1 was primarily designed to determine the appropriate dose and investigated various, gradually increasing doses of linvoseltamab across several cohorts.

In Phase 2 of the study, the intravenous administration of linvoseltamab following a dose escalation phase (5 to 25 mg) was investigated in 3 cohorts at doses of 50 mg (Cohort 1) and 200 mg (Cohorts 2 and 3).

The primary outcome in Phase 2 of LINKER-MM1 is tumour response. Secondary outcomes are being recorded in the categories of mortality, morbidity, health-related quality of life and side effects.

In Module 4 A, the company presented data on 3 data cuts from LINKER-MM1:

- First data cut-off date of 8 September 2023: prespecified primary analysis
- Second data cut-off date of 6 January 2024: requested by the European Medicines Agency (EMA)
- Third data cut-off date of 23 July 2024: non-prespecified current data cut

According to the information it provided, the company used the most recent available analysis for each outcome when deriving the added benefit.

Non-randomized comparison of LINKER-MM1 with R5458-ONC-21101

To put the results of the non-comparative pivotal study LINKER-MM1 into context, in Module 4 A the company presented a supplementary non-randomized comparison of linvoseltamab from LINKER-MM1 versus standard therapies from the non-interventional, retrospective cohort study R5458-ONC-21101.

R5458-ONC-21101 is primarily based on data from a multinational database maintained by the study centres of the International Myeloma Working Group (IMWG) and was specifically

designed to serve as an external control for the LINKER-MM1 study. R5458-ONC-21101 included adult patients with relapsed or refractory multiple myeloma who had previously received at least 3 prior lines of therapy with 3 different classes of drugs (including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody). Only patients treated between 16 November 2015 and 31 December 2021 were included. Otherwise, similar reasons for inclusion and exclusion to those in LINKER-MM1 had to be met.

The primary outcomes of R5458-ONC-21101 were the description of the distribution of treatment regimens and the objective response rate. Secondary outcomes were recorded in the categories of mortality and morbidity.

To ensure structural equality between the 2 analysis populations from LINKER-MM1 and R5458-ONC-21101, the company adjusted for potential confounders using the propensity score method. In doing so, the company used stabilized weighting based on inverse probability of treatment weighting (IPTW).

The company presented only results for the outcomes of overall survival, tumour response and progression-free survival when comparing the study populations from LINKER-MM1 and R5458-ONC-21101. Of these, only the outcome of overall survival is relevant to patients. The results for these outcomes were based on the non-prespecified 3rd data cut from 23 July 2024 for LINKER-MM1 and on the database lock of 12 September 2024 for R5458-ONC-21101.

Assessment of the evidence presented by the company

The evidence presented by the company was not suitable for the derivation of an added benefit of linvoseltamab in comparison with the ACT specified by the G-BA.

For LINKER-MM1, this was due to the fact that this is a non-comparative study with linvoseltamab and therefore no comparison versus the ACT is possible.

For the non-randomized comparison of linvoseltamab from LINKER-MM1 versus standard therapies from the non-interventional, retrospective cohort study R5458-ONC-21101, there were substantial shortcomings in the company's approach:

- As the company did not conduct an information retrieval for the ACT, the study pool on the comparator side was potentially incomplete.
- The majority of patients in R5458-ONC-21101 received treatment that did not correspond to the ACT as defined by the G-BA: 77% of patients did not receive a treatment option from the ACT for research question 1, and 70% of patients did not receive a treatment option from the ACT for research question 2.
- In Module 4 A, the company only presented results for the patient-relevant outcome of overall survival, but no results for patient-relevant outcomes in the categories of

morbidity, health-related quality of life and side effects. It is therefore not possible to weigh up the positive and negative effects across all outcome categories for the comparison presented.

Notwithstanding the deficiencies described, the non-randomized comparison of the outcome overall survival presented by the company showed no effect that could not be explained solely by systemic bias arising from potentially unknown confounding variables. Furthermore, regarding this non-randomized comparison, the company only presented results for a non-prespecified data cut from LINKER-MM1.

As the previously mentioned factors have already demonstrated that the comparison submitted by the company was not suitable, a detailed description and assessment of the identification of confounders and the methodology of the comparison are not included in the benefit assessment.

