IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A16-32

# Elotuzumab (multiple myeloma) –

## Benefit assessment according to §35a Social Code Book V[1]

## Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Elotuzumab (multiples Myelom) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 29 August 2016). 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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[3] Table numbers start with "2" as numbering follows that of the full dossier assessment.

**List of abbreviations**

| Abbreviation | Meaning |
|---|---|
| ACT | appropriate comparator therapy |
| CHMP | Committee for Medicinal Products for Human Use |
| IQWiG | Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care) |
| RCT | randomized controlled trial |
| SGB | Sozialgesetzbuch (Social Code Book) |
| SPC | Summary of Product Characteristics |

# 2 Benefit assessment

## 2.1 Executive summary of the benefit assessment

### Background

In accordance with §35a Social Code Book (SGB) 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 elotuzumab. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as "the company"). The dossier was sent to IQWiG on 1 June 2016.

### Research question

The aim of the present report was to assess the added benefit of elotuzumab in combination with lenalidomide and dexamethasone in comparison with the appropriate comparator therapy (ACT) for the treatment of multiple myeloma in adult patients who have received one or more prior therapies.

Table 2 shows the research question of the benefit assessment and the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of elotuzumab

| Research question | Therapeutic indication | Appropriate comparator therapy[a, b] |
|---|---|---|
| 1 | In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adults who have received one or more prior therapies | Bortezomib as monotherapy, or<br>bortezomib in combination with pegylated liposomal doxorubicin, or<br>bortezomib in combination with dexamethasone, or<br>**lenalidomide in combination with dexamethasone** |

a: Presentation of the appropriate comparator therapy specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.
b: It is assumed for the present therapeutic indication that the use of elotuzumab in combination with other drugs is conducted in the framework of a remission-inducing induction treatment. High-dose chemotherapy with stem cell transplantation, which may be a subsequent treatment option, is therefore not an option as part of the ACT.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

In accordance with the G-BA's specification, the company chose lenalidomide in combination with dexamethasone from the ACT options presented in Table 2.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier. Randomized controlled trials (RCTs) were to be used for the derivation of the added benefit.

**Results**

The company presented the ongoing multicentre, randomized, controlled, open-label approval study ELOQUENT-2 for the present research question. It included adult patients with multiple myeloma, at least one and at most 3 prior therapies and documented disease progression after their most recent therapy. Elotuzumab in combination with lenalidomide and dexamethasone (N = 321) was compared with lenalidomide in combination with dexamethasone (N = 325) in the study.

Due to the dosing regimen of dexamethasone in the comparator arm, which was not in compliance with the approval, the ELOQUENT-2 study was unsuitable to derive conclusions on the added benefit of elotuzumab versus the ACT.

The administration of dexamethasone in combination with elotuzumab and lenalidomide is described by the approval of elotuzumab, the combination with lenalidomide is described only by the approval of lenalidomide. The dosing regimen of dexamethasone differs depending on the combination it is given in. The dose of dexamethasone is lower in combination with elotuzumab and lenalidomide than in combination with lenalidomide alone and it is used without pulse administration (see below for the combination with lenalidomide alone). The dosing regimen in the intervention arm, but not in the comparator arm of the ELOQUENT-2 study, concurred with the specifications of the Summary of Product Characteristics (SPC).

***Reasons for the lack of suitability of the ELOQUENT-2 study for the benefit assessment***

- The dosing regimen in the comparator arm of the ELOQUENT-2 study deviated substantially from the approval, both in the different dosage of dexamethasone in the first 4 treatment cycles and in the generally missing pulse administration.

