Tislelizumab (squamous NSCLC, first line)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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Medical and scientific advice

No advisor on medical and scientific questions was involved in the present dossier assessment.

Patient and family involvement

No patients or families were involved in the present dossier assessment.

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Part I: Benefit assessment

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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
ECOG PS	Eastern Cooperative Oncology Group Performance Status
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
NSCLC	non-small cell lung cancer
RCT	randomized controlled trial
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)

I 1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug tislelizumab (in combination with carboplatin and paclitaxel or nab-paclitaxel). The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 20 December 2024.

Research question

The aim of this report is to assess the added benefit of tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (hereinafter referred to as tislelizumab + carboplatin + paclitaxel/nab-paclitaxel) compared with the appropriate comparator therapy (ACT) for the first-line treatment of squamous non-small cell lung cancer (NSCLC) in adult patients who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC.

The research questions presented in Table 2 result from the ACT specified by the G-BA.

Table 2: Research questions of the benefit assessment of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel

Research question	Therapeutic indication	ACT[a, b]
First-line treatment of squamous NSCLC in adult patients with locally advanced NSCLC who are not candidates for surgical resection or platinum-based chemoradiation, or with metastatic NSCLC		
1	with PD-L1 expression ≥ 50% and without treatable genetic alterations[c]	▪ 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)
2	with PD-L1 expression < 50% and without treatable genetic alterations[c]	▪ 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 ▪ carboplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed); see also Appendix VI to Section K of the Pharmaceutical Directive (only for patients with ECOG PS 2), or ▪ carboplatin in combination with nab-paclitaxel (only for patients with ECOG PS 2)

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against ALK, BRAF, EGFR, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The company followed the G-BA's specification of the ACT in both research questions.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) are used to derive the added benefit. This concurs with the company's inclusion criteria.

Since no suitable data are available for either of the research questions identified by the G-BA, the 2 research questions are assessed together below.

Results

A review of the completeness of the study pool did not identify any relevant studies for assessing the added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel in comparison with the G-BA's ACT for either of the research questions.

Results on added benefit

Since no suitable data are available for the 2 research questions of the benefit assessment, there is no hint of an added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel in comparison with the ACT; an added benefit is therefore not proven for either research question.

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

Table 3 shows a summary of probability and extent of the added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Tislelizumab + carboplatin + paclitaxel/nab-paclitaxel – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
First-line treatment of squamous NSCLC in adult patients with locally advanced NSCLC who are not candidates for surgical resection or platinum-based chemoradiation, or with metastatic NSCLC			
1	with PD-L1 expression ≥ 50% and without treatable genetic alterations[c]	▪ 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)	Added benefit not proven
2	with PD-L1 expression < 50% and without treatable genetic alterations[c]	▪ 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 ▪ carboplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed); see also Appendix VI to Section K of the Pharmaceutical Directive (only for patients with ECOG PS 2), or ▪ carboplatin in combination with nab-paclitaxel (only for patients with ECOG PS 2)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against ALK, BRAF, EGFR, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report is to assess the added benefit of tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (hereinafter referred to as tislelizumab + carboplatin + paclitaxel/nab-paclitaxel) compared with the ACT for the first-line treatment of squamous NSCLC in adult patients who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC.

The research questions presented in Table 4 result from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel

Research question	Therapeutic indication	ACT[a, b]
First-line treatment of squamous NSCLC in adult patients with locally advanced NSCLC who are not candidates for surgical resection or platinum-based chemoradiation, or with metastatic NSCLC		
1	with PD-L1 expression ≥ 50% and without treatable genetic alterations[c]	▪ 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)
2	with PD-L1 expression < 50% and without treatable genetic alterations[c]	▪ 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 ▪ carboplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed); see also Appendix VI to Section K of the Pharmaceutical Directive (only for patients with ECOG PS 2), or ▪ carboplatin in combination with nab-paclitaxel (only for patients with ECOG PS 2)

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against ALK, BRAF, EGFR, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The company followed the G-BA's specification of the ACT in both research questions.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs are used to derive the added benefit. This concurs with the company's inclusion criteria.

Since no suitable data are available for either of the research questions identified by the G-BA, the 2 research questions are assessed together below.

I 3 Information retrieval and study pool

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

Sources used by the company in the dossier:

- Study list on tislelizumab (status: 21 October 2024)
- Bibliographical literature search on tislelizumab (last search on 21 October 2024)
- Search of trial registries/trial results databases for studies on tislelizumab (last search on 21 October 2024)
- Search on the G-BA website for tislelizumab (last search on 21 October 2024)

To check the completeness of the study pool:

- Search of trial registries for studies on tislelizumab (last search on 16 January 2025); for search strategies, see I Appendix A of the full dossier assessment

The review did not identify any additional relevant studies.

Consistent with the findings of the company, the review of completeness of the study pool did not identify any relevant studies for assessing the added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel in comparison with the G-BA's ACT.

The company provided a supportive presentation of the pivotal study RATIONALE 307 [3] as best available evidence. This study compared tislelizumab + carboplatin + paclitaxel/nab-paclitaxel with carboplatin + paclitaxel in treatment-naive adult patients with squamous NSCLC, with locally advanced disease, who were not candidates for surgical resection or platinum-based chemoradiation, or with metastatic NSCLC, in each case without anaplastic lymphoma kinase (ALK) gene translocation or epidermal growth factor receptor (EGFR) gene mutation. Patients were enrolled in the study regardless of their programmed cell death ligand 1 status. Enrolment was limited to patients in good general health corresponding to an Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≤ 1. However, the combination of carboplatin + paclitaxel administered in the comparator arm of the study is only designated as ACT for research question 2 and only for patients with an ECOG PS of 2 (see Table 4). This treatment option therefore only represents an ACT for a limited patient population. However, these patients were not part of the study population. This means that there are no suitable data for the comparison of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel with the comparator therapy specified by the G-BA. In agreement with the company, the RATIONALE 307 study is therefore not used to assess the added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel for either research question.

I 4 Results on added benefit

For the assessment of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel for the first-line treatment of squamous NSCLC in adult patients who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC, there are no suitable data for the comparison of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel versus the comparator therapy specified by the G-BA for either research question. In each case, there is no hint of an added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel in comparison with the ACT; an added benefit is therefore not proven for either research question.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of tislelizumab + carboplatin + paclitaxel/nab-paclitaxel in comparison with the ACT is summarized in Table 5.

Table 5: Tislelizumab + carboplatin + paclitaxel/nab-paclitaxel – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
First-line treatment of squamous NSCLC in adult patients with locally advanced NSCLC who are not candidates for surgical resection or platinum-based chemoradiation, or with metastatic NSCLC			
1	with PD-L1 expression ≥ 50% and without treatable genetic alterations[c]	▪ 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)	Added benefit not proven
2	with PD-L1 expression < 50% and without treatable genetic alterations[c]	▪ 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 ▪ carboplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed); see also Appendix VI to Section K of the Pharmaceutical Directive (only for patients with ECOG PS 2), or ▪ carboplatin in combination with nab-paclitaxel (only for patients with ECOG PS 2)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against ALK, BRAF, EGFR, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The assessment described above concurs with that by the company.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 02.09.2024]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a24-126.html.