Gemeinsamer Bundesausschuss

Justification

of 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 Tislelizumab (new therapeutic indication: non-small cell lung cancer, squamous, first-line, combination with carboplatin and either paclitaxel or nab-paclitaxel)

of 18 June 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses 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 has 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 decides 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 tislelizumab (Tevimbra) was listed for the first time on 1 September 2024 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices.

On 15 May 2024, the pharmaceutical company filed an application to postpone the start of the benefit assessment procedure for tislelizumab in the therapeutic indication "Tevimbra, in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of adult patients with squamous NSCLC who have:

- locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or
- metastatic NSCLC. “

according to Section 35a paragraph 5b SGB V.

The pharmaceutical company expected marketing authorisation extensions for the active ingredient tislelizumab within the period specified in Section 35a paragraph 5b SGB V for multiple therapeutic indications at different times.

At their session on 4 July 2024, the G-BA approved the application pursuant to Section 35a paragraph 5b SGB V and postponed the relevant date for the start of the benefit assessment and the submission of a dossier for the benefit assessment for the therapeutic indication in question to four weeks after the marketing authorisation of the last approved therapeutic indication of the therapeutic indications covered by the application, at the latest six months after the first relevant date. The marketing authorisation for the other therapeutic indication covered by the application according to Section 35a paragraph 5b SGB V were granted within the 6-month period.

On 25 November 2024, tislelizumab was granted the extension of the marketing authorisation for the therapeutic indications "Gastric or gastroesophageal junction adenocarcinoma, PD-L1 expression TAP ≥ 5, HER2-, first-line, combination with platinum- and fluoropyrimidine-based chemotherapy" and "Oesophageal squamous cell carcinoma, PD-L1 expression TAP score ≥ 5%, first-line, combination with platinum-based chemotherapy" and "Oesophageal squamous cell carcinoma, after previous therapy". The extension of the marketing authorisation for the therapeutic indications "Non-small cell lung cancer, after previous therapy", "Non-small cell lung cancer, squamous, first-line, combination with carboplatin and either paclitaxel or nab-paclitaxel" and "Non-small cell lung cancer, non-squamous, PD-L1 expression ≥ 50%, first-line, combination with pemetrexed and platinum-containing chemotherapy" was granted on 8 July 2024. The mentioned extensions of the marketing authorisation are 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, 12.12.2008, sentence 7).

On 20 December 2024, the pharmaceutical company submitted in due time a dossier on tislelizumab with the therapeutic indication "Squamous non-small cell lung cancer, first-line therapy" in accordance with Section 4, paragraph 3, number 3 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 2 of the Rules of Procedure of the G-BA (VerfO).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 April 2025 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of tislelizumab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has 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 tislelizumab.

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

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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

2.1.1 Approved therapeutic indication of Tislelizumab (Tevimbra) in accordance with the product information

Tevimbra, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of adult patients with squamous NSCLC who have:

- locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or
- metastatic NSCLC.

Therapeutic indication of the resolution (resolution of 18 June 2025):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy

Appropriate comparator therapy for tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel:

– Pembrolizumab as monotherapy

or

– atezolizumab as monotherapy

or

– cemiplimab as monotherapy

or

– nivolumab in combination with ipilimumab and 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

or

– pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for patients with ECOG-PS 0-1)

or

– cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

or

– durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

Appropriate comparator therapy for tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel:

- Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for patients with ECOG-PS 0-1)

or

- atezolizumab as monotherapy (only for patients with PD-L1 expression ≥ 10% in tumour-infiltrating immune cells)

or

- nivolumab in combination with ipilimumab and 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

or

- cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

or

- durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

or

- carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel) cf. Annex VI to Section K of the Pharmaceuticals Directive (only for patients with ECOG-PS 2)

or

- carboplatin in combination with nab-paclitaxel (only for patients with ECOG-PS 2)

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

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

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

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

4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

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

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

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

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

On 1. In terms of authorisation status, in addition to the medicinal products to be assessed, the cytostatic agents cisplatin, docetaxel, etoposide, gemcitabine, ifosfamide, mitomycin, nab-paclitaxel, paclitaxel, vindesine, vinorelbine as well as the antibodies atezolizumab, cemiplimab, durvalumab, ipilimumab, nivolumab, pembrolizumab and tremelimumab are available.

Active ingredients approved for further molecularly stratified therapy (directed against ALK, EGFR, HER2, KRAS, METex-14, NTRK, RET or ROS1) were not considered.

On 2. For the present therapeutic indication, it is assumed that there is neither an indication for definitive chemoradiotherapy nor for definitive local therapy. Therefore, a non-medicinal treatment cannot be considered in the present therapeutic indication.

