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, after previous therapy)

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 "Monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC after prior platinum-based therapy. Patients with EGFR mutant or ALK positive NSCLC should also have received targeted therapies before receiving tislelizumab" in accordance with 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 its 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 other therapeutic indication of the therapeutic indication 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. Both 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 "Non-small cell lung cancer, after previous 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, as well of the addendum drawn up by the IQWiG on the benefit assessment. 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 as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior platinum-based therapy. Patients with EGFR-mutated or ALK-positive NSCLC should also have received targeted therapies prior to treatment with tislelizumab.

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:

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

Appropriate comparator therapy for tislelizumab as monotherapy:

- Docetaxel (only for patients with PD-L1 negative tumours)

  or

- pemetrexed (only for patients with PD-L1 negative tumours and except in cases of predominantly squamous histology)

  or

- Nivolumab

  or

- pembrolizumab (only for patients with PD-L1 expressing tumours (TPS ≥ 1%))

  or

- Atezolizumab

  or

- docetaxel in combination with nintedanib (only for patients with PD-L1 negative tumours and adenocarcinoma histology)

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 addition to tislelizumab, medicinal products with the active ingredients cisplatin, docetaxel, etoposide, ifosfamide mitomycin, paclitaxel, pemetrexed, vindesine, vinorelbine, afatinib, erlotinib, nintedanib, osimertinib, atezolizumab, nivolumab, pembrolizumab and ramucirumab are approved in the present therapeutic indication.

Medicinal products for the treatment of NSCLC with ALK translocation, BRAF, EGFR, Exon20, HER-2, KRAS G12C, METex14, ROS1 or RET mutations were excluded.

On 2. For the present therapeutic indication, it is assumed that the patients have no indication 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:

- Afatinib (resolution of 20.10.2016)
- Atezolizumab (resolution of 16.03.2018)
- Nintedanib (resolution of 18.06.2015)
- Nivolumab (resolutions of 04.02.2016 and 20.10.2016)
- Pembrolizumab (resolution of 02.02.2017)
- Ramucirumab (resolution of 01.09.2016)

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 therapeutic indication according to Section 35a, paragraph 7 SGB V. A written statement from the Drugs Commission of the German Medical Association (AkdÄ) as well as a joint written statement from the German Society for Haematology and Medical Oncology (DGHO), the German Respiratory Society (DGP) and the Working Group for Pneumological Oncology of the German Cancer Society (POA) are available.

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

For the present therapeutic indication, it is assumed that the patients have no indication for definitive local therapy.

In addition, it is assumed that no (further) molecularly stratified therapy (directed against ALK, BRAF, EGFR, Exon-20, KRAS G12C, METex14, RET or ROS1) is considered for patients at the time of therapy with tislelizumab.

According to the guidelines and the written statement of the AkdÄ, patients should be offered a PD1 or PD-L1 antibody in second-line therapy if an immune checkpoint inhibitor was not used in first-line therapy and there were no contraindications. In this regard, atezolizumab, nivolumab (each independent of the PD-L1 status) and pembrolizumab (PD-L1 ≥ 1%) are mentioned. For patients who have received platinum-based combination chemotherapy in combination with an immune checkpoint inhibitor as first-line treatment, further antineoplastic therapy is considered in this advanced treatment setting, particularly taking into account the tumour histology. In this regard, the guidelines and the written statement mention docetaxel, docetaxel in combination with nintedanib and pemetrexed as therapy options. Based on the respective marketing authorisations, pemetrexed is not indicated for predominantly squamous histology and docetaxel in combination with nintedanib is only indicated for adenocarcinoma histology.

Overall, it can be deduced from the guidelines that treatment with immune checkpoint inhibitors is already the first-line therapy standard for patients without contraindications. However, if patients have not previously received first-line therapy

with an immune checkpoint inhibitor and there were no contraindications to immune checkpoint inhibitors, treatment with an immune checkpoint inhibitor is preferred in the second line. However, PD-L1 negative tumours are a fundamental exception. In these cases, the guidelines predominantly do not recommend a regular preference of immune checkpoint inhibitors over chemotherapy. Therefore, the appropriate comparator therapy determined here for PD-L1 negative tumours sees cytotoxic chemotherapeutic agents as an alternative appropriate comparator therapy to immune checkpoint inhibitors in this case only.

