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Cemiplimab (cutaneous squamous cell carcinoma) –

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

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Cemiplimab (kutanes Plattenepithelkarzinom) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 30 October 2019). 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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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AD	absolute difference
AE	adverse event
CI	confidence interval
BSC	best supportive care
cSCC	cutaneous squamous cell carcinoma
DeCOG	Dermatologic Cooperative Oncology Group
ECOG PS	Eastern Cooperative Oncology Group – Performance Status
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
lacSCC	locally advanced cSCC
mcSCC	metastatic cSCC
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

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 cemiplimab. 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 2 August 2019.

Research question

The aim of the present report was to assess the added benefit of cemiplimab as monotherapy in comparison with the appropriate comparator therapy (ACT) in adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy.

Two research questions resulted for the assessment in accordance with the G-BA's specification of the ACT. These two research questions are presented in Table 2.

Table 2: Research questions of the benefit assessment of cemiplimab

Research question	Subindication	ACT[a]
1	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy, and who have not yet received prior drug therapy	Systemic antineoplastic treatment according to the physician's choice
2	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy and whose cancer disease has progressed after prior drug therapy	Best supportive care (BSC)[b]

a: Presentation of the respective ACT specified by the G-BA.
b: BSC refers to the therapy that provides the patient with the best possible, individually optimized, supportive treatment to alleviate symptoms and improve the quality of life.
ACT: appropriate comparator therapy; BSC: best supportive care; G-BA: Federal Joint Committee

In the present assessment, the following terms are used for the respective populations of the research questions:

- Research question 1: Patients who have not yet received prior drug therapy
- Research question 2: Patients whose cancer disease has progressed after drug therapy

The company followed the G-BA's specification on the ACT for research question 1.

For research question 2, the company subdivided the therapeutic indication into the following subgroups:

- patients whose cancer disease has progressed after prior drug therapy but who are still amenable to drug therapy, and
- patients whose cancer disease has progressed after prior drug therapy and for whom treatment to alleviate symptoms and improve quality of life is the only option

For the first subgroup, the company considered systemic antineoplastic treatment according to the physician's choice as comparator therapy and thus deviated from the ACT specified by the G-BA. For the second subgroup, the company considered best supportive care (BSC) as comparator therapy and thus followed the G-BA's specification of the ACT.

The present assessment was conducted for the two research questions 1 and 2 versus the ACT specified by the G-BA.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Results

Research question 1: Patients who have not yet received prior drug therapy

Since the company identified no randomized controlled trial (RCT) for a direct or indirect comparison, it presented a comparison of individual arms from different studies in the dossier. Based on its own study list and on the register search, it identified the study R2810-ONC-1540 on cemiplimab, and it further identified a retrospective study of the Dermatologic Cooperative Oncology Group (DeCOG) on the ACT "systemic antineoplastic therapy according to the physician's choice" (Hillen 2018) by means of bibliographical literature search.

The comparison presented by the company was unsuitable to derive an added benefit of cemiplimab in comparison with the ACT. This is explained below.

Lack of suitability of the data presented by the company for the derivation of an added benefit

The comparison of individual arms of different studies resulted in a high uncertainty of results. Based on such comparison, conclusions on the added benefit were only possible in the presence of very large effects. However, the effect estimations for the outcome "overall survival" presented by the company were not sufficiently large to exclude that they were based on systematic bias alone. Derivation on an added benefit for the outcome "overall survival" is therefore not possible on the basis of the results presented. Results for a comparison are not available for further patient-relevant outcomes on "symptoms", "health-related quality of life" and "AEs". The publication on the study Hillen 2018 provides no information on whether these outcomes were recorded. Balancing of benefit and harm is therefore not possible on the basis of the comparison presented by the company.

Formation of the subpopulation in the Hillen 2018 study not comprehensible

According to data presented by the company in Module 4 A, the individual patient data from the Hillen 2018 study, on the basis of which it formed the subpopulation on research question 1, were available to the company. The publication on the study Hillen 2018 is the only source for the present benefit assessment; however, the formation of the subpopulations by the company is not completely comprehensible under consideration of this study.