  According to the approval, dexamethasone in combination with lenalidomide for the treatment of pretreated patients with multiple myeloma is given at a dosage of 40 mg (orally) once daily on 4 consecutive days in pulse administration. Hence, dexamethasone is taken on days 1 to 4, 9 to 12, and 17 to 20 in the first 4 cycles. Starting from the fifth cycle, only one pulse is administered (on days 1 to 4). In the comparator arm of the ELOQUENT-2 study, dexamethasone 40 mg (orally) was only taken once weekly, however. Hence the total dose of dexamethasone in the ELOQUENT-2 study was only 160 mg per cycle in the comparator group, whereas the approval recommends a total dose of 480 mg dexamethasone per cycle in the first 4 cycles. In addition, there was no pulse administration in the ELOQUENT-2 study.
- It cannot be inferred from guidelines that dexamethasone dosage outside the approval status is to be used in pretreated multiple myeloma.
- For applicability of the results of the comparator arm of the ELOQUENT-2 study it has to be demonstrated with sufficient certainty and plausibility in appropriate scientific studies that effects regarding patient-relevant outcomes are not substantially influenced by the

different treatment situations (in this case the dosage of dexamethasone outside the approval status). The company did not provide this proof.

- The direction of a possible bias by the dosing regimen in the comparator arm of the ELOQUENT-2 study (underdosed and not pulsed), which was not in compliance with the approval, instead of the approved regimen cannot be estimated. Hence the results of the study were not interpretable for the benefit assessment.
- The aim of the benefit assessment was the investigation of the added benefit of elotuzumab versus the ACT. Because of the low-dose dexamethasone without pulse administration in the comparator arm of the ELOQUENT-2 study, an add-on therapy without proof of efficacy of elotuzumab in the sense of a placebo comparison was aimed at. Such a comparison is unsuitable for the benefit assessment.

## Extent and probability of added benefit, patient groups with therapeutically important added benefit[4]

Table 3 presents a summary of the extent and probability of the added benefit of elotuzumab.

Table 3: Elotuzumab – extent and probability of added benefit

| Therapeutic indication | Appropriate comparator therapy[a, b] | Extent and probability of added benefit |
|---|---|---|
| In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adults who have received one or more prior therapies | Bortezomib as monotherapy, or<br>bortezomib in combination with pegylated liposomal doxorubicin, or<br>bortezomib in combination with dexamethasone, or<br>**lenalidomide in combination with dexamethasone** | Added benefit not proven |

a: Presentation of the appropriate comparator therapy specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.
b: It is assumed for the present therapeutic indication that the use of elotuzumab in combination with other drugs is conducted in the framework of a remission-inducing induction treatment. High-dose chemotherapy with stem cell transplantation, which may be a subsequent treatment option, is therefore not an option as part of the ACT.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

[4] 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, no added benefit, or less benefit). For further details see [1,2].

## 2.2 Research question

The aim of the present report was to assess the added benefit of elotuzumab in combination with lenalidomide and dexamethasone in comparison with the ACT for the treatment of multiple myeloma in adult patients who have received one or more prior therapies.

Table 4 shows the research question of the benefit assessment and the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of elotuzumab

| Research question | Therapeutic indication | Appropriate comparator therapy[a, b] |
|---|---|---|
| 1 | In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adults who have received one or more prior therapies | Bortezomib as monotherapy, or<br>bortezomib in combination with pegylated liposomal doxorubicin, or<br>bortezomib in combination with dexamethasone, or<br>**lenalidomide in combination with dexamethasone** |

a: Presentation of the appropriate comparator therapy specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.
b: It is assumed for the present therapeutic indication that the use of elotuzumab in combination with other drugs is conducted in the framework of a remission-inducing induction treatment. High-dose chemotherapy with stem cell transplantation, which may be a subsequent treatment option, is therefore not an option as part of the ACT.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

In accordance with the G-BA's specification, the company chose lenalidomide in combination with dexamethasone from the ACT options presented in Table 4.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier. RCTs were to be used for the derivation of the added benefit.

## 2.3 Information retrieval and study pool

### 2.3.1 Information retrieval

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

Sources of the company in the dossier:

- study list on elotuzumab (status: 19 May 2016)
- bibliographical literature search on elotuzumab (last search on 19 May 2016)
- search in trial registries for studies on elotuzumab (last search on 6 May 2016)

To check the completeness of the study pool:

- search in trial registries for studies on elotuzumab (last search on 14 June 2016)

No relevant study was identified from the check.

### 2.3.2 Study pool of the company for the direct comparison

From the steps of information retrieval mentioned, the company identified the RCT ELOQUENT-2 [3] for the present research question.