In the benefit assessments of the immune checkpoint inhibitors nivolumab (squamous and non-squamous tumour histology), pembrolizumab and atezolizumab, an indication of a considerable additional benefit was found for the treatment of patients after prior chemotherapy compared with docetaxel (nivolumab: resolutions of 4 February and 20 October 2016, pembrolizumab: resolution of 2 February 2017, atezolizumab: resolution of 16 March 2018). According to the marketing authorisation for the present therapeutic indication, pembrolizumab is only indicated for patients with PD-L1 expressing tumours (TPS ≥ 1%).

For the combination of docetaxel and nintedanib, which is indicated for adenocarcinoma histology, an indication of a minor additional benefit was identified in the benefit assessment compared to docetaxel monotherapy (resolution of 18 June 2015).

The benefit assessment of the active ingredient afatinib, which is approved for the treatment of squamous histology, showed no additional benefit compared to docetaxel (resolution of 20 October 2016). Also for ramucirumab in combination with docetaxel, no additional benefit was shown in the benefit assessment compared to docetaxel (resolution of 1 September 2016).

Taking into account that benefit-assessed medicinal treatments with an additional benefit are available in the present indication, the treatment options afatinib as well as ramucirumab in combination with docetaxel, for which no additional benefit could be determined in each case, are not considered as an appropriate comparator therapy.

Overall, docetaxel, pemetrexed, nivolumab, pembrolizumab, atezolizumab, and docetaxel in combination with nintedanib were determined as appropriate comparator therapies. In this context, docetaxel only represents a suitable appropriate comparator therapy for patients with PD-L1 negative tumours, pemetrexed only for patients with PD-L1 negative tumours and except in the case of predominantly squamous histology, pembrolizumab only for patients with PD-L1 expressing tumours (TPS ≥ 1%) and docetaxel in combination with nintedanib only for patients with PD-L1 negative tumours and adenocarcinoma histology.

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.

2.1.3 Extent and probability of the additional benefit

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

<u>Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy</u>

a1) Patients with PD-L1 expression ≥ 1%

An additional benefit is not proven.

a2) Patients with tumour cell PD-L1 < 1%

An additional benefit is not proven.

Justification:

For the benefit assessment, the pharmaceutical company presented the results from the completed, open-label, randomised, controlled phase III RATIONALE 303 study comparing tislelizumab with docetaxel. The study was conducted in 109 study sites in Asia, Eastern Europe, North America and South America between November 2017 and January 2024.

Adults with locally advanced or metastatic NSCLC who showed disease progression on treatment with at least one prior platinum-based therapy, but who had not received more than two prior lines of systemic chemotherapy for their advanced or metastatic disease were enrolled in the study. Patients with known EGFR mutation or ALK translocation were excluded from participation in the study. PD-L1 expression status testing was planned for all enrolled patients at the time of enrolment in the study. However, enrolment in the study was independent of the PD-L1 expression status.

A total of 805 patients were enrolled in the study and randomised in a 2:1 ratio to treatment with tislelizumab (N = 535) or docetaxel (N = 270). Randomisation was stratified according to histology (squamous cell carcinoma vs non-squamous cell carcinoma), line of therapy (second vs third line) and PD-L1 expression (≥ 25% vs < 25%).

Treatment in both treatment arms was carried out in cycles of 3 weeks, largely in accordance with the requirements in the product information. According to the study design, treatment was planned until disease progression, occurrence of unacceptable toxicity or withdrawal of consent. In the intervention arm, treatment could also be continued beyond radiologically confirmed disease progression, provided that the patient benefited from the treatment according to the principal investigator's estimate and there was no deterioration of symptoms or unacceptable toxicity.

The primary endpoint of the RATIONALE 303 study is overall survival. Patient-relevant secondary endpoints are endpoints in the categories of morbidity, health-related quality of life and side effects.

The pharmaceutical company presented the results of the RATIONALE 303 study at the 3rd data cut-off from 18 January 2024. This is the evaluation at the end of the study. The benefit assessment is based on this data cut-off.

Relevant sub-population for the present benefit assessment

Patients were enrolled in the RATIONALE 303 study regardless of their PD-L1 expression status. However, according to the appropriate comparator therapy determined by the G-BA, the comparator docetaxel used in the study is only a suitable therapy option for patients with PD-L1-negative tumours. Thus, only the sub-population of patients from the RATIONALE 303 study with a negative PD-L1 expression status is relevant for the present benefit assessment. In the dossier, the pharmaceutical company presented evaluations of a sub-population with PD-L1 expression < 1%. As part of the written statement procedure, the pharmaceutical company explained that the percentage of PD-L1 positive tumour cells shown in the dossier is equivalent to the Tumour Proportion Score (TPS). The sub-population evaluated by the

pharmaceutical company is used for the present assessment. This includes 214 of the randomised patients for tislelizumab and 103 thereof for docetaxel.

