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 (oesophageal squamous cell carcinoma, 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 trials 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 submitted an application for postponement of the date for the start of the benefit assessment procedure for tislelizumab in the therapeutic indication "Monotherapy of unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma" 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 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 8 July 2024, tislelizumab was granted extension of the marketing authorisation for the therapeutic indications of 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-based chemotherapy. The extension of the marketing authorisation for the therapeutic indications of gastric or gastroesophageal junction adenocarcinoma, PD-L1 expression ≥ 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 was granted on 25 November 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 "Oesophageal squamous cell carcinoma, 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. 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

Oesophageal squamous cell carcinoma (OSCC)

Tevimbra as monotherapy is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic OSCC after prior platinum-based chemotherapy.

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 unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy

Appropriate comparator therapy for tislelizumab as monotherapy:

- Nivolumab

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.

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

On 1. The chemotherapeutic agents 5-fluorouracil, cisplatin and mitomycin as well as the immune checkpoint inhibitor nivolumab are approved for the present therapeutic indication.

On 2. A non-medicinal treatment option is not considered for the therapeutic indication in question. This does not affect the use of radiotherapy as a supportive therapy option.

On 3. The following resolutions or guidelines of the G-BA are available for the planned therapeutic indication:

Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Nivolumab: Resolution of 1 July 2021

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

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V (see “Information on Appropriate Comparator Therapy”). A joint written statement has been issued by the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS), the Working Group for Internal Oncology of the German Cancer Society (AIO), the German Cancer Society (DKG) and the German Society for Haematology and Medical Oncology (DGHO).

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.

The present authoritative S3 guideline of the German Cancer Society (DKG), German Cancer Aid and the Association of the Scientific-Medical Societies (AWMF) recommends second-line therapy with an immune checkpoint inhibitor for patients with metastatic or locally advanced, non-curatively treatable oesophageal squamous cell carcinoma after previous fluoropyrimidine- and platinum-based chemotherapy, provided that no immunotherapy has previously been carried out.

Alongside tislelizumab, nivolumab is the only approved immune checkpoint inhibitor in the present therapeutic indication.

In their written statement, the scientific-medical societies recommend immunotherapy with nivolumab for programmed cell death ligand 1 (PD-L1)-positive patients after prior chemotherapy without a checkpoint inhibitor in the event of tumour progression within 3 months. In the event of tumour progression more than three months after first-line therapy, the possibility of repeating first-line therapy is mentioned as a further option in addition to nivolumab.

By resolution of 1 July 2021, the benefit assessment on nivolumab showed a hint for a minor additional benefit over chemotherapy according to doctor's instructions in the treatment of patients with unresectable, advanced, recurrent or metastatic oesophageal cancer with squamous cell histology, after prior fluoropyrimidine- and platinum-based combination chemotherapy, for which chemotherapy is a suitable treatment option.

In the overall analysis of the available evidence, nivolumab is therefore determined to be an appropriate comparator therapy for adults with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy.

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:

An additional benefit is not proven.

Justification:

The pharmaceutical company presented the results of the randomised controlled trial RATIONALE 302 for the benefit assessment of tislelizumab for the treatment of adults with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy.

The RATIONALE 302 study is an open-label phase III study comparing tislelizumab with a therapy according to doctor's instructions with selection of docetaxel, paclitaxel and

irinotecan. The study was conducted at 132 study sites in Europe, Asia and North America between 2018 and 2022.

Patients with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after previous first-line systemic therapy with an Eastern Cooperative Oncology Group - Performance Status (ECOG-PS) of 0 or 1 were enrolled in the study. Of the 512 patients enrolled in the study, 498 (97.3%) had received pretreatment with platinum-based systemic therapy.

The primary endpoint of the RATIONALE 302 study was overall survival. Patient-relevant secondary endpoints were morbidity, health-related quality of life, and adverse events.

Assessment:

As the comparator therapy used in the RATIONALE 302 study does not correspond to the appropriate comparator therapy determined by the G-BA, it does not allow an assessment of the additional benefit of tislelizumab compared with the appropriate comparator therapy and is therefore unsuitable for the benefit assessment of tislelizumab.

An additional benefit of tislelizumab for the treatment of adults with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy is therefore not proven.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Tevimbra with the active ingredient tislelizumab.

Tislelizumab (Tevimbra) is approved for the treatment of adult patients with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy.

Nivolumab was determined as the appropriate comparator therapy for this therapeutic indication.

The pharmaceutical company presented the randomised controlled trial RATIONALE 302 for the benefit assessment, which compared tislelizumab with a therapy according to doctor's instructions with selection of docetaxel, paclitaxel and irinotecan. The RATIONALE 302 study is unsuitable for the benefit assessment because the comparator therapy of the study does not correspond to the appropriate comparator therapy. There are therefore no appropriate data for the benefit assessment.

An additional benefit of tislelizumab for the treatment of adults with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy 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).

The resolution is based on the information provided by the pharmaceutical company. This information is subject to uncertainties, partly due to a large percentage of missing information

on the IUCC stage in the registry analysis from 2020 used by the pharmaceutical company. Furthermore, there are uncertainties in connection with the differentiation between resectable and unresectable tumours within stage III. In addition, the pharmaceutical company assumes that tislelizumab is only suitable for those patients in the present therapeutic indication who do not have increased PD-L1 expression and consequently have not received any previous therapy with an immune checkpoint inhibitor. In contrast, in the benefit assessment procedure for nivolumab (resolution of 1 July 2021), the SHI target population was derived independently of the presence of PD-L1 expression, which is why a higher number of patients was determined in this previous resolution.

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 as well as specialists in internal medicine and gastroenterology and other specialists participating in the Oncology Agreement, all of whom are experienced in the treatment of patients with oesophageal cancer.

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).

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.

Treatment period:

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	Continuously, 1x every 21 days	17.4	1	17.4
Appropriate comparator therapy				
Nivolumab	Continuously, 1x every 14 days or continuously, 1x every 28 days	26.1 13.0	1 1	26.1 13.0

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.

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					
Nivolumab	240 mg or 480 mg	240 mg or 480 mg	2 x 120 mg or 4 x 120 mg	26.1 or 13.0	52.2 x 120 mg or 52.0 x 120 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:

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
Appropriate comparator therapy					
Nivolumab 120 mg	1 CIS	€ 1,539.71	€ 1.77	€ 84.64	€ 1,453.30
Abbreviations: CIS = concentrate for the preparation of an infusion solution					

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.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 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:

Adults with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma 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 21 February 2023, 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 27 February 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 1, sentence 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
Subcommittee on Medicinal Products	27 February 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
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