On 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Cemiplimab (resolutions of 20 January 2022 and 19 October 2023)
- Tremelimumab (resolution of 5 October 2023)
- Durvalumab (resolution of 5 October 2023)
- Atezolizumab (resolutions of 19 November 2021 and 11 March 2025)
- Ipilimumab (resolution of 3 June 2021)
- Nivolumab (resolution of 3 June 2021)

- Pembrolizumab (resolutions of 3 August 2017 and 19 September 2019)

Annex VI to Section K of the Pharmaceuticals Directive - Prescribability of approved medicinal products in non-approved therapeutic indications (off-label use):

- Carboplatin-containing medicinal products for advanced non-small cell lung cancer (NSCLC) - combination therapy

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic 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.

A joint written statement by the German Society for Haematology and Medical Oncology (DGHO), the German Respiratory Society (DGP), the Working Group for Thoracic Oncology in the Working Group for Internal Oncology of the German Cancer Society (AIO) and the Working Group for Pneumological Oncology of the German Cancer Society (POA) is available.

Among the approved active ingredients listed under 1., only certain active ingredients named below will be included in the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of care.

Based on the available evidence on therapy options depending on PD-L1 expression, the appropriate comparator therapy differentiated into two sub-populations with a cut-off value of PD-L1 expression of 50% of tumour cells is determined.

a) <u>Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy</u>

For first-line treatment of metastatic NSCLC with PD-L1 expression on ≥ 50% of tumour cells, the guidelines recommend monotherapy with the approved immune checkpoint inhibitors atezolizumab, cemiplimab and pembrolizumab, regardless of histological status. In addition, immunochemotherapies are recommended, whereby a distinction is made between patients with good general condition (Eastern Cooperative Oncology Group Performance Status (ECOG-PS) 0-1) and reduced general condition (ECOG-PS 2) with regard to selection of therapy. As the evidence for patients with ECOG-PS 2 is limited, the therapy recommendations for immunochemotherapies are based on patients with ECOG-PS 0-1. Within this defined framework, pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel are administered in patients with squamous NSCLC. The combination therapies of nivolumab and ipilimumab and two cycles of platinum-based chemotherapy as well as cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy are also available as histology-independent treatment options. In summary, based on the available body of evidence, the G-BA considers it appropriate to determine immune checkpoint inhibitors as monotherapies and in combination with platinum-containing chemotherapy as

appropriate comparator therapies, whereby the immunochemotherapies are restricted to patients with an ECOG-PS of 0-1. In this context, individual therapy options only represent a comparator therapy for the part of the patient population that has the patient and disease characteristics specified in brackets. The therapeutic alternatives are only to be considered equally appropriate in the therapeutic indication, where the patient populations have the same characteristics. It is pointed out that the marketing authorisation and dosage specifications in the product information for the active ingredients must be taken into account and any deviations must be justified separately.

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

In the first-line treatment of metastatic NSCLC with PD-L1 expression < 50% of the tumour cells, the therapy recommendations in the available evidence are also made, depending on ECOG-PS and tumour histology. For patients with an ECOG-PS of 0-1, the available evidence recommends combination therapies of the immune checkpoint inhibitors atezolizumab, nivolumab or pembrolizumab and chemotherapy, depending on the tumour histology. Within this defined framework, pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel can be administered in patients with squamous NSCLC.

The combination therapies of nivolumab and ipilimumab and two cycles of platinum-based chemotherapy as well as cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy as well as atezolizumab as monotherapy (for patients with PD-L1 expression ≥ 10 % in tumour-infiltrating immune cells) are also available as histology-independent treatment options.

For patients with an ECOG-PS 2, chemotherapy can also be a relevant therapy option according to the current guidelines. According to the written statements of the scientific-medical societies, combination chemotherapy with two cytostatic agents is more effective than monochemotherapy. In addition, it is stated that although significantly higher remission rates are achieved with cisplatin than with carboplatin, these differences not being shown in combinations with third-generation medicinal products. In terms of overall survival, the two platinum derivatives are described by the scientific-medical societies as having an equivalent effect. The choice of the platinum active ingredient is primarily based on the specific toxicity expected, with cisplatin having a higher toxicity. Taking into account the relevance of toxicity, particularly for patients with a reduced general condition (ECOG-PS 2), the G-BA considers it appropriate to designate carboplatin alone as the platinum active ingredient for patients with an ECOG-PS 2, thereby determining carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel) as the appropriate comparator therapy. The combination of carboplatin and nab-paclitaxel is also recommended and determined to be an appropriate comparator therapy for patients with an ECOG-PS 2. In contrast to cisplatin, carboplatin is not approved for the treatment of NSCLC, but can be prescribed for patients as "off-label use" (see Annex VI to Section K of the Pharmaceuticals Directive).

In summary, based on the current body of evidence, the G-BA considers it appropriate to determine atezolizumab as monotherapy as well as the above-mentioned immune checkpoint inhibitors in combination with platinum-containing chemotherapy as appropriate comparator therapies, whereby the combination immunochemotherapies are restricted to patients with an ECOG-PS of 0-1. In contrast, the combination chemotherapies of carboplatin with a third-generation cytostatic or carboplatin with nab-paclitaxel are only determined as appropriate comparator therapy for patients with ECOG-PS 2.