However, based on the relevant sub-population of the RATIONALE 303 study, only statements on the additional benefit for patients with PD-L1 negative tumours (PD-L1 expression status < 1%) are possible. In contrast, no suitable data are available from the RATIONALE 303 study for patients with PD-L1 positive tumours (PD-L1 expression status ≥ 1%). The G-BA therefore considers it appropriate to divide the patient population into patients with PD-L1 expression ≥ 1% and patients with PD-L1 expression < 1%.

a1) Patients with PD-L1 expression ≥ 1%

Extent and probability of the additional benefit

No data are available to allow an assessment of the additional benefit. In their dossier, the pharmaceutical company only presented data for patients with PD-L1 expression < 1%. No data are available for patients with PD-L1 expression ≥ 1%.

a2) Patients with tumour cell PD-L1 < 1%

Extent and probability of the additional benefit

Mortality

Overall survival in the RATIONALE 303 study was operationalised as the time from randomisation to death from any cause.

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

Morbidity

Progression-free survival (PFS) was operationalised in the RATIONALE 303 study as the time from randomisation to first objective disease progression or death from any cause. The endpoint was collected by principal investigators on site and was assessed according to the RECIST criteria version 1.1.
For the PFS endpoint, there was no statistically significant difference between the treatment groups.

The PFS endpoint is a composite endpoint composed of endpoints of the mortality and morbidity categories. The endpoint component "mortality" was already assessed as an independent endpoint in the present study via the endpoint "overall survival". The morbidity component assessment was not done in a symptom-related manner but exclusively by means of imaging (disease progression assessed by radiology according to the RECIST version 1.1 criteria).

Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient relevance of the endpoint PFS. The
overall statement on the additional benefit remains unaffected.

On symptomatology, health status and health-related quality of life

In the dossier, the pharmaceutical company presented both responder analyses and continuous evaluations using a mixed model for repeated measures (MMRM) for the change compared to the start of the study for the patient-reported endpoints of symptomatology (assessed using EORTC QLQ-C30 and EORTC QLQ-LC13), health status (assessed using EQ-5D VAS) and health-related quality of life (assessed using EORTC QLQ C30). As responder analyses, the pharmaceutical company presented evaluations up to the first confirmed deterioration by ≥ 15 points for the EQ-5D VAS and by ≥ 10 points for the EORTC QLQ-C30 and the EORTC QLQ-LC13.
However, the duration of observation for the patient-reported endpoints was, on the one hand, systematically and very clearly shortened compared to overall survival and, on the other, differed significantly between the treatment arms, which is why the responder analyses presented could not be meaningfully interpreted in the present data basis. The continuous evaluations presented for supportive purposes are unsuitable for the benefit assessment, as there were a large number of missing values in the evaluations (> 50%) and also large differences between the study arms. As part of the written statement procedure, the pharmaceutical company subsequently submitted evaluations of the time to first deterioration.

The evaluations on the time to first deterioration subsequently submitted as part of the written statement procedure show that only ≤ 10 patients are still under observation for the majority of endpoints in the comparator arm at month 6 (or week 24), and that censoring occurs to a considerable extent in the first 2.5 months after the start of observation. However, differences in the events occurring between the treatment arms only become apparent for most endpoints after month 3, thus being potentially influenced to a high degree by this censoring. Due to these major uncertainties, the subsequently submitted responder analyses on the time to first deterioration of the patient-reported endpoints cannot be meaningfully interpreted in the present data basis.

Symptomatology (EORTC QLQ-C30 and EORTC QLQ-LC13)

The presented evaluations on the time to first confirmed deterioration and the time to first deterioration cannot be interpreted meaningfully. The reasons are explained in the "*On symptomatology, health status and health-related quality of life*" section.

The results for the endpoint of alopecia (EORTC QLQ-LC13), which are used for the benefit assessment, are an exception, as the Kaplan-Meier curves are split here immediately after the start of the study and a clear difference in the course of the curves is recognisable. This shows a statistically significant difference to the advantage of tislelizumab over docetaxel.

Health status (EQ-5D VAS)

The presented evaluations on the time to first confirmed deterioration and the time to first deterioration cannot be interpreted meaningfully. The reasons are explained in the "*On symptomatology, health status and health-related quality of life*" section.