The RCT presented by the company was unsuitable to draw conclusions on the added benefit of elotuzumab in comparison with the ACT. This is because the dosing regimen of dexamethasone in the comparator arm deviated substantially from the approval. Hence no comparison with the ACT was possible. The company's arguments regarding the applicability of the results from the ELOQUENT-2 study despite this substantial deviation were inadequate. The direction of a potential bias by the dosing regimen that was not in compliance with the approval instead of the approved regimen could not be estimated so that the results of the study were not interpretable for the benefit assessment.

### 2.3.3 Assessment of the study pool presented

The characteristics of the studies and of the interventions of the ELOQUENT-2 study are presented in Appendix A of the full dossier assessment.

The ELOQUENT-2 study is an ongoing, multicentre, randomized, controlled, open-label approval study. It included adult patients with multiple myeloma, at least one and at most 3 prior therapies and documented disease progression after their most recent therapy. Elotuzumab in combination with lenalidomide and dexamethasone (N = 321) was compared with lenalidomide in combination with dexamethasone (N = 325) in the study. The final analyses are planned after 466 events for progression-free survival and after 427 events for overall survival.

The treatments were administered in cycles both in the intervention arm and in the comparator arm of the ELOQUENT-2 study. One cycle has 28 days. The approved dosing regimen of dexamethasone differs depending on whether it is administered in combination with elotuzumab and lenalidomide or in combination with lenalidomide alone. The administration of dexamethasone in combination with elotuzumab and lenalidomide is described by the approval of elotuzumab [4]. According to the approval, dexamethasone is administered weekly with a total dose of 112 mg orally and 32 mg intravenously per cycle in the first 2 cycles, and, starting with the third cycle, with a total dose of 136 mg orally and 16 mg intravenously. The dosing regimen in the intervention arm therefore concurs with the specifications of the SPC.

**Comparator arm of the ELOQUENT-2 study: use of dexamethasone not in compliance with the approval**

In the comparator arm of the ELOQUENT-2 study lenalidomide was given in compliance with the approval [5]. The administration of dexamethasone in combination with lenalidomide

is also described by the approval of lenalidomide. In the comparator arm of the ELOQUENT-2 study, dexamethasone was not given in compliance with this approval for the patient population of pretreated patients relevant in the present dossier assessment. Instead, the dosing regimen used concurred with the approved regimen for the treatment of patients with newly diagnosed multiple myeloma.

Table 5 compares the approval-compliant dosage of dexamethasone with the dosage given in the comparator arm of the ELOQUENT-2 study.

Table 5: Comparison of the approval-compliant dexamethasone dosage with the dexamethasone dosage given in the ELOQUENT-2 study

| **Dexamethasone dosage** | **Cycle[a] 1–4** | | | | **From cycle[a] 5** | | | |
|---|---|---|---|---|---|---|---|---|
| **According to the approval [5][b]** | **Cycle day** | | | | | | | |
| | **1–4** | | **9–12** | **17–20** | **1–4** | | **9–12** | **17–20** |
| Daily dose (mg) | 40 | | 40 | 40 | 40 | | – | – |
| Total dose per cycle[a] (mg) | 480 (pulse administration) | | | | 160 (pulse administration) | | | |
| **In the comparator arm of the ELOQUENT-2 study** | **Cycle day** | | | | | | | |
| | **1** | **8** | **15** | **22** | **1** | **8** | **15** | **22** |
| Daily dose (mg) | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Total dose per cycle[a] (mg) | 160 (non-pulse administration) | | | | 160 (non-pulse administration) | | | |

a: 28-day cycle
b: In combination with lenalidomide in patients with multiple myeloma with at least one prior therapy.
–: no dexamethasone given

According to the approval, dexamethasone in combination with lenalidomide for the treatment of pretreated patients with multiple myeloma is given at a dosage of 40 mg (orally) once daily on 4 consecutive days in so-called pulse administration. Hence, dexamethasone is taken on days 1 to 4, 9 to 12, and 17 to 20 in the first 4 cycles. Starting from the fifth cycle, only one pulse is administered (on days 1 to 4). In the comparator arm of the ELOQUENT-2 study, dexamethasone 40 mg (orally) was only taken once weekly, however. Hence the total dose of dexamethasone in the ELOQUENT-2 study was only 160 mg per cycle in the comparator group, whereas the approval recommends a total dose of 480 mg dexamethasone per cycle in the first 4 cycles. In addition, there was no pulse administration in the ELOQUENT-2 study.