Overall, the data presented by the company were not suitable for the benefit assessment and did not allow an adequate comparison of linvoseltamab with the ACT.

Results on added benefit

Since no suitable data were available for the research questions of the benefit assessment, there is no hint of an added benefit of linvoseltamab in comparison with the ACT in either case; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 shows a summary of the probability and extent of the added benefit of linvoseltamab.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) “proof”, (2) “indication”, (3) “hint”, or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Linvoseltamab – probability and extent of added benefit (multipage table)

Research question	**Therapeutic indication**	**ACT**[a]	**Probability and extent of added benefit**
1	Adults with relapsed or refractory multiple myeloma who have received 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, e] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ carfilzomib in combination with dexamethasone	Added benefit not proven

Table 3: Linvoseltamab – probability and extent of added benefit (multipage table)

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
2	Adults with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, h, i] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ panobinostat in combination with bortezomib and dexamethasone ▪ carfilzomib in combination with dexamethasone ▪ pomalidomide in combination with dexamethasone[j] ▪ lenalidomide in combination with dexamethasone[j] ▪ bortezomib in combination with pegylated liposomal doxorubicin[j] ▪ bortezomib in combination with dexamethasone[j] ▪ daratumumab monotherapy[k] ▪ cyclophosphamide as monotherapy or in combination with dexamethasone[k] ▪ melphalan as monotherapy or in combination with prednisolone or prednisone[k]	Added benefit not proven

Table 3: Linvoseltamab – probability and extent of added benefit (multipage table)

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
a. Presented is the respective ACT specified by the G-BA. b. The term 'individualized treatment' is used instead of previously used terms such as 'patient-specific therapy' or 'treatment of physician's choice'. This ensures consistency with the terms used in European health technology assessments (EU HTAs). c. According to the G-BA, for the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study). The decision on individualized treatment with regard to the comparator therapy was to be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment. d. One criterion for individualized treatment is the duration of response to previous treatment. In this regard, in accordance with generally accepted medical knowledge, the unsuitability of retreatment with the drugs or combinations of drugs used in the prior therapy is defined as disease progression during that therapy, or a duration of response of less than 12 months following the completion of that therapy. Accordingly, for patients with relapsed disease who show a response in the form of CR, VGPR and PR of more than 12 months after completion of the prior therapy, treatment using the drugs or drug combinations used in the prior therapy may also be a suitable treatment option. e. According to the G-BA, the decision on treatment should be made taking particular account of the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments. f. Only for patients whose tumour is refractory to a CD38 antibody and lenalidomide. g. Only for patients whose tumour is refractory to bortezomib, carfilzomib and a CD38 antibody. h. According to the G-BA, the decision on treatment should be made taking particular account of the patient's general condition, the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments. According to the G-BA, the unsuitability of triplet or doublet therapy should be justified on the basis of the patients' refractoriness and comorbidity, and also taking into account the toxicity of the respective therapy. i. It is assumed that patients in the given therapeutic indication generally continue antineoplastic treatment. Best supportive care is therefore not considered an ACT. j. Only for patients whose tumour is at least double-refractory and for whom triplet therapy is not suitable. k. Only for patients whose tumour is at least triple-refractory and for whom triplet or doublet therapy are not suitable. ACT: appropriate comparator therapy; CD: cluster of differentiation; CR: complete remission; EU: European Union; GB-A: Federal Joint Committee; HTA: health technology assessment; PR: partial response; VGPR: very good partial response			

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report is to assess the added benefit of linvoseltamab as monotherapy compared with individualized treatment as the appropriate comparator therapy (ACT) in adult patients with relapsed and refractory multiple myeloma who have received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-cluster of differentiation (CD)38 monoclonal antibody, and have demonstrated disease progression on the last therapy.

The research questions presented in Table 4 were defined in accordance with the ACT specified by the Federal Joint Committee (G-BA).