Quality of life

EORTC QLQ-C30
The presented evaluations on the time to first confirmed deterioration and the time to first deterioration cannot be interpreted meaningfully. The reasons are explained in the "*On symptomatology, health status and health-related quality of life*" section.

Side effects

Adverse events (AEs) in total

In the RATIONALE 303 study, AEs occurred in both study arms in almost all patients. The results were only presented additionally.

Serious AE (SAE), therapy discontinuation due to AEs

There was no statistically significant difference between the treatment groups for the endpoints of SAEs and discontinuation due to AEs.

Severe AEs (CTCAE grade ≥ 3)

For the endpoint of severe AEs, there was a statistically significant advantage of tislelizumab over docetaxel.

Specific AE

Immune-mediated AEs

In the dossier, the pharmaceutical company presented evaluations of the immune-mediated AEs, which are however not suitable to fully represent the immune-mediated AEs. Although the evaluations are based on an appropriate collection of PTs, not all events of the listed PTs were evaluated as immune-mediated AEs, but only a selection of these PTs when certain conditions were met.

As part of the written statement procedure, the pharmaceutical company presented further information on the evaluations submitted in the dossier. However, no evaluations taking into account all potentially immune-mediated events were subsequently submitted. Thus, no suitable data are still available for the benefit assessment. The immune-mediated AEs are therapeutically relevant and known side effects of tislelizumab, as of other active ingredients from the class of immune checkpoint inhibitors.

Gastrointestinal disorders (AEs), asthenia (AEs) and insomnia (AEs), alopecia (AEs), blood and lymphatic system disorders (severe AEs) and investigations (severe AEs), infections and infestations (severe AEs) and metabolism and nutrition disorders (severe AEs)

For the endpoints of gastrointestinal disorders (AEs), asthenia (AEs) and insomnia (AEs), alopecia (AEs), blood and lymphatic system disorders (severe AEs; included therein: neutropenia, leukopenia and febrile neutropenia (each severe AEs)) and investigations (severe AEs; included therein: neutropenia and leukopenia (both severe AEs)), infections and infestations (severe AEs) and metabolism and nutrition disorders (severe AEs) each show a statistically significant difference to the advantage of tislelizumab compared to docetaxel.

Respiratory, thoracic and mediastinal disorders (SAEs)

For the endpoint of respiratory, thoracic and mediastinal disorders (SAEs), there was a statistically significant difference to the disadvantage of tislelizumab compared to docetaxel.

Conclusion on side effects:

Overall, tislelizumab showed a statistically significant improvement in severe AEs (CTCAE grade ≥ 3) compared to docetaxel. In detail, the specific AEs predominantly show advantages. No suitable data on immune-mediated AEs are available.

Overall assessment

For the benefit assessment of tislelizumab compared with docetaxel for the treatment of adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy,

results of the RATIONALE 303 study are available for the endpoint categories of mortality, morbidity, health-related quality of life and side effects.

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

With regard to symptomatology, there was a statistically significant advantage of tislelizumab in the endpoint of alopecia assessed using EORTC QLQ-LC13. No assessable data are available for the other endpoints on symptomatology assessed using EORTC QLQ-LC13 and EORTC QLQ-C30 and for health status (assessed using EQ-5D VAS).

No assessable data are available for health-related quality of life (assessed using EORTC QLQ-C30).

In terms of side effects, there was a statistically significant improvement for tislelizumab compared to docetaxel for severe AEs (CTCAE grade ≥ 3). In detail, the specific AEs predominantly show advantages of tislelizumab. However, the evaluations on immune-mediated AEs relevant to the product class of immune checkpoint inhibitors were not assessable.

In the overall analysis of the results, there was a statistically significant improvement for tislelizumab in the endpoint of alopecia assessed using EORTC QLQ-LC13 and a clear advantage in severe adverse events.

However, the fact that no assessable data on other morbidity endpoints apart from the endpoint of alopecia (assessed using EORTC QLQ-LC13) are available results in assessment-relevant limitations. There are also no assessable data on health-related quality of life. Particularly in the present advanced, palliative treatment setting, data on health-related quality of life assumes high significance. An advantage in overall survival could not be proven.

It is also taken into account that the study population investigated is only transferable to the reality of care to a very limited extent, as treatment with an immune checkpoint inhibitor in addition to the previous platinum-based therapy is now the therapy standard.

As a result of a weighted decision, the G-BA concluded that an additional benefit of tislelizumab as monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC after prior platinum-based therapy is 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:

"Tevimbra as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior platinum-based therapy. Patients with EGFR mutant or ALK positive NSCLC should also have received targeted therapies before receiving tislelizumab."