Photographic documentation

In Module 3 A, Section 3.2.1, and Module 5 of its dossier, the company presented photographs of patients of the study R2810-ONC-1540 to support its conclusions on the added benefit. A comparative photographic documentation or analysis on Hillen 2018 is not available. In addition, the comparison with Module 5 shows that the photographic documentation presented by the company is exclusively based on pictures of patients from groups 1 and 2 of study R2810-ONC-1540 who were treated with a cemiplimab dose not compliant with the approval. Therefore, the company itself indicated that these two groups were not to be taken into account when presenting the results of the patient-relevant outcomes and that the derivation of the added benefit was to be carried out exclusively on the basis of group 3 treated in compliance with the approval. There was no photographic documentation or comparative analysis available for the latter.

Shortcomings in the bibliographical literature search

There were shortcomings in the company's bibliographical literature search resulting in the non-suitability of the company's information retrieval to guarantee the completeness of the search results. Moreover, it is unclear why it excluded the study Jarkowski 2016.

Research question 2: patients whose cancer disease has progressed after drug therapy

The company divided the patient population on research question 2 into two subgroups and, deviating from the G-BA's specification, considered a systemic antineoplastic treatment according to the physician's choice as ACT for one of these subgroups. This division of the patient population with regard to the ACT by the company was not followed. For all patients of research question 2, "BSC" is determined as ACT in line with the G-BA's specification. The company presented no data for the assessment of the added benefit of cemiplimab in comparison with the ACT.

Summarizing result

The company presented no suitable data for the assessment of the added benefit of cemiplimab versus the ACT for any of the two research questions. This resulted in no hint of an added benefit of cemiplimab in comparison with the ACT; an added benefit is therefore not proven.

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

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

Table 3: Cemiplimab – probability and extent of added benefit

Research question	Subindication	ACT[a]	Probability and extent of added benefit
1	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy, and who have not yet received prior drug therapy	Systemic antineoplastic treatment according to the physician's choice	Added benefit not proven
2	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy and whose cancer disease has progressed after prior drug therapy	Best supportive care (BSC)[b]	Added benefit not proven

a: Presentation of the respective ACT specified by the G-BA.
b: BSC refers to the therapy that provides the patient with the best possible, individually optimized, supportive treatment to alleviate symptoms and improve the quality of life.
ACT: appropriate comparator therapy; BSC: best supportive care; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

[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].

2.2 Research question

The aim of the present report was to assess the added benefit of cemiplimab as monotherapy in comparison with the ACT in adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy.

Two research questions resulted for the assessment in accordance with the G-BA's specification of the ACT. These two research questions are presented in Table 4.

Table 4: Research questions of the benefit assessment of cemiplimab

Research question	Subindication	ACT[a]
1	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy, and who have not yet received prior drug therapy	Systemic antineoplastic treatment according to the physician's choice
2	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy and whose cancer disease has progressed after prior drug therapy	Best supportive care (BSC)[b]

a: Presentation of the respective ACT specified by the G-BA.
b: BSC refers to the therapy that provides the patient with the best possible, individually optimized, supportive treatment to alleviate symptoms and improve the quality of life.
ACT: appropriate comparator therapy; BSC: best supportive care; G-BA: Federal Joint Committee

In the present assessment, the following terms are used for the respective populations of the research questions:

- Research question 1: Patients who have not yet received prior drug therapy
- Research question 2: patients whose cancer disease has progressed after drug therapy

The company followed the G-BA's specification on the ACT for research question 1.

For research question 2, the company subdivided the therapeutic indication into the following subgroups:

- Patients whose cancer disease has progressed after prior drug therapy but who are still amenable to drug therapy, and
- Patients whose cancer disease has progressed after prior drug therapy and for whom treatment to alleviate symptoms and improve quality of life is the only option

For the first subgroup, the company considered systemic antineoplastic treatment according to the physician's choice as comparator therapy and thus deviated from the ACT specified by the

G-BA. For the second subgroup, the company considered BSC as comparator therapy and thus followed the G-BA's specification of the ACT.

The present assessment was conducted for the two research questions 1 and 2 versus the ACT specified by the G-BA (see Section 2.6.1 of the full dossier assessment).