For patient group b), it should be noted that the appropriate comparator therapy determined here comprises several therapy options. In this context, the therapy options only represent a comparator therapy for the part of the patient population that has the patient and disease characteristics specified in brackets. The therapeutic alternatives are only to be considered equally appropriate in the therapeutic indication, where the patient populations have the same characteristics.

It is pointed out that the marketing authorisation and dosage specifications in the product information for the active ingredients must be taken into account and any deviations must be justified separately.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

Change of the appropriate comparator therapy:

Compared to the originally determined appropriate comparator therapy, this is supplemented in the present resolution by the therapeutic alternatives "Cemiplimab in combination with platinum-based chemotherapy" and "Durvalumab in combination with tremelimumab and platinum-based chemotherapy" in both patient groups a) and b). According to current evidence, immunochemotherapies should be offered for first-line treatment of metastatic NSCLC for patients with a good general condition (ECOG-PS 0-1), regardless of histological status and regardless of PD-L1 status.

For patients with squamous NSCLC, cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy are also unanimously named in this regard.

For this reason, the G-BA considers it appropriate to change the appropriate comparator therapy for the present resolution, thus adapting it to the current state of medical knowledge.

In addition, the cytostatic agent "pemetrexed" specified in brackets for patient group b) in the therapy option "carboplatin in combination with a third-generation cytostatic" has been deleted from the originally determined appropriate comparator therapy in the present resolution. Pemetrexed is not approved for predominantly squamous histology of NSCLC and is therefore not determined to be part of the appropriate comparator therapy for the present therapeutic indication.

Furthermore, the characteristic "without treatable genetic alterations" for the patient group designations a) and b) has been deleted from the originally determined appropriate

comparator therapy in the present resolution. This allows subsequent adaptation to the approved therapeutic indication.

The present assessment of the additional benefit of tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel remains unaffected by these changes to the appropriate comparator therapy.

2.1.3 Extent and probability of the additional benefit

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

An additional benefit is not proven.

Justification:

In the dossier for the benefit assessment, the pharmaceutical company submitted the results of the RATIONALE 307 approval study on tislelizumab. This is an open-label, randomised phase III study comparing tislelizumab in combination with carboplatin and either paclitaxel (study arm A) or nab-paclitaxel (study arm B) versus carboplatin in combination with paclitaxel (study arm C).

The RATIONALE 307 study with a total of 360 adults with locally advanced or metastatic (stage IIIB or IV) squamous NSCLC with no EGFR or ALK aberrations and without prior treatment was conducted in 43 study sites in China between July 2018 and April 2023. Enrolment in the study was restricted to patients with a good general condition, corresponding to an ECOG-PS ≤ 1. Patients were stratified in a 1:1:1 ratio to the intervention and control arms according to disease stage (IIIB vs IV) and PD-L1 expression on the tumour cells (< 1% vs 1% to 49% vs ≥ 50%).

For the benefit assessment, the results of the third data cut-off from 28.04.2023 are available.

Assessment:

The data from the RATIONALE 307 study are unsuitable for the assessment of the additional benefit. The combination of carboplatin with paclitaxel constituted the comparator arm of the study. This does not correspond to the determined appropriate comparator therapy. Consequently, the appropriate comparator therapy has not been implemented. Thus, no suitable data are available for an assessment of the additional benefit of tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel. An additional benefit of tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel for the first-line treatment of locally advanced squamous NSCLC that is not suitable for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is a benefit assessment of a new therapeutic indication for the active ingredient tislelizumab. The therapeutic indication assessed here is as follows:

"Tevimbra, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of adult patients with squamous NSCLC who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC."

In the therapeutic indication to be considered, two patient groups were distinguished by PD-L1 expression:

a) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

The G-BA determined the appropriate comparator therapy for the patient group a) to be immune checkpoint inhibitors, if applicable, in combination with chemotherapy, and for the patient group b), atezolizumab as monotherapy as well as combination immunochemotherapy for patients with ECOG-PS 0-1 and various combination chemotherapies for patients with ECOG-PS 2.

The pharmaceutical company presented results from the open-label phase III RATIONALE 307 study comparing tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel versus carboplatin in combination with paclitaxel. The therapy in the comparator arm of the study therefore does not correspond to the appropriate comparator therapy. Thus, no suitable data are available. It was concluded that an additional benefit of tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel for the first-line treatment of locally advanced squamous NSCLC that is not suitable for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, is therefore not proven.

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

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

For the number of German patients with lung cancer, the projected incidence for 2024 (59,851 patients)[2] is used as the basis for the calculations. The current publications lack projected data. This is why later developments cannot be presented here.

