Gemeinsamer Bundesausschuss

Justification

for the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Cemiplimab (new therapeutic indication: cutaneous squamous cell carcinoma, following resection and radiotherapy, adjuvant treatment)

From 4 June 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical studies the pharmaceutical company have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decide on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient cemiplimab (Libtayo) was listed for the first time on 1 August 2019 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 17 November 2025, cemiplimab received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334 from 12.12.2008, sentence 7).

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

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

"LIBTAYO as monotherapy is indicated for the adjuvant treatment of adult patients with cutaneous squamous cell carcinoma (CSCC) at high risk of recurrence after surgery and radiation".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 16 March 2026 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of cemiplimab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of cemiplimab.

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

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

2.1.1 Approved therapeutic indication of Cemiplimab (Libtayo) in accordance with the product information

LIBTAYO as monotherapy is indicated for the adjuvant treatment of adult patients with cutaneous squamous cell carcinoma (CSCC) at high risk of recurrence after surgery and radiation.

Therapeutic indication of the resolution (resolution of 04.06.2026):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with cutaneous squamous cell carcinoma at high risk of recurrence following resection and radiotherapy; adjuvant treatment

Appropriate comparator therapy for cemiplimab as monotherapy:

– Monitoring wait-and-see approach

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

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved for the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved for the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1. No medicinal products are approved for the therapeutic indication.

On 2. Non-medicinal treatment is not considered.

On 3. No resolutions are available in the therapeutic indication.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V. There is a joint written statement from the German Society for Haematology and Medical Oncology (DGHO) and the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (DGHNO).

When determining the appropriate comparator therapy, it was assumed that patients had undergone an R0 resection or achieved a complete radiological response.

In this context, based on the available evidence, no specific standard therapy has yet been established in the treatment setting of cutaneous squamous cell carcinoma at high risk of recurrence following resection and radiotherapy.

In their written statement, the scientific-medical societies also point out that there is currently no medicinal standard for the adjuvant treatment of cutaneous squamous cell carcinoma following resection and radiotherapy, including patients at high risk of recurrence. The wait-and-see approach is considered to be the standard.

In accordance with the guideline recommendations, regular after-care for patients is indicated in this treatment setting.

Against this background, the monitoring wait-and-see approach is determined to be the appropriate comparator therapy in this treatment setting.

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

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

2.1.3 Extent and probability of the additional benefit

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

Indication of non-quantifiable additional benefit

Justification:

The pharmaceutical company presented the results of the C-POST study to demonstrate the additional benefit of cemiplimab.

The C-POST study is an ongoing, multicentre, double-blind, randomised controlled phase III study comparing cemiplimab as monotherapy with placebo, following surgery and subsequent radiotherapy in each case. Adult patients with cutaneous squamous cell carcinoma (CSCC) at high risk of recurrence, who have previously undergone surgery and completed postoperative radiotherapy with curative intent, were examined. In accordance with the inclusion criteria, the enrolled patients met at least 1 of the following criteria for high-risk CSCC: Lymph node involvement (nodal disease), in-transit metastases, T4 lesion (head and neck tumour and non-head and neck tumour), perineural invasion or local recurrence. Furthermore, the study participants had to have an Eastern Cooperative Oncology Group-Performance Status (ECOG-PS) of 0 or 1. Radiotherapy must have been administered at a minimum radiation dose of 50 Gray (Gy), within 4 to 6 weeks of the surgery and 2 to 10 weeks prior to randomisation. The enrolment of patients who underwent chemoradiotherapy was also permitted.

A total of 415 patients were enrolled in the study and randomised in a 1:1 ratio to either treatment with cemiplimab (N = 209) or placebo (N = 106).

The placebo comparison carried out in the C-POST study sufficiently corresponds to an implementation of the appropriate comparator therapy - monitoring wait-and-see approach.

The study was started in June 2019 and is being conducted at 166 study sites across North America, South America, Australia, Asia and Europe.

In the dossier, the pharmaceutical company presented the results as of the data cut-offs from 04.10.2024 and 07.04.2025.