In the RATIONALE 303 study, tislelizumab was compared with docetaxel.

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

With regard to symptomatology, there was a statistically significant advantage of tislelizumab in the endpoint of alopecia. No assessable data are available for the other endpoints of symptomatology and health status.

Likewise, no assessable data are available on health-related quality of life.

In terms of side effects, there was a statistically significant advantage of tislelizumab in severe AEs (CTCAE grade ≥ 3). In detail, the specific AEs predominantly show advantages of tislelizumab. However, the evaluations on immune-mediated AEs relevant to the product class of immune checkpoint inhibitors were not assessable.

In the overall analysis of the results, there was a statistically significant improvement for tislelizumab in the endpoint of alopecia assessed using EORTC QLQ-LC13 and a clear advantage in severe adverse events.

However, the fact that there are no assessable data on other endpoints of morbidity and no assessable data on health-related quality of life apart from the endpoint of alopecia results in assessment-relevant limitations. Particularly in the present advanced, palliative treatment setting, data on health-related quality of life assumes high significance. An advantage in overall survival could not be proven.

In addition, the study population investigated is only transferable to the reality of care to a very limited extent, as treatment with an immune checkpoint inhibitor in addition to the previous platinum-based therapy is now the therapy standard.

As a result of a weighted decision, the G-BA determined that an additional benefit of tislelizumab is 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).

The resolution is based on information provided by the pharmaceutical company in the dossier on the benefit assessment.

The pharmaceutical company's procedure for estimating the number of patients in the SHI target population is mathematically plausible. Overall, the information is however subject to uncertainties, which result primarily from the following aspects:

The pharmaceutical company determines the number of patients with locally advanced or metastasised NSCLC (stages IIIB to IV) at first diagnosis by adding the percentages from different sources, which leads to uncertainties, as the comparability of the patients enrolled and the observation periods in the three different data bases is not given. In addition, there are further uncertainties in the individual publications regarding the percentages of patients with NSCLC and the staging.

The percentage of patients in stages I to IIIA at initial diagnosis and progression to stage IV in the year under review 2024 is also subject to uncertainty, as patients who were already in the locally advanced or metastatic stage in the previous year were not considered. Moreover, patients who progress from an earlier stage to stage IIIB/IIIC were not considered and, on the other hand, progression events from stage IIIB/IIIC to stage IV within 15 years were also collected for metastases, resulting in overall deviations in the opposite direction.

The used percentage of the lower limit of patients with advanced NSCLC receiving first-line systemic therapy is subject to uncertainty, as it was obtained exclusively on the basis of patients with stage IV NSCLC. In addition, the underlying data date back to 2009 and 2010, meaning that they are only transferable to the current healthcare context to a limited extent due to the treatment options newly approved since then. There are also uncertainties

regarding the upper limit based on the SHI routine data analysis: On the one hand, some patients who had received platinum-based therapy were excluded. On the other, the percentage with systemic lines of therapy may be overestimated, as only patients with a therapy specific to NSCLC were enrolled. In addition, further treatment options were approved following the present observation period, which may influence the distribution or number of lines of therapy undergone.

With regard to the percentage of patients who are eligible for further lines of therapy after the first-line, further patients could be added if applicable at the upper limit based on patients with progression after the previous line of therapy. It should also be noted that it also includes those who have not received systemic therapy in the calculation.

It should also be noted that the number of patients receiving chemotherapy alone as first-line therapy is subject to uncertainty in that the current guidelines recommend offering chemoimmunotherapy as early as the first-line therapy, particularly in the metastatic stage of the disease, which already contains an immune checkpoint inhibitor, regardless of PD-L1 status. Based on this, the significance of the percentage of platinum-based chemotherapy alone for the current German healthcare context is questionable.

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: 20 February 2025):

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

Therapy 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 carcinoma, 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).

Treatment period:

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.

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

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	1 x every 21 days	17.4	1	17.4
Appropriate comparator therapy				
Docetaxel (only for patients with PD-L1 negative tumours)				
Docetaxel	1 x every 21 days	17.4	1	17.4
Pemetrexed (only for patients with PD-L1 negative tumours and except in cases of predominantly squamous histology)				
Pemetrexed	1 x every 21 days	17.4	1	17.4
Nivolumab				
Nivolumab	1 x every 14 days	26.1	1	26.1
Pembrolizumab (only for patients with PD-L1 expressing tumours (TPS ≥ 1%))				
Pembrolizumab	1 x every 21 days	17.4	1	17.4
	or			
	1 x every 42 days	8.7	1	8.7
Atezolizumab				
Atezolizumab	1 x every 21 days	17.4	1	17.4
Docetaxel in combination with nintedanib (only for patients with PD-L1 negative tumours and adenocarcinoma histology)				
Docetaxel	1 x every 21 days	17.4	1	17.4
Nintedanib	2 x daily on day 2-21 of a 21-day cycle	17.4	20	348.0

Consumption:

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.