The following calculation steps are used to narrow down this patient group to the target population:

1. The percentage of lung cancer patients with NSCLC is between 73.6% and 83.6%[3] (44,050 to 50,035 patients).
2. Of these, 46.63% of patients are in stage IV at initial diagnosis.[4] Of the remaining 53.37% of patients who are in stage I-IIIB, 37.7% will progress to stage IV in 2022.[5] The percentage of patients in stage IIIB/IIIC is 4.5% to 6.1%.[6] The total number of patients is 32,273 to 36,658.
3. First-line therapy is given in 76.9% to 96.1%[3] of cases (24,818 - 35,228 patients).

[2] Robert Koch Institute, Society of Epidemiological Cancer Registries in Germany. Cancer in Germany for 2019/2020. 2024
[3] Benefit assessment procedure D-655 selpercatinib
[4] Benefit assessment procedure D-923 tremelimumab
[5] 5 Tumour Registry Munich ICD-10 C34: Non-small cell BC Survival [online]. 2022. URL: https://www.tumorregister-muenchen.de/facts/surv/sC34N_G-ICD-10-C34-Nicht-kleinzell.-BC-Survival.pdf
[6] Benefit assessment procedure D-935 cemiplimab

4 In 35.9% (8,909 to 12,647 patients), there is squamous histology.[7]
5 In 28.9% of patients, PD-L1 expression was ≥ 50% (2,575 to 3,655 patients) and in 71.9% of patients, PD-L1 expression was < 50% (6,335 to 8,992 patients).[8]
6 Taking into account the percentage of SHI-insured patients of 87.28%, the following result in the first-line therapy of tumours with squamous histology:

6a. Patient group a) (PD-L1 expression ≥ 50%): 2,247 to 3,190 patients

6b. Patient group b) (PD-L1 expression< 50%): 5,529 to 7,848 patients

Due to uncertainties regarding the data basis in the target population in Germany, both an overestimation and an underestimation of patient numbers are possible.

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 Tevimbra (active ingredient: tislelizumab) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 5 May 2025):

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

Treatment with tislelizumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology who are experienced in the treatment of patients with non-small cell lung cancer, as well as specialists in internal medicine and pulmonology or specialists in pulmonary medicine and other doctors from specialist groups participating in the Oncology Agreement.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (including patient identification card). The training material contains, in particular, instructions on the management of immune-mediated side effects potentially occurring with tislelizumab.

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 June 2025).

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

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies 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.

The dosage regimens used in the BGB-A317-307 approval study are used for tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

[7] Benefit assessment procedure D-184 nivolumab, D-448 pembrolizumab and D-226 afatinib
[8] Benefit assessment procedure D-705 cemiplimab

The dosage of carboplatin as part of the combination therapy of the medicinal product to be assessed (tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel) is calculated using the Calvert formula and the estimation of renal function using the Cockcroft-Gault equation, whereby average values of body height (women: 166 cm, men: 179 cm)[13], body weight (women: 69.2 kg, men: 85.8 kg)[13], age (women: 46 years, men: 43.4 years)[9] and the mean standard serum creatinine concentration (women: 0.75 mg/dl, men: 0.9 mg/dl)[10] for women and men in Germany in 2021 are used.

The mean value (AUC 5 = 700.8 mg) formed from these doses for women (AUC 5 = 637 mg) and men (AUC 5 = 764.5 mg) was used as the basis for calculating the cost of carboplatin.

A cycle duration of 3 weeks is used as the basis for carboplatin as a component of the appropriate comparator therapy. For the use of carboplatin in the off-label indication "combination therapy for advanced NSCLC", Annex VI of the Pharmaceuticals Directive specifies the following dosage: up to 500 mg/m² BSA (body surface area) or AUC 6.0 (area under the curve). For the use of carboplatin in combination with nab-paclitaxel, a dosage of AUC 6.0 is also used, according to the product information.

The two pembrolizumab doses of 200 mg every 3 weeks or 400 mg every 6 weeks recommended according to the product information are listed in the cost representation.

For nivolumab, the recommended dose is 360 mg every 3 weeks in combination with 1 mg/kg BW (body weight) ipilimumab every 6 weeks and platinum-based chemotherapy every 3 weeks, whereby treatment with 360 mg nivolumab intravenously every 3 weeks in combination with 1 mg/kg ipilimumab intravenously every 6 weeks continues after 2 cycles of chemotherapy. According to the product information, carboplatin and paclitaxel are considered as components of platinum-based chemotherapy due to the squamous tumour histology.

Durvalumab is administered in combination with tremelimumab and platinum-based chemotherapy every 3 weeks for 4 cycles, followed by durvalumab monotherapy including a fifth dose of tremelimumab in week 16.

According to the product information, cisplatin is dosed differently depending on the concomitant active ingredient - in combination with paclitaxel, the product information specifies a dosage of 80 mg/m² BSA.