The 1st data cut-off from 04.10.2024 represents the pre-specified interim analysis following 89 DFS events (50% of 165 DFS events). The 2nd data cut-off from 07.04.2025 is a non-pre-specified data cut-off following 97 DFS events (59% of 165 events). The pharmaceutical company stated in the dossier that the 2nd data cut-off was carried out in accordance with the European Medicines Agency (EMA) requirements. The available information, including the documents submitted during the written statement procedure, clearly show that further data was requested; however, no specific data cut-off or point of time of such an updated analysis was defined. However, results-based implementation of the 2nd data cut-off is not assumed.

Consequently, given the longer duration of observation, the results of the 2nd data cut-off from 07.04.2025 are used for the resolution.

The suitability of risk classification for assessment of the additional benefit

The risk factors for a high risk of recurrence selected by the pharmaceutical company in the C-POST study differ from those in the S3 guideline[2]. In general, the S3 guideline states that there is no standard classification system for categorising patients as those with high-risk CSCC.

In the C-POST study, all patients were required to have undergone prior surgery and adjuvant radiotherapy. The S3 guideline does not recommend adjuvant radiotherapy by default, but only in the presence of specific risk factors for recurrence, such as an R1 resection. The characteristics selected by the pharmaceutical company to identify a high risk of recurrence largely correspond to the factors for which adjuvant radiotherapy is recommended in the guidelines.

At the oral hearing, the clinical experts confirmed that there is no standardised classification of high-risk CSCC, but that the high-risk group is well defined in the C-POST study, even though it does not cover the full range of possible risk definitions.

Overall, it can therefore be assumed that the factors of high-risk CSCC listed in the C-POST study adequately represent the high-risk group.

Extent and probability of the additional benefit

Mortality

Overall survival is a secondary endpoint in the C-POST study and is defined as the time between randomisation and death from any cause.

For the endpoint of overall survival, there was no statistically significant difference between the treatment groups.

Morbidity

Failure of the curative therapeutic approach

The failure of a curative therapeutic approach is fundamentally patient-relevant.

In the dossier, the pharmaceutical company presented analyses of the disease-free survival (DFS) endpoint, which are used as an approximation of the endpoint of failure of the curative therapeutic approach.

According to the dossier, the DFS was defined as the time from randomisation to first documented recurrence of the disease (local, regional and/or distant, or death from any cause):

- Locoregional recurrence at one of the following sites:
  - in head and neck CSCC: recurrence in the soft tissues of the neck or the cervical lymph nodes
  - in non-head and neck CSCC: recurrence in the first regional lymph node adjacent to the resected tumour (or in the soft tissue associated with the first adjacent lymph node basin)

[2] Guideline programme on oncology, actinic keratosis and squamous cell carcinoma of the skin; S3 guideline, extended version, version 2.0. AWMF registry number: 032/022OL. Berlin (GER); 2022.

- in-transit metastases, defined as skin or subcutaneous metastases at a distance > 2 cm from the resected primary tumour but not outside the regional lymph node basin

- Distant recurrence at one of the following sites:
  - in head and neck CSCC: nodal recurrence below the clavicle
  - in non-head and neck CSCC: recurrence extending beyond the first adjacent lymph node basin of the resected tumour bed. A recurrence in 2 lymph node basins is considered a distant recurrence, even if they are adjacent (i.e. 2 mediastinal lymph node basins, 2 lymph nodes in the pelvic cavity).
  - recurrence in non-nodal tissue (including, but not limited to, the lungs, liver, bones and brain)
  - epidermotropic metastases (EDM), defined as distant lesion(s) in the dermis without involvement of the epidermis

The pharmaceutical company does not consider the endpoint of new CSCC lesions to be a recurrence event. However, the occurrence of a new primary tumour means that patients are not disease-free. In order to assess whether patients have been cured by the treatment, it is therefore necessary to take these events into account when interpreting the endpoint of failure of the curative therapeutic approach and to at least present sensitivity analyses of both DFS and the recurrence rate, taking into account new CSCC lesions. As part of the written statement procedure, the pharmaceutical company submitted sensitivity analyses of the DFS endpoint, taking into account new-onset tumours.