**Arguments by the company for including the ELOQUENT-2 study in the benefit assessment**

The company argued why it considered the ELOQUENT-2 study to be suitable for the derivation of the added benefit of elotuzumab versus the ACT for the present research question despite dosage outside the approval status in the comparator arm. It described that the low dexamethasone dosage in the "induction phase" is current standard of care in the present therapeutic indication. It considered the scientific advice [6] by the Committee for

Medicinal Products for Human Use (CHMP) of the European regulatory authority to support this view.

The company based its approach on the studies by Rajkumar 2010 [7] and San Miguel 2007 [8]. Furthermore, citing the assessment report of the European regulatory authority [9] it compared the results on the objective response rate of the ELOQUENT-2 study with those of the approval studies of lenalidomide (MM-009, MM-010).

The company concluded from study designs of the current approval studies on carfilzomib [10] und ixazomib [11], in which low dosages of dexamethasone had been given, that the CHMP accepts the low dexamethasone dosage as study comparator. It claimed that the study design of the ELOQUENT-2 study allowed an unbiased investigation of elotuzumab as "add-on therapy" in comparison with lenalidomide and dexamethasone alone.

The company's arguments were not followed for the following reasons.

***Low dexamethasone dosage in pretreated multiple myeloma cannot be inferred from guidelines as standard of care***

The company's statement that the dosage of dexamethasone in the comparator arm of the ELOQUENT-2 study (hereinafter referred to as "low dosage") was current standard of care was not comprehensible. The company considered the CHMP scientific advice to confirm its view that this dosage was current standard of care. The company did not describe further contents of the advice, which also addressed the choice of the comparator. It provided no evidence in its dossier that the low dosage concurred with the current standard of care.

It cannot be inferred from guidelines that a lower dexamethasone dosage is to be used in pretreated multiple myeloma [12-17]. The majority of these guidelines [12,13,15,16] refer to the corresponding approval studies on lenalidomide for the treatment of patients with pretreated multiple myeloma (MM-009 and MM-010 [18,19]). These 2 approval studies used exactly the dosage of lenalidomide in combination with dexamethasone recommended by the approval.

***Studies Rajkumar 2010 and San Miguel 2007 do not support the use of low-dose dexamethasone in pretreated patients with multiple myeloma***

The company cited the studies Rajkumar 2010 und San Miguel 2007, which showed "lower toxicity and better efficacy" in a low dosage of dexamethasone compared with a high dosage of dexamethasone, each in combination with lenalidomide. However, neither of the 2 studies cited by the company provided proof that the low dexamethasone dosage was preferable to the approval-compliant dosage.

*Rajkumar 2010*

The Rajkumar 2010 study compared the low dexamethasone dosage with a high dexamethasone dosage, each in combination with lenalidomide, in newly diagnosed multiple myeloma.

One of the 2 reasons that the Rajkumar 2010 study was unsuitable to prefer the low dexamethasone dosage to the approval-compliant dosage is that the population investigated in the study did not concur with the target population of elotuzumab. It remained unclear whether the results would be transferable to pretreated patients.

The second reason for the lack of suitability of the Rajkumar 2010 study was that the dose given in the study arm with the high dexamethasone dosage was higher than recommended by the approval in the present therapeutic indication.

Table 6 compares the approval-compliant dexamethasone dosage with the dosage given in the Rajkumar 2010 study in the study arm with high-dose dexamethasone.