Treatment period:

a) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy

[9] Federal Institute for Population Research, average age of the population in Germany (1871-2021) https://www.bib.bund.de/DE/Fakten/Fakt/B19-Durchschnittsalter-Bevoelkerung-ab-1871.html

[10] DocCheck Flexikon – Serum creatinine, URL: https://flexikon.doccheck.com/de/Serumkreatinin [last access: 05.05.2025]

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel				
Tislelizumab	1 x per 21-day cycle	17.4	1	17.4
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	3 x per 21-day cycle	17.4	3	52.2
Appropriate comparator therapy				
Monotherapies with immune checkpoint inhibitors				
Atezolizumab	1 x per 21-day cycle	17.4	1	17.4
Cemiplimab	1 x per 21-day cycle	17.4	1	17.4
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)				
Nivolumab	1 x per 21-day cycle	17.4	1	17.4
Ipilimumab	1 x per 42-day cycle	8.7	1	8.7
Carboplatin	1 x per 21-day cycle	2	1	2.0
Paclitaxel	1 x per 21-day cycle	2	1	2.0
Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for patients with ECOG-PS 0-1)				
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	3 x per 21-day cycle	17.4	3	52.2
cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[11]				
Cemiplimab	1 x per 21-day cycle	17.4	1	17.4

[11] The treatment options for platinum-based chemotherapy were carboplatin or cisplatin in combination with paclitaxel.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Carboplatin				
Cisplatin				
Paclitaxel				
Durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[12]				
Durvalumab	1 x per 21-day cycle	4	1	4.0
Tremelimumab	1 x per 21-day cycle	4	1	4.0
Carboplatin	1 x per 21-day cycle	4	1	4.0
Cisplatin	1 x per 21-day cycle	4	1	4.0
Gemcitabine	2 x per 21-day cycle	4	2	8.0
nab-paclitaxel	3 x per 21-day cycle	4	3	12.0
Antibody maintenance treatment				
Durvalumab	1 x per 28-day cycle	10		10.0
Tremelimumab	1 x in week 16	1		1.0

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel				
Tislelizumab	1 x per 21-day cycle	17.4	1	17.4
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	3 x per 21-day cycle	17.4	3	52.2
Appropriate comparator therapy				
Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for patients with ECOG-PS 0-1)				
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4

[12] The treatment options for platinum-based chemotherapy were gemcitabine + cisplatin or gemcitabine + carboplatin or nab-paclitaxel + carboplatin for squamous NSCLC.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
	or			
	1 x per 42-day cycle	8.7	1	8.7
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	3 x per 21-day cycle	17.4	3	52.2
Atezolizumab as monotherapy (only for patients with PD-L1 expression ≥ 10% in tumour-infiltrating immune cells)				
Atezolizumab	1 x per 21-day cycle	17.4	1	17.4
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)				
Nivolumab	1 x per 21-day cycle	17.4	1	17.4
Ipilimumab	1 x per 42-day cycle	8.7	1	8.7
Carboplatin	1 x per 21-day cycle	2	1	2.0
Paclitaxel	1 x per 21-day cycle	2	1	2.0
Cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[11]				
Cemiplimab	1 x per 21-day cycle	17.4	1	17.4
Carboplatin				
Cisplatin				
Paclitaxel				
Durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[12]				
Durvalumab	1 x per 21-day cycle	4	1	4.0
Tremelimumab	1 x per 21-day cycle	4	1	4.0
Carboplatin	1 x per 21-day cycle	4	1	4.0
Cisplatin	1 x per 21-day cycle	4	1	4.0
Gemcitabine	2 x per 21-day cycle	4	2	8.0
nab-paclitaxel	3 x per 21-day cycle	4	3	12.0
Antibody maintenance treatment				
Durvalumab	1 x per 28-day cycle	10	1	10.0
Tremelimumab	1 x in week 16	1	1	1.0
Carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel) cf. Annex VI to Section K of the Pharmaceuticals Directive (only for patients with ECOG-PS 2)				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Gemcitabine	2 x per 21-day cycle	17.4	2	34.8
Vinorelbine	2 x per 21-day cycle	17.4	2	34.8
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
Carboplatin in combination with nab-paclitaxel (only for patients with ECOG-PS 2)				
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	3 x per 21-day cycle	17.4	3	52.2

Consumption:

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements of the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg). This results in a body surface area of 1.91 m² (calculated according to Du Bois 1916)[13].