Overall, the primary analyses as well as the sensitivity analyses of the endpoint of failure of curative therapeutic approach showed a statistically significant difference in favour of cemiplimab compared with the monitoring wait-and-see approach, both in terms of the event rate and the time-dependent analysis. It should however be noted that as of the 2nd data cut-off, there were still a large number of early censoring events for the DFS endpoint, suggesting that the duration of observation is not yet sufficient to allow for a definitive assessment of the endpoint. The EMA has also criticised the duration of observation and originally called for a fixed observation period of 3 years.

As described, all patients in the C-POST study were required to have undergone prior surgery and adjuvant radiotherapy, and adjuvant radiotherapy is only recommended for the constellation of specific risk factors. An R1 resection is a factor for which adjuvant radiotherapy is recommended according to the S3 guideline. An unperformed R0 resection does not therefore mean that a curative therapeutic approach no longer applies to the patients in question.

At the oral hearing, the clinical experts explained that a curative approach can be assumed for postoperative radiotherapy following R1 resection of a cutaneous squamous cell carcinoma, and that these patients are formally in a tumour-free status.

As the present C-POST study only included patients who had undergone R0 and R1 resections, it can therefore be assumed that patients in the present therapeutic indication are being treated with a curative therapeutic approach.

Symptomatology (assessed using EORTC QLQ-C30)

In the C-POST study, patients' symptomatology was assessed using the EORTC QLQ-C30.

For the benefit assessment, evaluations of the time to first deterioration by at least 10 points were submitted by the pharmaceutical company and used as the basis for the present assessment.

No statistically significant differences between cemiplimab and monitoring wait-and-see approach were observed across all scales of the EORTC QLQ-C30 (global health status, physical functioning, role functioning, emotional functioning, cognitive functioning and social functioning).

Health status (assessed using EQ-5D VAS)

The health status was assessed using the visual analogue scale (VAS) of the EQ-5D questionnaire. Of the analyses presented by the pharmaceutical company, analyses of the time to first deterioration by at least 15 points form the basis of the present assessment.

There was no statistically significant difference between the treatment groups.

Overall assessment of the morbidity endpoints showed a clear effect in the avoidance of recurrences in the context of the endpoint of failure of the curative therapeutic approach; taking the sensitivity analyses into account, this effect indicates an improvement with cemiplimab compared to the monitoring wait-and-see approach. However, the extent of this improvement cannot be reliably quantified due to the high number of censoring events in the DFS endpoint. However, the significant difference between the treatment arms does not call the effect into question. A longer observation period would be necessary to allow for quantification of the extent of the improvement achieved.

Quality of life

The quality of life of patients in the C-POST study was assessed using the functional scales of the EORTC QLQ-C30 questionnaire.

Of the analyses presented, analyses of the time to first deterioration by at least 10 points form the basis of the present assessment.

For all functional scales of the EORTC QLQ-C30, there were no statistically significant differences between the treatment groups.

Overall, there was neither an advantage nor a disadvantage of cemiplimab with regard to health-related quality of life.

Side effects

Total adverse events

Adverse events (AEs) occurred in almost all patients. The results for the endpoint "Total adverse events" are only presented additionally.

Serious AEs (SAEs), severe AEs (CTCAE grade ≥ 3), therapy discontinuation due to AEs

A statistically significant difference to the disadvantage of cemiplimab over the monitoring wait-and-see approach was observed for each of the endpoints of SAEs, severe AEs (CTCAE grade ≥ 3) and therapy discontinuation due to AEs.

Specific AEs

Immune-mediated SAEs, immune-mediated severe AEs (CTCAE ≥ 3)

For the endpoints of immune-mediated SAEs and immune-mediated severe AEs, there was a statistically significant difference to the disadvantage of cemiplimab over the monitoring wait-and-see approach.

Hypothyroidism (PT, AEs)

Detailed analysis of the specific AE of hypothyroidism (PT, AEs) showed a statistically significant difference to the disadvantage of cemiplimab over the monitoring wait-and-see approach.

In summary, in the endpoint category of side effects, a disadvantage of cemiplimab was observed due to negative effects on SAEs, severe AEs (CTCAE grade ≥ 3) and therapy discontinuation due to AEs. Detailed analysis of specific adverse events showed a disadvantage of cemiplimab.