For dosages depending on body weight or body surface area, the average body measurements from the official representative statistics “Microcensus 2021 – body measurements of the

population"[2]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).

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

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	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
Appropriate comparator therapy					
Docetaxel (only for patients with PD-L1 negative tumours)					
Docetaxel	75 mg/m² BSA = 143.3 mg	143.3 mg	1 x 160 mg	17.4	17.4 x 160 mg
Pemetrexed (only for patients with PD-L1 negative tumours and except in cases of predominantly squamous histology)					
Pemetrexed	500 mg/m² BSA = 955 mg	955 mg	1 x 1000 mg	17.4	17.4 x 1000 mg
Nivolumab					
Nivolumab	240 mg	240 mg	2 x 120 mg	26.1	52.2 x 120 mg
Pembrolizumab (only for patients with PD-L1 expressing tumours (TPS ≥ 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
Atezolizumab					
Atezolizumab	1875 mg	1875 mg	1 x 1875 mg	17.4	17.4 x 1875 mg
Docetaxel in combination with nintedanib (only for patients with PD-L1 negative tumours and adenocarcinoma histology)					
Docetaxel	75 mg/m² BSA = 143.3 mg	143.3 mg	1 x 160 mg	17.4	17.4 x 160 mg
Nintedanib	200 mg	400 mg	4 x 100 mg	348.0	1392 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

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

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 locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

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 g	1 CIS	€ 2,288.43	€ 1.77	€ 127.40	€ 2,159.26
Appropriate comparator therapy					
Atezolizumab 1,875 mg	1 SFI	€ 4,129.23	€ 1.77	€ 232.53	€ 3,894.93
Docetaxel 160 mg	1 CIS	€ 515.78	€ 1.77	€ 23.94	€ 490.07
Nintedanib 100 mg	120 SC	€ 2,761.30	€ 1.77	€ 0.00	€ 2,759.53
Nivolumab 120 mg	1 CIS	€ 1,539.71	€ 1.77	€ 85.64	€ 1,453.30
Pembrolizumab 100 mg	2 CIS	€ 4,962.26	€ 1.77	€ 280.10	€ 4,680.39
Pemetrexed 1,000 mg	1 CIS	€ 1,124.81	€ 1.77	€ 52.84	€ 1,070.20
Abbreviations: CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; SC = soft capsules					

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							
Not applicable							
Appropriate comparator therapy:							
Pemetrexed							
Dexamethasone[3,4] (2 x 4 mg PO)	100 TAB 4 mg each	€ 79.54	€ 1.77	€ 5.40	€ 72.37	52.2	€ 75.55
Folic acid[5] (350 – 1,000 µg/day, PO)	100 TAB 400 µg each	€ 17.60	€ 0.88	€ 2.12	€ 14.60	365.0	€ 53.29 – € 106.58
Vitamin B12[4] (1,000 µg/day, every 3 cycles, IM)	10 ILO each 1,000 µg	€ 8.19	€ 0.41	€ 0.37	€ 7.41	5.8	€ 4.30
Docetaxel							
Dexamethasone[3,4] (2 x 4 mg PO)	100 TAB 4 mg each	€ 79.54	€ 1.77	€ 5.40	€ 72.37	€ 52.2	€ 75.55
Abbreviations: TAB = tablets; SFI = solution for injection							

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

[3] To reduce the frequency and severity of skin reactions, a corticosteroid must be given the day before and on the day of pemetrexed administration as well as the day after.

[4] Fixed reimbursement rate

[5] The cost calculation for folic acid is based on the single dose of 400 µg of the non-divisible tablets available for cost calculation related to a dose range of 400 - 800 µg per day, even if a dose range of 350 - 1000 µg is given in the product information.

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:

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

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 authorised in monotherapy.

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 9 February 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 7 May 2024.

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.

By letter dated 6 May 2025, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 28 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	9 February 2022	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	7 May 2024	New 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, Commissioning of the IQWiG with the supplementary assessment of documents
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