Table 4: Research questions for the benefit assessment of linvoseltamab (multipage table)

Research question	Therapeutic indication	ACT[a]
1	Adults with relapsed or refractory multiple myeloma who have received 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, e] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ carfilzomib in combination with dexamethasone

Table 4: Research questions for the benefit assessment of linvoseltamab (multipage table)

Research question	Therapeutic indication	ACT[a]
2	Adults with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, h, i] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ panobinostat in combination with bortezomib and dexamethasone ▪ carfilzomib in combination with dexamethasone ▪ pomalidomide in combination with dexamethasone[j] ▪ lenalidomide in combination with dexamethasone[j] ▪ bortezomib in combination with pegylated liposomal doxorubicin[j] ▪ bortezomib in combination with dexamethasone[j] ▪ daratumumab monotherapy[k] ▪ cyclophosphamide as monotherapy or in combination with dexamethasone[k] ▪ melphalan as monotherapy or in combination with prednisolone or prednisone[k]

a. Presented is the respective ACT specified by the G-BA.
b. The term 'individualized treatment' is used instead of previously used terms such as 'patient-specific therapy' or 'treatment of physician's choice'. This ensures consistency with the terms used in European health technology assessments (EU HTAs).
c. According to the G-BA, for the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study). The decision on individualized treatment with regard to the comparator therapy was to be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment.
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e. According to the G-BA, the decision on treatment should be made taking particular account of the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments.
f. Only for patients whose tumour is refractory to a CD38 antibody and lenalidomide.
g. Only for patients whose tumour is refractory to bortezomib, carfilzomib and a CD38 antibody.

Table 4: Research questions for the benefit assessment of linvoseltamab (multipage table)

Research question	Therapeutic indication	ACT[a]
h. According to the G-BA, the decision on treatment should be made taking particular account of the patient's general condition, the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments. According to the G-BA, the unsuitability of triplet or doublet therapy should be justified on the basis of the patients' refractoriness and comorbidity, and also taking into account the toxicity of the respective therapy. i. It is assumed that patients in the given therapeutic indication generally continue antineoplastic treatment. Best supportive care is therefore not considered an ACT. j. Only for patients whose tumour is at least double-refractory and for whom triplet therapy is not suitable. k. Only for patients whose tumour is at least triple-refractory and for whom triplet or doublet therapy are not suitable. ACT: appropriate comparator therapy; CD: cluster of differentiation; CR: complete remission; EU: European Union; GB-A: Federal Joint Committee; HTA: health technology assessment; PR: partial response; VGPR: very good partial response		

The G-BA adjusted the ACT on 27 May 2025. The company deviated from the current ACT specified by the G-BA. Whilst the company also regarded individualized treatment as an ACT, taking into account prior treatments as well as the nature and duration of the response to those treatments, it listed further treatment options at the same time. The company considered the following additional treatment options to be ACTs for both research questions:

- elranatamab
- teclistamab
- talquetamab
- idecabtagene vicleucel
- ciltacabtagene autoleucel

The fact that the company deviated from the G-BA's ACT had no bearing on this benefit assessment, as the company did not provide suitable data versus the G-BA's recommended treatment options or versus the treatment options specified by the company.

The assessment of the added benefit was conducted in comparison with the G-BA's current ACT as shown in Table 4. The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Since no suitable data were available for either of the research questions specified by the G-BA, the assessment below is provided in a joint section of the report.

I 3 Information retrieval and study pool

The study pool for the assessment was compiled on the basis of the following information:

Sources used by the company in the dossier:

- Study list on linvoseltamab (status: 24 July 2025)
- Bibliographical literature search on linvoseltamab (last search on 24 July 2025)
- Search of trial registries / trial results databases for studies on linvoseltamab (last search on 28 July 2025)
- Search on the G-BA website for linvoseltamab (last search on 24 July 2025)

To check the completeness of the study pool:

- Search of trial registries for studies on linvoseltamab (last search on 7 October 2025); for search strategies, see I Appendix A of the full dossier assessment

Direct comparison

As per the company's findings, a review of the completeness of the study pool for both research questions failed to identify any randomized controlled trials (RCTs) that would allow a direct comparison or an adjusted indirect comparison via a common comparator of linvoseltamab versus the ACT specified by the G-BA.