Although the disadvantages relating to side effects are classified as significant in the overall assessment, this does not lead to a downgrading of the overall conclusion on the additional benefit.

Overall assessment

Results from the C-POST study for comparison with the monitoring wait-and-see approach in the endpoint categories of mortality, morbidity, quality of life and side effects are available for the assessment of the additional benefit of cemiplimab in the adjuvant treatment of adults with cutaneous squamous cell carcinoma at high risk of recurrence after surgery and radiation. The analyses of the 2nd data cut-off from 07.04.2025 were used for the resolution.

However, there were no statistically significant differences between the treatment groups for the overall survival.

The results on symptomatology, health status and health-related quality of life (assessed using the EORTC QLQ-C30 and EQ 5D-VAS) indicate neither an advantage nor a disadvantage of cemiplimab compared to the monitoring wait-and-see approach.

The results on the failure of the curative therapeutic approach, presented as the recurrence rate and disease-free survival, show a clear advantage of cemiplimab over the monitoring wait-and-see approach. The avoidance of recurrences is an essential therapeutic goal in the present curative treatment setting. It should however be noted that as of the 2nd data cut-off, there were a large number of early censoring events for the DFS endpoint, suggesting that the duration of observation is not yet sufficient to allow for a definitive assessment of the endpoint. The EMA has also criticised the duration of observation and originally called for a fixed observation period of 3 years.

The results on side effects showed a disadvantage of cemiplimab. This was based on statistically significant differences to the disadvantage of cemiplimab in terms of serious adverse events (AEs), severe AEs (CTCAE grade ≥ 3) and therapy discontinuation due to AEs. Detailed analysis of the specific AEs showed a disadvantage of cemiplimab over the monitoring wait-and-see approach.

In the overall analysis, the advantage in the endpoint of failure of the curative approach is offset by a disadvantage in terms of side effects.

Given the high number of early censoring events, the extent of improvement in the endpoint of failure of the curative approach cannot be reliably quantified. However, the significant difference between the treatment arms does not call the effect into question. A longer observation period would be necessary to allow for quantification of the extent of the improvement achieved.

Although the disadvantage in terms of side effects is classified as significant, this does not lead to a downgrading of the overall conclusion on the additional benefit.

As a result, a non-quantifiable additional benefit of cemiplimab over the monitoring wait-and-see approach was identified for the adjuvant treatment of adult patients with cutaneous squamous cell carcinoma at high risk of recurrence after resection and radiotherapy.

Reliability of data (probability of additional benefit)

The present benefit assessment is based on the results of the ongoing, double-blind, randomised, multicentre phase III C-POST study.

At the study level, the risk of bias is rated as low.

The risk of bias for the endpoints of overall survival, failure of the curative therapeutic approach and side effects is also rated as low.

The risk of bias is rated as high for the endpoints on symptomatology and health-related quality of life (each assessed using the EORTC QLQ-C30) as well as health status (assessed using the EQ-5D VAS). This is due to the lack of data on the endpoint-specific durations of observation and the decline in the return rate of questionnaires observed over the course of the study. It remains unclear to what extent this is due to administrative censoring at this point in time.

Overall, the available data basis is subject to uncertainties. However, these uncertainties are not rated so high as to justify a downgrading of the reliability of data of the overall assessment. In summary, the G-BA therefore derive an indication for the identified additional benefit with regard to the reliability of data (probability of additional benefit).

2.1.4 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the benefit assessment of cemiplimab finds its legal basis in Section 35a, paragraph 3, sentence 7 SGB V. Thereafter, the G-BA may limit the validity of the resolution on the benefit assessment of a medicinal product. In the present case, the limitation is justified by objective reasons consistent with the purpose of the benefit assessment pursuant to Section 35a paragraph 1 SGB V.

The C-POST study data on overall survival forming the basis of the present assessment are preliminary and show a low number of events as of the 2nd data cut-off. Furthermore, there is a high number of early censoring events for the DFS endpoint, suggesting that the observation period is not yet sufficiently long. The final results from the study, which is still ongoing, are still pending. In this context, the EMA requested submission of the final study report by 31 July 2028.