Table 6: Comparison of the approval-compliant dexamethasone dosage with the dexamethasone dosage given in the Rajkumar 2010 study in the study arm with high-dose dexamethasone

| **Dexamethasone dosage** | **Cycle[a] 1–4** | | | **From cycle[a] 5** | | |
|---|---|---|---|---|---|---|
| **According to the approval [5][b]** | **Cycle day** | | | | | |
| | **1–4** | **9–12** | **17–20** | **1–4** | **9–12** | **17–20** |
| Daily dose (mg) | 40 | 40 | 40 | 40 | – | – |
| Total dose per cycle[a] (mg) | 480 (pulse administration) | | | 160 (pulse administration) | | |
| **High-dose dexamethasone (Rajkumar 2010)** | **Cycle day** | | | | | |
| | **1–4** | **9–12** | **17–20** | **1–4** | **9–12** | **17–20** |
| Daily dose (mg) | 40 | 40 | 40 | 40 | 40 | 40 |
| Total dose per cycle[a] (mg) | 480 (pulse administration) | | | 480 (pulse administration) | | |

a: 28-day cycle
b: In combination with lenalidomide in patients with multiple myeloma with at least one prior therapy.
–: no dexamethasone given

The administration in the first 4 cycles in the study arm with high-dose dexamethasone of the Rajkumar 2010 study concurred with the approval-compliant dosage of dexamethasone (in combination with lenalidomide) for the treatment of patients with multiple myeloma and at least one prior therapy. The decisive factor was, however, that in the Rajkumar 2010 study the total dose was not reduced to 160 mg per cycle after the fourth cycle, but that the threefold dose, i.e. 480 mg per cycle, was continued.

Since the approved dosage of dexamethasone was exceeded to a marked extent from the fifth cycle, the comparison of the Rajkumar 2010 study was unsuitable to cite advantages in

"toxicity" and "efficacy", as the company named it, of a low dosage versus the approval-compliant dosage. The authors of the publication on the Rajkumar 2010 study themselves considered this aspect to be an important limitation of their study. They discussed that one reason for the poorer survival rate in the study arm with high-dose dexamethasone might have been the "inadequate" use of high-dose dexamethasone beyond the fourth cycle. The authors also discussed that no thrombosis or antibiotic prophylaxis was conducted in the study, which also might have contributed to the higher mortality in the study arm with high-dose dexamethasone.

*San Miguel 2007*

The San Miguel 2007 study cited by the company conducted a post-hoc analysis on the basis of the respective intervention arms (lenalidomide + dexamethasone) of the approval studies of lenalidomide in pretreated patients with multiple myeloma. The patients in the lenalidomide and dexamethasone arms of both studies were divided into 2 groups based on whether the dexamethasone dose was reduced due to adverse events or not. Subsequently, the results of these 2 patient groups within the lenalidomide and dexamethasone arms were compared. The analyses were only available as abstracts. In addition, this post-hoc analysis was unsuitable anyway to show that a low dexamethasone dose has advantages over the approval-compliant dosage because the analysis investigated a different research question and it was not a controlled comparison.

***Applicability of the results of the ELOQUENT-2 study not shown***

According to the company, the CHMP saw a risk of bias for the "proof of efficacy" for the ELOQUENT-2 study only in case of insufficient response of the patients in the arm with low dexamethasone dosage. This conclusion was not comprehensible from the documents on the scientific advice. Again, the company did not provide further aspects of the CHMP scientific advice.

To show that there was no risk of bias as described above, the company descriptively compared the objective response rate in the comparator arm of the ELOQUENT-2 study with the pooled rate of the intervention arms of the lenalidomide approval studies. The company concluded from the higher objective response rates in the ELOQUENT-2 study of 65.5% versus 60.1% in the pooled response rates of the lenalidomide studies that there seemed to be no risk of bias "regarding the proof of efficacy due to insufficient response" of the patients with low dexamethasone dosage. The company conceded that this comparison had limitations, but did not address this issue further.

The approach of the company was inadequate. For applicability of the results of the comparator arm of the ELOQUENT-2 study it has to be demonstrated with sufficient certainty and plausibility in appropriate scientific studies that effects regarding patient-relevant outcomes are not substantially influenced by the different treatment situations (in this case the underdosed and non-pulse administration of dexamethasone outside the approval status). The company did not present such proof. The use of only a parameter that is not patient-relevant,

in this case the objective response rate, which the company also only presented as "additional analysis" in its dossier, is inadequate.