It should be noted that in Module 4 A, the company excluded the RCT LINKER-MM3 [3] from its study pool, on the grounds that it is an ongoing study currently recruiting participants for which no results are yet available. LINKER-MM3 is an open-label RCT that is potentially relevant to both research questions; it compares linvoseltamab versus elotuzumab in combination with pomalidomide and dexamethasone in adults with relapsed or refractory multiple myeloma who have previously received 1 to 4 prior treatments, including a proteasome inhibitor and lenalidomide (with or without prior treatment with an anti-CD38 antibody), and who have shown disease progression during their last treatment. The study may therefore include subpopulations that are potentially relevant to the research questions addressed in this benefit assessment. However, results were not available at the time of the benefit assessment. In accordance with the study design, an interim analysis of the overall survival outcome is planned for LINKER-MM3 following 81 events in the subpopulation that received prior treatment with an anti-CD38 monoclonal antibody; this is expected to occur approximately 28 months after randomization of the first patient. According to the study registry entry, the study was started on 18 September 2023 [3].

Further investigations

As the company did not identify any studies for a direct comparison, it conducted an information retrieval for further investigations on linvoseltamab. In doing so, it identified the pivotal, non-comparative study LINKER-MM1 [4,5] regarding treatment with linvoseltamab and used this to perform the derivation of the added benefit.

The company did not conduct an information retrieval for further investigations with the ACT. Notwithstanding the lack of information retrieval for the ACT, the company nevertheless presented the cohort study R5458-ONC-21101 [6] as a non-randomized comparison versus LINKER-MM1. The company also presented this comparison in the description of the results from further investigations (Section 4.3.2 in Module 4 A). The company indicated that the underlying methodology had limitations and that this comparison could not therefore be used as a basis for the derivation of the added benefit of linvoseltamab. For this reason, the company did not include a detailed account in the dossier. Nevertheless, the company included the results of these investigations as supporting information in its derivation of the added benefit.

In addition, in the summary description of the added benefit (Section 4.4.2 in Module 4 A), the company also presented the results of non-randomized comparisons of linvoseltamab with the bispecific antibodies teclistamab, talquetamab and elranatamab using matching-adjusted indirect comparison (MAIC) analysis. No systematic information retrieval was carried out regarding the comparators selected by the company for these analyses either. For these comparisons, the company drew on individual patient data from LINKER-MM1 for linvoseltamab and aggregate data from the MajesTEC-1 (teclistamab), MonumenTAL-1 (talquetamab) and MagnetisMM-3 (elranatamab) studies [7-9] for the comparator side. Notwithstanding the fact that the data presented by the company for comparing individual arms from different studies were not adequately analysed, these analyses were not suitable for the assessment of the added benefit of linvoseltamab. Firstly, the drugs used for comparison with linvoseltamab – teclistamab, talquetamab and elranatamab – were not included in the comparator therapy specified by the G-BA. And secondly, MAIC analyses without a common comparator are generally not an appropriate option for confounder adjustment [1]. This benefit assessment therefore does not include a further examination or description of the MAIC analyses.

No review was carried out to verify the completeness of the study pool submitted by the company for further investigations, as the data submitted by the company for further investigations were in general unsuitable for the benefit assessment. This is explained below.

I 3.1 Evidence provided by the company

LINKER-MM1

LINKER-MM1 is an ongoing non-comparative, open-label, multicentre phase 1/2 study investigating treatment with linvoseltamab. The study enrolled adult patients with relapsed or refractory multiple myeloma who had received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory drug and an anti-CD38 antibody, and who had demonstrated disease progression on the last therapy. For Phase 1 of the study, patients who had received fewer than 3 prior lines of therapy were also eligible if they had shown disease progression following treatment with an anti-CD38 antibody and the disease was double-refractory to both an immunomodulatory drug and a proteasome inhibitor. In Phase 2 of the study, patients could also be enrolled if they were triple refractory, regardless of the number of previous treatments. Patients with plasma cell leukaemia, primary systemic light-chain amyloidosis (excluding myeloma-associated amyloidosis), Waldenström's macroglobulinaemia, or polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes (POEMS syndrome) were excluded from participating in the study. To be enrolled in the study, patients had to have an Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≤ 1.