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

a) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy

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					
Tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel					
Tislelizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
Carboplatin	AUC 5 = 700.8 mg	700.8 mg	1 x 150 mg + 1 x 600 mg	17.4	17.4 x 150 mg + 17.4 x 600 mg
Paclitaxel	175 mg/m2 =	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	334.3 mg				
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	52.2	104.4 x 100 mg
Appropriate comparator therapy					
Monotherapies with immune checkpoint inhibitors					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	17.4	17.4 x 1,875 mg
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 x 350 mg
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)					
Nivolumab	360 mg	360 mg	3 x 120 mg	17.4	52.2 x 120 mg
Ipilimumab	1 mg/kg = 77.7 mg	77.7 mg	2 x 50 mg	8.7	17.4 x 50 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	2.0	4 x 450 mg + 4 x 50 mg
Paclitaxel	175 mg/m^2 = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	2.0	4 x 100 mg + 2 x 150 mg
Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for patients with ECOG-PS 0-1)					
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	17.4	34.8 x 450 mg + 34.8 x 50 mg
Paclitaxel	175 mg/m^2 = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	52.2	104.4 x 100 mg
Cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[11]					
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 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
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	17.4	17.4 x 600 mg + 17.4 x 450 mg
Cisplatin	80 mg/m^2 = 152.8 mg	152.8 mg	1 x 10 mg + 1 x 50 mg + 1 x 100 mg	17.4	17.4 x 10 mg + 17.4 x 50 mg + 17.4 x 100 mg
Paclitaxel	175 mg/m^2 = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
Durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[12]					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	4.0	12.0 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	4.0	12.0 x 25 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	4.0	4.0 x 600 mg + 4.0 x 450 mg
Cisplatin	75 mg/m^2 = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	4.0	4.0 x 50 mg + 4.0 x 100 mg
Gemcitabine	1,250 mg/m^2 = 2,387.5 mg	2,387.5 mg	2 x 200 mg + 2 x 1,000 mg	8.0	16.0 x 200 mg + 16.0 x 1,000 mg
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	12.0	24.0 x 100 mg
Antibody maintenance treatment					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	10.0	30 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	1.0	3.0 x 25 mg

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

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					
Tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel					
Tislelizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
Carboplatin	AUC 5 = 700.8 mg	700.8 mg	1 x 150 mg + 1 x 600 mg	17.4	17.4 x 150 mg + 17.4 x 600 mg
Paclitaxel	175 mg/m^2 = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	52.2	104.4 x 100 mg
Appropriate comparator therapy					
Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for patients with ECOG-PS 0-1)					
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	17.4	34.8 x 450 mg + 34.8 x 50 mg
Paclitaxel	175 mg/m^2 = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	52.2	104.4 x 100 mg
Atezolizumab as monotherapy (only for patients with PD-L1 expression ≥ 10% in tumour-infiltrating immune cells)					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	17.4	17.4 x 1,875 mg
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)					
Nivolumab	360 mg	360 mg	3 x 120 mg	17.4	52.2 x 120 mg
Ipilimumab	1 mg/kg = 77.7 mg	77.7 mg	2 x 50 mg	8.7	17.4 x 50 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
Carboplatin	500 mg/m² = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	2.0	4 x 450 mg + 4 x 50 mg
Paclitaxel	175 mg/m² = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	2.0	4 x 100 mg + 2 x 150 mg
Cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[11]					
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 x 350 mg
Carboplatin	500 mg/m² = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	17.4	34.8 x 450 mg + 34.8 x 50 mg
Cisplatin	80 mg/m² = 152.8 mg	152.8 mg	1 x 10 mg + 1 x 50 mg + 1 x 100 mg	17.4	17.4 x 10 mg + 17.4 x 50 mg + 17.4 x 100 mg
Paclitaxel	175 mg/m² = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
Durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[12]					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	4.0	12.0 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	4.0	12.0 x 25 mg
Carboplatin	500 mg/m² = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	4.0	8.0 x 450 mg + 8.0 x 50 mg
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	4.0	4.0 x 50 mg + 4.0 x 100 mg
Gemcitabine	1,250 mg/m² = 2,387.5 mg	2,387.5 mg	2 x 200 mg + 2 x 1,000 mg	8.0	16.0 x 200 mg + 16.0 x 1,000 mg
nab-paclitaxel	100 mg/m² = 191 mg	191 mg	2 x 100 mg	12.0	24.0 x 100 mg
Antibody maintenance treatment					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	10.0	30 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	1.0	3.0 x 25 mg
Carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel) cf. Annex VI to Section K of the Pharmaceuticals Directive (only for patients with ECOG-PS 2)					
Carboplatin	500 mg/m² = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	17.4	34.8 x 450 mg + 34.8 x 50 mg
Gemcitabine	1,250 mg/m² = 2,387.5 mg	2,387.5 mg	2 x 200 mg + 2 x 1,000 mg	34.8	69.6 x 200 mg + 69.6 x 1,000 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
Vinorelbine	25 mg/m² – 30 mg/m² = 47.8 mg – 57.3 mg	47.8 mg – 57.3 mg	1 x 50 mg – 1 x 50 mg + 1 x 10 mg	34.8	34.8 x 50 mg – 34.8 x 50 mg + 34.8 x 10 mg
Docetaxel	75 mg/m² = 143.3 mg	143.3 mg	1 x 160 mg	17.4	17.4 x 160 mg
Paclitaxel	175 mg/m² = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
Carboplatin in combination with nab-paclitaxel (only for patients with ECOG-PS 2)					
Carboplatin	500 mg/m² = 955 mg	955 mg	2 x 450 mg + 2 x 50 mg	17.4	34.8 x 450 mg + 34.8 x 50 mg
nab-paclitaxel	100 mg/m² = 191 mg	191 mg	2 x 100 mg	52.2	104.4 x 100 mg