Since more clinical data which could be relevant for the benefit assessment of the medicinal product are expected, it is justified to set a time limit for the resolution until further scientific knowledge is available for the assessment of the additional benefit of cemiplimab. The time

limit allows inclusion of the expected final results from the C-POST study in the benefit assessment of the medicinal product in accordance with Section 35a SGB V.

For this purpose, setting a time limit for the resolution until 1 November 2028 is considered appropriate.

Conditions of the time limitation:

For the new benefit assessment of cemiplimab after expiry of the deadline, the results from the final clinical study report of the C-POST study on overall survival as well as on all other patient-relevant endpoints used for demonstrating an additional benefit are to be submitted in the dossier.

A change in the time limit can generally be granted if it is justified and clearly demonstrated that the period leading to the set time limit is insufficient or too long.

In accordance with Section 3, paragraph 1, number 5 AM-NutzenV in conjunction with Chapter 5, Section 1, paragraph 2, number 7 VerfO, the benefit assessment procedure of the medicinal product with the active ingredient cemiplimab recommences when the deadline has expired. For this purpose, the pharmaceutical company must present a dossier to the G-BA at the latest on the date of expiry of the deadline for proof of an additional benefit of cemiplimab in comparison with the appropriate comparator therapy (Section 4, paragraph 3, number 5 AM-NutzenV in conjunction with Chapter 5, Section 8, paragraph 1, number 5 VerfO). If the dossier is not submitted or is incomplete, the G-BA may determine that an additional benefit is considered not proven.

This does not affect the possibility that a benefit assessment of the medicinal product with the active ingredient cemiplimab may be carried out at an earlier date for other reasons (see Chapter 5, Section 1, paragraph 2, numbers 2 to 6 or 8 VerfO).

2.1.5 Summary of the assessment

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

The therapeutic indication assessed here is as follows:

"LIBTAYO as monotherapy is indicated for the adjuvant treatment of adult patients with cutaneous squamous cell carcinoma (CSCC) at high risk of recurrence after surgery and radiation."

The G-BA determined the monitoring wait-and-see approach as the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company presented the ongoing, double-blind phase III C-POST study comparing cemiplimab with placebo.

For the endpoint of overall survival, there was no statistically significant difference between the treatment arms.

No statistically significant difference between the treatment groups could be derived from the results on symptomatology, health status and health-related quality of life.

Considering the present curative therapeutic approach, the avoidance of recurrences represents a significant therapeutic goal. The results presented for the endpoint of failure of the curative therapeutic approach show a clear advantage of cemiplimab over the monitoring wait-and-see approach. It should however be noted that as of the 2nd data cut-off, there were a large number of early censoring events for the DFS endpoint, suggesting that the duration of observation is not yet sufficient to allow for a definitive assessment of the endpoint. The

EMA has also criticised the duration of observation and originally called for a fixed observation period of 3 years.

For side effects, there was a disadvantage of cemiplimab due to statistically significant differences in terms of serious adverse events (AEs), severe AEs (CTCAE grade ≥ 3) and therapy discontinuation due to AEs.

In the overall analysis, the advantage in the endpoint of failure of the curative approach is offset by a disadvantage in terms of side effects.

Given the high number of early censoring events, the extent of improvement in the endpoint of failure of the curative approach cannot be reliably quantified. However, the significant difference between the treatment arms does not call the effect into question. A longer observation period would be necessary to allow for quantification of the extent of the improvement achieved.

Although the disadvantage in terms of side effects is classified as significant, this does not lead to a downgrading of the overall conclusion on the additional benefit.

As a result, a non-quantifiable additional benefit of cemiplimab over the monitoring wait-and-see approach was identified for the adjuvant treatment of adult patients with cutaneous squamous cell carcinoma at high risk of recurrence after resection and radiotherapy.

The reliability of data for the identified additional benefit is classified as an indication.

The period of validity of the resolution is limited to 1 November 2028, as further clinical data, particularly regarding the DFS and overall survival endpoints, are expected.

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

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

The resolution is based on information provided by the pharmaceutical company in the dossier. The pharmaceutical company's derivation of the patient numbers in the dossier is mathematically comprehensible, but tends to be underestimated.