The direction of a possible bias by the dosing regimen in the comparator arm of the ELOQUENT-2 study (underdosed and not pulsed), which was not in compliance with the approval, instead of the approved regimen cannot be estimated. Hence the results of the study were not interpretable for the benefit assessment.

***"Add-on therapy" with elotuzumab in the sense of a placebo comparison unsuitable for the benefit assessment***

The company cited the approval studies of carfilzomib and ixazomib, which used the dexamethasone dosage that was also used in the comparator arm of the ELOQUENT-2 study in their respective comparator arms. The company concluded from this that the CHMP accepted the low dexamethasone dosage as study comparator. Due to the low dexamethasone dosage in combination with lenalidomide in each of both study arms, it was possible to investigate the effect of the "add-on therapy" (in ELOQUENT-2: elotuzumab) "alone in an unbiased way".

Apart from the fact that the approval study on ixazomib did not use the combination of lenalidomide and dexamethasone alone and also investigated a different therapeutic indication (solitary plasmocytoma of bone), it is generally inadequate to conclude from the acceptance of studies for the approval that certain treatment regimens are per se relevant also for research questions of the benefit assessment. A treatment described by the company and called "add-on" as the one which was the goal in the ELOQUENT-2 study, targets the efficacy of elotuzumab in the sense of a placebo comparison. Since the aim of the benefit assessment is the investigation of the added benefit of elotuzumab versus the ACT, such a comparison is unsuitable for the benefit assessment.

***Company did not discuss lack of pulse administration of dexamethasone in the comparator arm of the ELOQUENT-2 study***

The company's arguments only addressed the dexamethasone dose, which was not in compliance with the approval, in the comparator arm of the ELOQUENT-2 study. The company did not comment on the fact that the study arm also did not use pulse administration of dexamethasone as recommended by the approval.

It was inadequate that the company did not address the question whether not using pulse administration might have consequences for pretreated patients with multiple myeloma and which consequences that might be. It can be inferred from the literature that the rationale behind a pulse administration of steroids is the prevention of complications and side effects as well as faster and greater "efficacy". Another goal is the reduction of long-term steroid treatment [20,21]. It is conceivable in the present therapeutic indication that the pulse dosage of dexamethasone is important particularly in pretreated patients and in advanced disease to control the disease more rapidly.

## 2.4 Results on added benefit

In its dossier, the company presented no suitable data to assess the added benefit of elotuzumab in combination with lenalidomide and dexamethasone in comparison with the ACT for the treatment of multiple myeloma in adult patients who have received one or more prior therapies. This resulted in no hint of an added benefit; an added benefit is therefore not proven.

## 2.5 Extent and probability of added benefit

The company presented no suitable data for the assessment of the added benefit of elotuzumab. An added benefit of elotuzumab is therefore not proven.

The result of the assessment of the added benefit of elotuzumab in combination with lenalidomide and dexamethasone in comparison with the ACT is presented in Table 7.

Table 7: Elotuzumab – extent and probability of added benefit

| **Therapeutic indication** | **Appropriate comparator therapy[a, b]** | **Extent and probability of added benefit** |
|---|---|---|
| In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adults who have received one or more prior therapies | Bortezomib as monotherapy, or<br>bortezomib in combination with pegylated liposomal doxorubicin, or<br>bortezomib in combination with dexamethasone, or<br>**lenalidomide in combination with dexamethasone** | Added benefit not proven |

a: Presentation of the appropriate comparator therapy specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.
b: It is assumed for the present therapeutic indication that the use of elotuzumab in combination with other drugs is conducted in the framework of a remission-inducing induction treatment. High-dose chemotherapy with stem cell transplantation, which may be a subsequent treatment option, is therefore not an option as part of the ACT.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

This assessment deviates from the company's approach, which derived an indication of a minor added benefit of elotuzumab on the basis of the data presented by the company.

## 2.6 List of included studies

Not applicable as no studies were included in the benefit assessment.

**References for English extract**

Please see full dossier assessment for full reference list.

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