Phase 1 of LINKER-MM1 was primarily designed to determine the appropriate dose and investigated various, gradually increasing doses of linvoseltamab across several cohorts. In only one of these cohorts (Cohort DL 7, comprising 12 patients) were patients administered the on-label target dose of 200 mg; however, this was also not in compliance with the regimen defined in the summary of product characteristics (SmPC) [10].

In Phase 2 of the study, the intravenous administration of linvoseltamab following a dose escalation phase (5 to 25 mg) was investigated in 3 cohorts at doses of 50 mg (Cohort 1) and 200 mg (Cohorts 2 and 3). Patients in Cohort 3 of Phase 2 were treated with a single dose of an anti-IL-6R therapy prior to receiving their first intravenous dose of linvoseltamab. The results for Cohort 3 were not yet available when the company dossier was submitted. Only the treatment administered to 105 patients in Cohort 2 (Phase 2) complied with the specifications set out in the SmPC [10] in terms of dosage and prior treatment.

The primary outcome in Phase 2 of LINKER-MM1 is tumour response. Secondary outcomes are being recorded in the categories of mortality, morbidity, health-related quality of life and side effects.

Data cuts from LINKER-MM1 presented by the company

In Module 4 A, the company presented data on 3 data cuts from LINKER-MM1.

- First data cut-off date of 8 September 2023: prespecified primary analysis

- Second data cut-off date of 6 January 2024: requested by the European Medicines Agency (EMA)
- Third data cut-off date of 23 July 2024: non-prespecified current data cut

In Module 4 A and Appendix 4 G, the company presented results for all 3 data cuts for the majority of the outcomes it examined. An exception to this were the patient-reported outcomes in the categories of morbidity and health-related quality of life, for which the company only provided results for the first data cut in each case. According to the information it provided, the company used the most recent available analysis for each outcome when deriving the added benefit.

It should be noted that the 3rd data cut-off was neither prespecified in the study protocol nor required by a regulatory authority as part of the marketing authorization process.

Non-randomized comparison of LINKER-MM1 with R5458-ONC-21101

To put the results of the non-comparative pivotal study LINKER-MM1 into context, in Module 4 A the company presented a supplementary non-randomized comparison of linvoseltamab from LINKER-MM1 versus standard therapies from the non-interventional, retrospective cohort study R5458-ONC-21101.

R5458-ONC-21101 is primarily based on data from a multinational database maintained by the study centres of the International Myeloma Working Group (IMWG) and was specifically designed to serve as an external control for the LINKER-MM1 study. R5458-ONC-21101 included adult patients with relapsed or refractory multiple myeloma who had previously received at least 3 prior lines of therapy with 3 different classes of drugs (including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody). Only patients treated between 16 November 2015 and 31 December 2021 were included. Otherwise, similar reasons for inclusion and exclusion to those in LINKER-MM1 had to be met.

The primary outcomes of R5458-ONC-21101 were the description of the distribution of treatment regimens and the objective response rate. Secondary outcomes were recorded in the categories of mortality and morbidity.

To ensure structural equality between the 2 analysis populations from LINKER-MM1 and R5458-ONC-21101, the company adjusted for potential confounders using the propensity score method. In doing so, the company used stabilized weighting based on inverse probability of treatment weighting (IPTW).

The company presented only results for the outcomes of overall survival, tumour response and progression-free survival when comparing the study populations from LINKER-MM1 and R5458-ONC-21101. Of these, only the outcome of overall survival is relevant to patients. The

results for these outcomes were based on the non-prespecified 3rd data cut from 23 July 2024 for LINKER-MM1 and on the database lock of 12 September 2024 for R5458-ONC-21101.

I 3.2 Assessment of the evidence presented by the company

LINKER-MM1

The company drew on the results from patients treated on-label (Cohort 2 of Phase 2) in the non-comparative LINKER-MM1 study. In addition, results were available from a combined analysis of this cohort and the results of the DL 7 cohort from Phase 1 of the study (for further details, see Section I 3.1). The data on treatment with linvoseltamab from LINKER-MM1 allowed no comparison with the ACT and was therefore not suitable for the derivation of the added benefit.

Non-randomized comparison of LINKER-MM1 with R5458-ONC-21101

The non-randomized comparison of LINKER-MM1 and R5458-ONC-21101, submitted by the company as supplementary evidence, was not suitable for the derivation of the added benefit of linvoseltamab. In Module 4 A, the company itself noted that the underlying methodology had limitations and could not be used as a basis for the derivation of an added benefit.