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

2.3 Research question 1: Patients who have not yet received prior drug therapy

2.3.1 Information retrieval and study pool

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 cemiplimab (status: 5 June 2019)
- bibliographical literature search on cemiplimab (last search on 3 June 2019)
- search in trial registries for studies on cemiplimab (last search on 27 May 2019)
- bibliographical literature search on the ACT (last search on 29 May 2019)
- search in trial registries for studies on the ACT (last search on 27 May 2019)

To check the completeness of the study pool:

- search in trial registries for studies on cemiplimab (last search on 15 August 2019)

The check of the completeness of the study pool identified no RCTs for a direct or indirect comparison for the assessment of the added benefit of cemiplimab.

The company also identified no randomized or non-randomized comparative studies for the assessment of the added benefit of cemiplimab for the present research question. Therefore, the company presented a comparison of individual arms from different studies. However, this comparison was unsuitable to derive an added benefit of cemiplimab in comparison with the ACT. This is explained below.

Study pool of the company

In the dossier, the company presented a comparison of individual arms from different studies. Based on its own study list and on the register search, it identified the study R2810-ONC-1540 on cemiplimab [3-8], and it further identified a retrospective study of the DeCOG on the ACT "systemic antineoplastic therapy according to the physician's choice" (Hillen 2018) by means of bibliographical literature search [8,9]).

R2810-ONC-1540

The study R2810-ONC-1540 is an ongoing, open-label, multicentre study investigating several dosages of cemiplimab. The study included adult patients with histologically confirmed invasive cutaneous squamous cell carcinoma (cSCC) differentiating between patients with locally advanced cSCC (lacSCC) and patients with metastatic cSCC (mcSCC). The group of patients with mcSCC comprised patients with distant metastases and those with lymph node metastasis. Patients with lacSCC were only included when curative treatment by means of resection and/or radiation was contraindicated. To be included, the patients had to have an Eastern Cooperative Oncology Group – Performance Status (ECOG PS) of 0 or 1 at baseline.

Partially separated by lacSCC and mcSCC, the patients were allocated to different groups, each of them receiving different cemiplimab dosage (see Table 9 in Appendix A of the full dossier assessment). In Module 4 A, the company only considered group 3, because this was the only one treated with the approved cemiplimab dosage (350 mg IV, every 3 weeks). Only patients with mcSCC were included in group 3 (N = 56). Treatment was to be performed over a period of up to 54 weeks. Palliative radiotherapy was only possible after a completed 24-week treatment period with the study medication and only after consultation with the sponsor. Primary outcome of the study was the objective response rate. “Overall survival”, “symptoms”, “health-related quality of life” and “AEs” were some of the secondary outcomes. At the time point of the last data cut-off (20 September 2018), the median observation period for patients of group 3 was 8.1 months, whereas the shortest observation period was 0.6 months and the longest observation period was 14.1 months.

Table 9 and Table 10 describe the study design as well as the interventions on study R2810-ONC-1540.

Hillen 2018

The publication Hillen 2018 [9] describes a retrospective, non-interventional cohort study conducted by DeCOG. Therefore, the company refers to the study as DeCOG study in Module 4 A. From 1 October 2012 to 4 March 2013, centres participating in the study were requested to ensure retrospective entry of all patients treated by them (irrespective of the type of intervention) who had received first diagnosis of their advanced cSCC between 1 January 2010 and 31 December 2011 into the database. Both patients with mcSCC (distant metastases and lymph node metastasis) and patients with lacSCC were included. Patients with lacSCC were only eligible for the study when curative treatment by means of resection and/or radiation was contraindicated. There was no restriction to a specific ECOG-PS. Data on overall survival, disease status (complete remission, partial response, stable disease, progression, local recurrence), objective response rate, duration of response and time to progression were queried. A single follow-up was performed in May 2014. No information on the median observation period was available.

Table 9 and Table 10 present the study characteristics as well as the reported systemic therapies of the Hillen 2018 study.

Approach of the company for the derivation of the added benefit

For research question 1, the company reported having considered only the results of patients without prior therapy, referred to by it as subpopulation A in Module 4 A. For study R2810-ONC-1540, it therefore presented the results on "overall survival", "progression-free survival", "tumour response", "duration of response", "symptoms", "health-related quality of life" and "AEs" separated by patients with or without prior drug therapy. In Module 4 A, the company stated having used individual patient data regarding the Hillen 2018 study. It presented results on "overall survival", "tumour response" and "duration of response" separated by patients with ECOG-PS 0/1 and ECOG-PS 0/1/not reported, each of them separated by patients with and without prior therapy. To derive the added benefit, the company conducted an unadjusted comparison of the two studies based on the outcomes "overall survival", "tumour response" and "duration of response". The company stated that a comparison based on the other outcomes was impossible, because these were not recorded in Hillen 2018. Based on its comparison, the company derived a hint of a non-quantifiable added benefit of cemiplimab versus the ACT. Moreover, the company requested the clinically relevant added benefit achieved by the response to treatment with cemiplimab to be considered in addition to the presented data; it stated that this benefit was particularly illustrated by the photographic documentation.