The main reason for this is the underestimated incidence of non-melanotic skin cancer (ICD-10 code C44).

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Libtayo (active ingredient: cemiplimab) at the following publicly accessible link (last access: 27 May 2026):

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

Therapy with cemiplimab should only be initiated and monitored by specialists in internal medicine, haematology, and oncology, who are experienced in the treatment of patients with cutaneous squamous cell carcinoma, specialists in skin and sexually transmitted diseases, as well as other doctors from other specialist groups participating in the Oncology Agreement.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (incl. patient identification card).

The training material contains, in particular, information and warnings about immune-mediated side effects as well as infusion-related reactions.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 April 2026).

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

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is different from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

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

Treatment period:

Adults with advanced cutaneous squamous cell carcinoma at high risk of recurrence following resection and radiotherapy; adjuvant treatment

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed:				
Cemiplimab	1 x per 21-day cycle	4	1	4.0
	followed by			
	1 x per 21-day cycle	12	1	12.0
	or			
	1 x per 42-day cycle	6	1	6.0
Appropriate comparator therapy				
Monitoring wait-and-see approach	Not calculable			

Consumption:

The (daily) doses recommended in the product information were used as the calculation basis.

For the adjuvant treatment of cutaneous squamous cell carcinoma at high risk of recurrence, the underlying product information recommends 350 mg cemiplimab infusion every 3 weeks for 12 weeks, followed by 700 mg every 6 weeks or 350 mg every 3 weeks, with a total treatment duration of 48 weeks over the course of the year.

Adults with advanced cutaneous squamous cell carcinoma at high risk of recurrence following resection and radiotherapy; adjuvant treatment

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed:					
Cemiplimab	350 mg	350 mg	1 x 350 mg	4.0	4.0 x 350 mg
	followed by				
	350 mg	350 mg	1 x 350 mg	12.0	12.0 x 350 mg
	or				
	700 mg	700 mg	2 x 350 mg	6.0	12.0 x 350 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Appropriate comparator therapy					
Monitoring wait-and-see approach	Not calculable				

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Adults with advanced cutaneous squamous cell carcinoma at high risk of recurrence following resection and radiotherapy; adjuvant treatment

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed:					
Cemiplimab 350 mg	1 CIS	€ 4,321.44	€ 1.77	€ 243.51	€ 4,076.16
Appropriate comparator therapy					
Monitoring wait-and-see approach	Not calculable				
Abbreviations: CIS = concentrate for the preparation of an infusion solution					

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Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary use of medical treatment or in the

prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-apply unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with

regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include data from the product information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic

indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA have decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between statutory health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

Adults with advanced cutaneous squamous cell carcinoma at high risk of recurrence following resection and radiotherapy; adjuvant treatment

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient approved as monotherapy.

References:
Product information for cemiplimab (Libtayo); product information for Regeneron Libtayo 350 mg concentrate for the preparation of an infusion solution; last revised: November 2025

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At their session on 11 June 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. At their session on 7 October 2025, the Subcommittee on Medicinal Products newly determined the appropriate comparator therapy.

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

By letter dated 15 December 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products

with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient cemiplimab.

The dossier assessment by the IQWiG was submitted to the G-BA on 12 March 2026, and the written statement procedure was initiated with publication on the G-BA website on 16 March 2026. The deadline for submitting written statements was 7 April 2026.

The oral hearing was held on 27 April 2026.

By letter dated 29 April 2026, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by the IQWiG was submitted to the G-BA on 15 May 2026.

On 28 May 2026, the IQWiG submitted a new version of the addendum to the G-BA. This addendum version 1.1 from 28 May 2026 replaces its version 1.0 from 15 May 2026. The assessment result was not affected by the changes in version 1.1 compared to version 1.0.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing were discussed at the Subcommittee's session on 27 May 2026, and deliberation of the draft resolution was concluded.

At their session on 4 June 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 June 2025	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	7 October 2025	New determination of the appropriate comparator therapy
Working group Section 35a	15 April 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	27 April 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	6 May 2026 20 May 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	27 May 2026	Concluding discussion of the draft resolution
Plenum	4 June 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 4 June 2026

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

Prof. Hecken