Irrespective of this, the company's approach showed the following substantial shortcomings:

- As the company did not conduct an information retrieval for the ACT, the study pool on the comparator side was potentially incomplete.
- The majority of patients in R5458-ONC-21101 received treatment that did not correspond to the ACT as defined by the G-BA: 77% of patients did not receive a treatment option from the ACT for research question 1, and 70% of patients did not receive a treatment option from the ACT for research question 2.
- In Module 4 A, the company only presented results for the patient-relevant outcome of overall survival, but no results for patient-relevant outcomes in the categories of morbidity, health-related quality of life and side effects. It is therefore not possible to weigh up the positive and negative effects across all outcome categories for the comparison presented.

Notwithstanding the deficiencies described, the non-randomized comparison of the outcome overall survival presented by the company showed no effect that could not be explained solely by systemic bias arising from potentially unknown confounding variables. Furthermore, regarding this non-randomized comparison, the company only presented results for a non-prespecified data cut from LINKER-MM1.

As the previously mentioned factors have already demonstrated that the comparison submitted by the company was not suitable, a detailed description and assessment of the

identification of confounders and the methodology of the comparison are not included in the benefit assessment. Overall, the data presented by the company were not suitable for the benefit assessment and did not allow an adequate comparison of linvoseltamab with the ACT.

I 4 Results on added benefit

No suitable data were available for the assessment of the added benefit of linvoseltamab as monotherapy compared with individualized treatment as the ACT in adult patients with relapsed and refractory multiple myeloma who have received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy. This applied to both research questions. In each case, there is no hint of an added benefit of linvoseltamab in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of linvoseltamab in comparison with the ACT is summarized in Table 5.

Table 5: Linvoseltamab – probability and extent of added benefit (multipage table)

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Adults with relapsed or refractory multiple myeloma who have received 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, e] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ carfilzomib in combination with dexamethasone	Added benefit not proven

Table 5: Linvoseltamab – probability and extent of added benefit (multipage table)

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
2	Adults with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and have demonstrated disease progression on the last therapy	An individualized treatment[b, c, d, h, i] with a choice of: ▪ carfilzomib in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with lenalidomide and dexamethasone ▪ elotuzumab in combination with pomalidomide and dexamethasone ▪ daratumumab in combination with bortezomib and dexamethasone ▪ daratumumab in combination with lenalidomide and dexamethasone ▪ daratumumab in combination with carfilzomib and dexamethasone ▪ daratumumab in combination with pomalidomide and dexamethasone ▪ isatuximab in combination with carfilzomib and dexamethasone ▪ isatuximab in combination with pomalidomide and dexamethasone ▪ pomalidomide in combination with bortezomib and dexamethasone[f] ▪ ixazomib in combination with lenalidomide and dexamethasone[g] ▪ panobinostat in combination with bortezomib and dexamethasone ▪ carfilzomib in combination with dexamethasone ▪ pomalidomide in combination with dexamethasone[j] ▪ lenalidomide in combination with dexamethasone[j] ▪ Bortezomib in combination with pegylated liposomal doxorubicin[j] ▪ bortezomib in combination with dexamethasone[j] ▪ daratumumab monotherapy[k] ▪ cyclophosphamide as monotherapy or in combination with dexamethasone[k] ▪ melphalan as monotherapy or in combination with prednisolone or prednisone[k]	Added benefit not proven

Table 5: Linvoseltamab – probability and extent of added benefit (multipage table)