Assessment of the evidence presented by the company

Lack of suitability of the data presented by the company for the derivation of an added benefit

For the outcome "overall survival", the company presented the number of events that had occurred during the respective course of the study. However, due to different observation periods, these numbers cannot be meaningfully compared. The Kaplan-Meier curves (see Figure 1 to Figure 3 in Appendix B of the full dossier assessment) show that observation of "overall survival" was clearly longer in the Hillen 2018 study than in study R2810-ONC-1540. Moreover, the company presented survival rates at different time points (months 4, 6, 8 and 12) which it had estimated on the basis of the Kaplan-Meier method in the individual study arms. In Section 4.2.5.6 of Module 4 A, the company stated having used the absolute difference (AD) as well as a 95% confidence interval (CI) based on the respective standard errors of the two survival rates for this purpose. The company provided no justification for having chosen this absolute effect measure instead of a relative effect measure, such as the hazard ratio. According to the results presented by the company, no statistically significant results were shown at any time for patients with an ECOG PS of 0/1/not reported without prior drug therapy. When restricted to patients with an ECOG PS 0/1, a statistically significant difference was only shown at month 12 (difference in survival rates: −24.8; 95% CI: [−48.3; −1.2]). Here, it should be noted that the results presented in Section 4.3.2.3.3.1 of Module 4 A were not obtained by applying the methodology presented in Section 4.2.5.6 of Module 4 A. Thus, it remains unclear which calculation the company used for the 95% CIs of the absolute difference. However, use of the methodology described in Section 4.2.5.6 of Module 4 A yielded no statistically significant difference between the patients with ECOG PS 0/1 at month 12. The uncertainty of results was high due to the comparison of individual arms of different studies conducted by the

company. Based on such comparison, an added benefit can only be derived in the presence of very large effects. Even if the calculation method is adequate for the confidence intervals presented by the company, there are no sufficiently large effect estimations that cannot be based on systematic bias alone. Derivation on an added benefit for the outcome "overall survival" is therefore not possible on the basis of the results presented.

Results for a comparison are not available for further patient-relevant outcomes on "symptoms", "health-related quality of life" and "AEs". The publication on the study Hillen 2018 provides no information on whether these outcomes were recorded. Balancing of benefit and harm is therefore not possible on the basis of the comparison presented by the company.

Formation of the subpopulation in the Hillen 2018 study not comprehensible

According to data presented by the company in Module 4 A, individual patient data from the Hillen 2018 study, on the basis of which it formed the subpopulation on research question 1, were available to the company. However, the only source for the present benefit assessment is the publication Hillen 2018 [9]. However, the formation of the subpopulations by the company is not completely comprehensible under consideration of this publication. It can only be inferred from the publication that a total of 190 patients were included, 41 of whom had received any kind of systemic therapy.

Photographic documentation

In Module 3 A, Section 3.2.1, and Module 5 of its dossier, the company presented photographs of patients of the study R2810-ONC-1540 to support its conclusions on the added benefit. A comparative photographic documentation or analysis on Hillen 2018 is not available. In addition, the comparison with Module 5 shows that the photographic documentation presented by the company is exclusively based on pictures of patients from groups 1 and 2 of study R2810-ONC-1540 who were treated with a cemiplimab dose not compliant with the approval. In Section 4.3.2.3.2.1 of Module 4 A, the company indicated that these two groups were therefore not taken into account when presenting the results of the patient-relevant outcomes and that the derivation of the added benefit was carried out exclusively on the basis of group 3 treated in compliance with the approval. There was no photographic documentation or comparative analysis available for the latter.

Shortcomings in the bibliographical literature search

There were shortcomings in the company's bibliographical literature search resulting in the non-suitability of its information retrieval to guarantee the completeness of the search results. Moreover, it is unclear why it excluded the study Jarkowski 2016 [10] (see Section 2.6.3 of the full dossier assessment).