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:

a) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

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					
Tislelizumab 100 mg	1 CIS	€ 2,288.43	€ 1.77	€ 127.40	€ 2,159.26
Carboplatin 150 mg	1 CIS	€ 83.04	€ 1.77	€ 3.40	€ 77.87
Carboplatin 600 mg	1 CIS	€ 300.84	€ 1.77	€ 13.74	€ 285.33
Paclitaxel 100 mg	1 CIS	€ 289.47	€ 1.77	€ 13.20	€ 274.50
Paclitaxel 150 mg	1 CIS	€ 428.54	€ 1.77	€ 19.80	€ 406.97
nab-paclitaxel 100 mg	1 PIS	€ 429.36	€ 1.77	€ 19.84	€ 407.75
Appropriate comparator therapy					
Atezolizumab 1,875 mg	1 SFI	€ 4,129.23	€ 1.77	€ 232.53	€ 3,894.93
Carboplatin 450 mg	1 CIS	€ 228.27	€ 1.77	€ 10.30	€ 216.20
Carboplatin 50 mg	1 CIS	€ 34.70	€ 1.77	€ 1.11	€ 31.82
Cemiplimab 350 mg	1 CIS	€ 4,321.44	€ 1.77	€ 243.51	€ 4,076.16
Docetaxel 160 mg	1 CIS	€ 515.78	€ 1.77	€ 23.94	€ 490.07
Durvalumab 500 mg	1 CIS	€ 2,105.19	€ 1.77	€ 116.94	€ 1,986.48
Gemcitabine 1,000 mg	1 PIF	€ 102.35	€ 1.77	€ 10.62	€ 89.96
Gemcitabine 200 mg	1 PIF	€ 28.85	€ 1.77	€ 0.83	€ 26.25
Ipilimumab 50 mg	1 CIS	€ 3,489.23	€ 1.77	€ 195.98	€ 3,291.48
nab-paclitaxel 100 mg	1 PIS	€ 429.36	€ 1.77	€ 19.84	€ 407.75
Cisplatin 100 mg	1 CIS	€ 76.59	€ 1.77	€ 3.10	€ 71.72
Cisplatin 50 mg	1 CIS	€ 47.71	€ 1.77	€ 1.73	€ 44.21
Cisplatin 10 mg	1 CIS	€ 17.53	€ 1.77	€ 0.30	€ 15.46
Nivolumab 120 mg	1 CIS	€ 1,539.71	€ 1.77	€ 84.64	€ 1,453.30
Paclitaxel 100 mg	1 CIS	€ 289.47	€ 1.77	€ 13.20	€ 274.50
Paclitaxel 150 mg	1 CIS	€ 428.54	€ 1.77	€ 19.80	€ 406.97
Pembrolizumab 100 mg	2 CIS	€ 4,962.26	€ 1.77	€ 280.10	€ 4,680.39
Tremelimumab 25 mg	1 CIS	€ 1,779.95	€ 1.77	€ 98.36	€ 1,679.82
Vinorelbine 50 mg	1 CIS	€ 152.64	€ 1.77	€ 6.71	€ 144.16
Vinorelbine 10 mg	1 CIS	€ 38.90	€ 1.77	€ 1.31	€ 35.82
Abbreviations: CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PIF = powder for the preparation of an infusion solution, PIS = powder for the preparation of an infusion suspension					

LAUER-TAXE® last revised: 1 June 2025

Costs for additionally required SHI services:

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

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

expenditure in the course of the treatment are not shown.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5aSGB V, when a non-prescription medicinal product is dispensed and invoiced in accordance with Section 300, a medicinal product dispensing price in the amount of the dispensing price of the pharmaceutical company plus the surcharges in accordance with Sections 2 and 3 of the Pharmaceutical Price Ordinance in the version valid on 31 December 2003 applies to the insured.

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Medicinal product to be assessed							
Paclitaxel							
17.4 cycles of 21 days each (Tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel)							
Dexamethasone[14] 2 x 20 mg PO	50 x 20 mg TAB	€ 118.88	€ 1.77	€ 0.00	€ 117.11	17.4	€ 81.51
Dimetindene IV 1 mg/10 kg BW = 7.8 mg	5 x 4 mg SFI	€ 26.24	€ 1.77	€ 7.02	€ 17.45	17.4	€ 121.45
Cimetidine 300 mg IV	10 x 200 mg AMP	€ 22.31	€ 1.77	€ 1.39	€ 19.15	17.4	€ 66.64
Appropriate comparator therapy							
Paclitaxel							
17.4 cycles of 21 days each (Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel) (Cemiplimab in combination with carboplatin and paclitaxel)							
Dexamethasone[14] 2 x 20 mg PO	50 x 20 mg TAB	€ 118.88	€ 1.77	€ 0.00	€ 117.11	17.4	€ 81.51
Dimetindene IV 1 mg/10 kg BW = 7.8 mg	5 x 4 mg SFI	€ 26.24	€ 1.77	€ 7.02	€ 17.45	17.4	€ 121.45
Cimetidine 300 mg IV	10 x 200 mg AMP	€ 22.31	€ 1.77	€ 1.39	€ 19.15	17.4	€ 66.64
4 cycles of 21 days each (Durvalumab in combination with tremelimumab, cisplatin and nab-paclitaxel; induction phase)							
Dexamethasone[144] 2 x 20 mg PO	10 x 20 mg TAB	€ 32.42	€ 1.77	€ 0.00	€ 30.65	4	€ 30.65