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
a. Presented is the respective ACT specified by the G-BA. b. The term 'individualized treatment' is used instead of previously used terms such as 'patient-specific therapy' or 'treatment of physician's choice'. This ensures consistency with the terms used in European health technology assessments (EU HTAs). c. According to the G-BA, for the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study). The decision on individualized treatment with regard to the comparator therapy was to be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment. d. One criterion for individualized treatment is the duration of response to previous treatment. In this regard, in accordance with generally accepted medical knowledge, the unsuitability of retreatment with the drugs or combinations of drugs used in the prior therapy is defined as disease progression during that therapy, or a duration of response of less than 12 months following the completion of that therapy. Accordingly, for patients with relapsed disease who show a response in the form of CR, VGPR and PR of more than 12 months after completion of the prior therapy, treatment using the drugs or drug combinations used in the prior therapy may also be a suitable treatment option. e. According to the G-BA, the decision on treatment should be made taking particular account of the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments. f. Only for patients whose tumour is refractory to a CD38 antibody and lenalidomide. g. Only for patients whose tumour is refractory to bortezomib, carfilzomib and a CD38 antibody. h. According to the G-BA, the decision on treatment should be made taking particular account of the patient's general condition, the drugs and combinations of drugs used in prior treatments, as well as the nature and duration of the response to those prior treatments. According to the G-BA, the unsuitability of triplet or doublet therapy should be justified on the basis of the patients' refractoriness and comorbidity, and also taking into account the toxicity of the respective therapy. i. It is assumed that patients in the given therapeutic indication generally continue antineoplastic treatment. Best supportive care is therefore not considered an ACT. j. Only for patients whose tumour is at least double-refractory and for whom triplet therapy is not suitable. k. Only for patients whose tumour is at least triple-refractory and for whom triplet or doublet therapy are not suitable. ACT: appropriate comparator therapy; CD: cluster of differentiation; CR: complete remission; EU: European Union; G-BA: Federal Joint Committee; HTA: health technology assessment; PR: partial response; VGPR: very good partial response			

The assessment described above deviates from that of the company, which derived a hint of a non-quantifiable added benefit.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 02.09.2025]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

2. Skipka G, Wieseler B, Kaiser T et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2016; 58(1): 43-58. https://doi.org/10.1002/bimj.201300274.

3. Regeneron Pharmaceuticals. A Trial to Learn How Well Linvoseltamab Works Compared to the Combination of Elotuzumab, Pomalidomide and Dexamethasone for Adult Participants With Relapsed/Refractory Multiple Myeloma (LINKER-MM3) [online]. 2025 [Accessed: 27.10.2025]. URL: https://clinicaltrials.gov/study/NCT05730036.

4. Regeneron Pharmaceuticals. Phase 1/2 Study of Linvoseltamab in Adult Patients With Relapsed or Refractory Multiple Myeloma (LINKER-MM1) [online]. 2025 [Accessed: 19.11.2025]. URL: https://clinicaltrials.gov/study/NCT03761108.

5. Bumma N, Richter J, Jagannath S et al. Linvoseltamab for Treatment of Relapsed/Refractory Multiple Myeloma. J Clin Oncol 2024; 42(22): 2702–2712. https://doi.org/10.1200/JCO.24.01008.

6. Regeneron Pharmaceuticals. A Study to Characterize Treatment Patterns and Real-World Outcomes in Heavily Pretreated Patients With Relapsed and Refractory Multiple Myeloma (RRMM) and Similar Clinical Characteristics to Patients in the Phase 2 Cohort 2 of the R5458-ONC-1826 Trial [online]. 2025 [Accessed: 19.11.2025]. URL: https://clinicaltrials.gov/study/NCT05673967.

7. Lee HC, Bumma N, Richter J et al. Indirect Comparison of Linvoseltamab Versus Teclistamab for the Treatment of Triple-Class Exposed Relapsed/Refractory Multiple Myeloma. Clin Lymphoma Myeloma Leuk 2025. https://doi.org/10.1016/j.clml.2025.06.014.

8. Richter J, Jagannath S, Lee HC et al. P-415 Indirect comparison of linvoseltamab versus talquetamab for triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM). 21st International Myeloma Society (IMS) Annual Meeting, September 25–28, 2024, Rio de Janeiro, Brazil.

9. Jagannath S, Lee HC, Richter JR et al. Indirect comparison of linvoseltamab versus teclistamab for triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM). J Clin Oncol 2024; 42. https://doi.org/10.1200/JCO.2024.42.16_suppl.7560.

10. Regeneron. Lynozyfic 5 mg, 200 mg Konzentrat zur Herstellung einer Infusionslösung [online]. 07.2025 [Accessed: 06.10.2025]. URL: https://www.fachinfo.de/.

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