2.3.2 Results on added benefit

The company provided no suitable data for an assessment of the added benefit of cemiplimab versus the ACT in adult patients with metastatic or locally advanced cutaneous squamous cell

carcinoma who are not amenable to curative surgery or curative radiation therapy and who have not yet received prior drug therapy. This resulted in no hint of an added benefit of cemiplimab in comparison with the ACT; an added benefit is therefore not proven.

2.3.3 Probability and extent of added benefit

Since the company provided no suitable data for the assessment of the added benefit of cemiplimab as monotherapy in comparison with the ACT in adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or radiation therapy and who have not yet received prior drug therapy, an added benefit of cemiplimab is not proven for these patients.

This assessment deviates from that of the company, which derived a hint of a non-quantifiable added benefit on the basis of the presented data.

2.3.4 List of included studies

Not applicable as the company presented no relevant data for the benefit assessment.

2.4 Research question 2: Patients whose cancer disease has progressed after drug therapy

2.4.1 Information retrieval and study pool

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 cemiplimab (status: 5 June 2019)
- bibliographical literature search on cemiplimab (last search on 3 June 2019)
- search in trial registries for studies on cemiplimab (last search on 27 May 2019)
- bibliographical literature search on the ACT (last search on 29 May 2019)
- search in trial registries for studies on the ACT (last search on 27 May 2019)

To check the completeness of the study pool:

- search in trial registries for studies on cemiplimab (last search on 15 August 2019)

The check of the completeness of the study pool produced no suitable data for the assessment of the added benefit of cemiplimab for the present research question.

The company also identified no suitable data for the assessment of the added benefit of cemiplimab in comparison with the ACT “BSC” specified by the G-BA. However, the company divided the patient population into two subgroups and, deviating from the G-BA’s specification, considered a systemic antineoplastic treatment according to the physician’s choice as ACT for

one of these subgroups. This division of the patient population by the company with regard to the ACT was not followed (see Section 2.6.1 of the full dossier assessment). Therefore, BSC is considered the ACT for all patients of research question 2. Irrespective of this, principally the same points of criticism as in research question 1 apply to the results on patients with prior drug therapy (see Section 2.3.1 as well as Section 2.6.3.1 of the full dossier assessment) presented by the company.

2.4.2 Results on added benefit

Data suitable for the assessment of the added benefit of cemiplimab as monotherapy for adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy and whose cancer disease has progressed after prior drug therapy are not available. Hence, there was no hint of an added benefit of cemiplimab in comparison with BSC; an added benefit is therefore not proven.

2.4.3 Probability and extent of added benefit

Since the company provided no suitable data for the assessment of the added benefit of cemiplimab as monotherapy in adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy and whose cancer disease has progressed after prior drug therapy, an added benefit of cemiplimab is not proven for these patients.

This deviates from the assessment of the company insofar as the company divided the patient population into 2 subgroups (patients who were still eligible for drug therapy and patients who were only amenable to treatment to alleviate symptoms and improve quality of life). For the first subgroup, the company considered systemic antineoplastic treatment according to the physician’s choice as ACT and derived a hint of a non-quantifiable added benefit. For the second subgroup, the company considered BSC as ACT and derived no added benefit.

2.4.4 List of included studies

Not applicable as the company presented no relevant data for the benefit assessment.

2.5 Probability and extent of added benefit – summary

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

Table 5: Cemiplimab – probability and extent of added benefit

Research question	**Subindication**	**ACT**[a]	**Probability and extent of added benefit**
1	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy, and who have not yet received prior drug therapy	Systemic antineoplastic treatment according to the physician's choice	Added benefit not proven
2	Adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not amenable to curative surgery or curative radiation therapy and whose cancer disease has progressed after prior drug therapy	Best supportive care (BSC)[b]	Added benefit not proven

a: Presentation of the respective ACT specified by the G-BA.
b: BSC refers to the therapy that provides the patient with the best possible, individually optimized, supportive treatment to alleviate symptoms and improve the quality of life.
ACT: appropriate comparator therapy; BSC: best supportive care; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

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.

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The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a19-60-cemiplimab-benefit-assessment-according-to-35a-social-code-book-v.12496.html.