[14] Fixed reimbursement rate

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Dimetindene IV 1 mg/10 kg BW = 7.8 mg	5 x 4 mg SFI	€ 26.24	€ 1.77	€ 7.02	€ 17.45	4	€ 34.90
Cimetidine 300 mg IV	10 x 200 mg AMP	€ 22.31	€ 1.77	€ 1.39	€ 19.15	4	€ 19.15
2 cycles of 21 days each (Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy)							
Dexamethasone[14] 2 x 20 mg PO	10 x 20 mg TAB	€ 32.42	€ 1.77	€ 0.00	€ 30.65	2	€ 30.65
Dimetindene IV 1 mg/10 kg BW = 7.8 mg	5 x 4 mg SFI	€ 26.24	€ 1.77	€ 7.02	€ 17.45	2	€ 17.45
Cimetidine 300 mg IV	10 x 200 mg AMP	€ 22.31	€ 1.77	€ 1.39	€ 19.15	2	€ 19.15
Cisplatin							
Antiemetic treatment: In clinical practice, an appropriate antiemetic treatment is established before and/or after administration of cisplatin. The product information for cisplatin does not provide any specific information on this, which is why the necessary costs cannot be quantified.							
Hydration and forced diuresis							
4 cycles of 21 days each (Durvalumab in combination with tremelimumab + cisplatin and either nab-paclitaxel or gemcitabine)							
Mannitol 10% infusion solution, 37.5 g/day	10 x 500 ml INF	€ 105.54	€ 5.28	€ 4.26	€ 96.00	4	€ 96.00
Sodium chloride 0.9% Inf. Sol., 3 l - 4.4 l/day	10 x 500 ml INF	€ 13.28	€ 0.66	€ 0.96	€ 11.66	4	€ 34.98 – € 40.10
	10 x 1,000 ml INF	€ 23.10	€ 1.16	€ 1.89	€ 20.05		
17.4 cycles of 21 days each (Cemiplimab in combination with cisplatin and paclitaxel)							
Mannitol 10% infusion solution, 37.5 g/day	10 x 500 ml INF	€ 105.54	€ 5.28	€ 4.26	€ 96.00	17.4	€ 167.04
Sodium chloride 0.9% infusion solution, 3 - 4.4 l/day	10 x 1,000 ml INF	€ 23.10	€ 1.16	€ 1.89	€ 20.05	17.4	€ 104.66 – € 174.44

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Abbreviations: INF = infusion solution; AMP = ampoules; SFI = solution for injection; TAB = tablets							

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

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

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

According to Section 35a, paragraph 3, sentence 4, the G-BA designates 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 has 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 has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

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

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

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

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

Concomitant active ingredient

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

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

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

In addition, there must be no reasons for exclusion of the concomitant active ingredient from

a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

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

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

Designation

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

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

Exception to the designation

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

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

Legal effects of the designation

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

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

Justification for the findings on designation in the present resolution:

a) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression ≥ 50%, first-line therapy

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:
Product information for tislelizumab (Tevimbra); BeiGene Tevimbra 100 mg concentrate for the preparation of an infusion solution; last revised: November 2024

b) Adults who have locally advanced squamous non-small cell lung cancer (NSCLC) and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic squamous NSCLC, with PD-L1 expression < 50%, first-line therapy

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:
Product information for tislelizumab (Tevimbra); BeiGene Tevimbra 100 mg concentrate for the preparation of an infusion solution; last revised: November 2024

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 21 February 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 20 December 2024, the pharmaceutical company submitted a dossier for the benefit assessment of tislelizumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 20 December 2024 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient tislelizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 March 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 April 2025. The deadline for submitting statements was 22 April 2025.

The oral hearing was held on 5 May 2025.

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

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 11 June 2025, and the proposed draft resolution was approved.

At their session on 18 June 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	21 February 2023	Determination of the appropriate comparator therapy
Working group Section 35a	29 April 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	5 May 2025	Conduct of the oral hearing
Working group Section 35a	13 May 2025 3 June 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 June 2025	Concluding discussion of the draft resolution
Plenum	18 June 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 18 June 2025

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken