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 Tepotinib (advanced non-small cell lung cancer, METex14 skipping, pretreated patients)

of 1 September 2022

Contents

Courtesy translation – only the German version is legally binding.

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 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 relevant date for the first placing on the (German) market of the active ingredient tepotinib in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 1 March 2022. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 22 February 2022.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de) on 1 June 2022, 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 tepotinib compared to 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

Courtesy translation – only the German version is legally binding.

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 tepotinib.

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:

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

2.1.1 Approved therapeutic indication of Tepotinib (Tepmetko) in accordance with the product information

TEPMETKO as monotherapy is indicated for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping, who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

Therapeutic indication of the resolution (resolution of 01.09.2022):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

Appropriate comparator therapy for tepotinib as monotherapy:

- Cisplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed (except in the case of predominantly squamous histology))

or

- Carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed (except in the case of predominantly squamous histology)) cf. Annex VI to Section K of the Pharmaceuticals Directive

or

- Carboplatin in combination with nab-paclitaxel

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Courtesy translation – only the German version is legally binding.

or

– Monotherapy with gemcitabine or vinorelbine (only for patients with ECOG performance status 2 as an alternative to platinum-based combination treatment)

b) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a platinum-containing chemotherapy

Appropriate comparator therapy for tepotinib 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, Tumour Proportion Score (TPS) ≥ 1%)

or

– Atezolizumab

or

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

c) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-based chemotherapy or after sequential therapy with a-PD-1/PD-L1 antibody and a platinum-containing chemotherapy

Appropriate comparator therapy for tepotinib as monotherapy:

Patient-individual therapy, taking into account previous therapy and histology with selection of afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab and docetaxel in combination with nintedanib and vinorelbine.

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

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

Courtesy translation – only the German version is legally binding.

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.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. In terms of the authorisation status, the following active ingredients are available for the treatment of advanced NSCLC: cisplatin, docetaxel, etoposide, gemcitabine, ifosfamide, mitomycin, paclitaxel, nab-paclitaxel, pemetrexed, vindesine, vinorelbine; alectinib, amivantamab, brigatinib, capmatinib, cemiplimab, ceritinib, crizotinib, dabrafenib, dacomitinib, erlotinib, gefitinib, lorlatinib, nintedanib, osimertinib, pralsetinib, sotorasib, selpercatinib, trametinib, atezolizumab, bevacizumab, durvalumab, necitumumab, nivolumab, pembrolizumab and ramucirumab.

Apart from tepotinib and capmatinib, there are currently no other medicinal therapies specifically approved for the treatment of NSCLC with alterations leading to METex14 skipping.

The active ingredient capmatinib was only recently approved on 20.06.2022. The benefit assessment procedure for capmatinib started on 15.08.2022.

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. For advanced NSCLC, there are resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V on the active ingredients afatinib, alectinib, amivantamab, atezolizumab, brigatinib, cemiplimab, ceritinib, crizotinib, dabrafenib, dacomitinib, durvalumab, lorlatinib, necitumumab, nintedanib, nivolumab, osimertinib, pembrolizumab, ramucirumab, pralsetinib, sotorasib, selpercatinib and trametinib.

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

Courtesy translation – only the German version is legally binding.

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.

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 health care provision.

At this time, it is assumed that no other molecularly stratified therapy (directed against ALK, BRAF, EGFR, exon-20, KRAS G12C, RET or ROS1) will be considered for patients at the time of therapy with tepotinib.

For the present therapeutic indication, it is also assumed that the patients are generally eligible for active antineoplastic therapy, which is why best supportive care is not considered as an appropriate comparator therapy in the present case.

It should be noted that there is no higher-quality evidence for the treatment of advanced NSCLC with alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping in relation to MET overexpression. So far, apart from tepotinib and capmatinib, there are no other medicinal therapies specifically approved for the treatment of NSCLC with alterations leading to METex14 skipping. The active ingredient capmatinib was only recently approved, on 20.06.2022, and has been in the benefit assessment procedure since 15.08.2022. The therapeutic significance of capmatinib cannot be conclusively assessed at present, which is why this active ingredient is not currently being considered as an appropriate comparator therapy. Any change in the appropriate comparator therapy requires a decision by the G-BA.

Therefore, those therapy options that are applied independently of a MET alteration are basically considered for the present treatment setting.

In the second-line treatment, depending on the first-line therapy, a distinction is made between a) patients with a PD-1/PD-L1 antibody as monotherapy pretreatment, b) patients with cytotoxic chemotherapy pretreatment and c) after first-line therapy with a-PD-1/PD-L1 antibody in combination with a platinum-containing chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy as pretreatment.

a) Following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

In the guidelines, whose recommendations already include first-line therapy with immune checkpoint inhibitor (ICI), cytotoxic chemotherapy is also recommended for this patient group in the 2nd line, with platinum-containing chemotherapy being given the highest priority overall. In this regard, platinum-based (cisplatin or carboplatin)

Courtesy translation – only the German version is legally binding.

combination chemotherapy with a third-generation cytostatic (vinorelbine, gemcitabine, docetaxel, paclitaxel or pemetrexed) represents the previous and current therapy standard. It cannot be deduced from the available evidence that a combination is clearly inferior or superior in terms of therapeutic benefit.

In contrast to cisplatin, carboplatin is not approved for the treatment of NSCLC, but can be prescribed as "off-label use" (see Annex VI to Section K of the Pharmaceuticals Directive), whereby the selection of the platinum component (carboplatin or cisplatin) should be based in the specific case on the different toxicity profile of the two substances and on the existing comorbidities of the patients; cf. Annex VI to Section K of the Pharmaceuticals Directive.

The carboplatin combination with nab-paclitaxel is approved for the treatment of NSCLC and is also recommended in the guidelines.

The question of the extent to which platinum-based combination chemotherapy should also be considered in patients with ECOG performance status 2 is not clearly answered in the present guidelines. In particular, for patients with reduced general condition, the toxicity profile of a platinum-based combination chemotherapy must be weighed against the expected benefit, taking into account patient-individual criteria. Alternatively, for patients with ECOG performance status 2, monochemotherapy with gemcitabine or vinorelbine is considered appropriate for this patient group, in addition to platinum-based combination chemotherapy.

With regard to the approved therapeutic indications of pemetrexed, gemcitabine and nab-paclitaxel, the use of a PD-1/ PD-L1 inhibitor in prior therapy is not interpreted as a line of therapy to be considered with regard to the marketing authorisation of the medicinal products.

In the overall assessment, the G-BA determined cisplatin in combination with a third-generation cytostatic, carboplatin in combination with a third-generation cytostatic, carboplatin in combination with nab-paclitaxel and monotherapy with gemcitabine or vinorelbine as equally appropriate comparator therapies for this patient group. The additional benefit can be demonstrated compared to one of the treatment options mentioned.

b) Following first-line therapy with cytotoxic chemotherapy

For patients with NSCLC for whom further antineoplastic therapy is indicated after first-line chemotherapy, several treatment options are available on the basis of the available evidence with the cytotoxic chemotherapeutic agents docetaxel and pemetrexed, in each case as monotherapy, docetaxel in combination with nintedanib and the ICIs nivolumab, pembrolizumab and atezolizumab, partly only under certain conditions.

With docetaxel and pemetrexed, both as monotherapy, two established chemotherapeutic agents are available for second-line chemotherapy, although pemetrexed is unsuitable for predominantly squamous histology. 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

Courtesy translation – only the German version is legally binding.

compared to docetaxel monotherapy (resolution of 18 June 2015). In the guidelines, docetaxel in combination with nintedanib is recommended alongside the other chemotherapy options, but is not regularly preferred over them. Based on the available evidence and corresponding therapy recommendations in the guidelines, docetaxel and pemetrexed, each as monotherapy, as well as docetaxel in combination with nintedanib, are considered therapeutically comparable, subject to tumour histology and the different side effect profile.

For nivolumab for the treatment of adults after prior chemotherapy and squamous tumour histology, an indication of a considerable additional benefit was identified in the benefit assessment compared to docetaxel (resolution of 4 February 2016). For nivolumab for the treatment of adults after prior chemotherapy and non-squamous tumour histology, an indication of a considerable additional benefit was also identified in the benefit assessment compared to docetaxel (resolution of 20 October 2016).

For pembrolizumab and atezolizumab, used after prior chemotherapy, the benefit assessment also found an indication of a considerable additional benefit compared to docetaxel (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%).

Nivolumab, pembrolizumab and atezolizumab each lead to a significant prolongation in overall survival compared with docetaxel and also to a significant reduction in side effects. Accordingly, the guidelines regularly prefer immune checkpoint inhibitors over cytotoxic chemotherapeutic agents. 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 cytotoxic chemotherapy. Therefore, in PD-L1 negative tumours, alternative cytotoxic chemotherapeutic agents are also determined as an appropriate comparator therapy for the immune checkpoint inhibitors.

For ramucirumab in combination with docetaxel, no additional benefit was shown in the benefit assessment compared to docetaxel (resolution of 1 September 2016). Likewise, no additional benefit was identified in the benefit assessment of afatinib compared to docetaxel (resolution of 20 October 2016). Taking into account that benefit-assessed medicinal therapies with an additional benefit are available in the present indication, the treatment options ramucirumab in combination with docetaxel as well as afatinib, for which no additional benefit could be determined in each case, are not considered as an appropriate comparator therapy.

In the overall assessment, the G-BA determined docetaxel, pemetrexed, nivolumab, pembrolizumab, atezolizumab and docetaxel in combination with nintedanib as equally appropriate comparator therapies for this patient group. The additional benefit can be demonstrated compared to one of the treatment options mentioned.

c) *Following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-containing chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy*

Courtesy translation – only the German version is legally binding.

The treatment setting addressed in the present case may include patients who have either already received a platinum-containing chemotherapy in combination with a PD-1/PD-L1 antibody therapy as part of first-line therapy or have received a platinum-containing chemotherapy and a PD-1/PD-L1 antibody therapy sequentially in the first and second line of therapy (regardless of which of the therapies was administered first).

For the first-mentioned option of platinum-containing chemotherapy in combination with a PD-1/PD-L1 antibody therapy, it is true that this is a fairly new treatment option for advanced and metastatic NSCLC. For both the treatment setting after platinum-containing chemotherapy in combination with a PD-1/PD-L1 antibody therapy and for further treatment after sequential therapy with a platinum-containing chemotherapy and a PD-1/PD-L1 antibody therapy in the first and second line of therapy, there is no higher-quality evidence based on clinical studies.

According to the guidelines, patients in the present therapeutic indication are eligible for antineoplastic subsequent therapy, taking into account the prior therapy and tumour histology, with docetaxel, pemetrexed, docetaxel in combination with ramucirumab or nintedanib, erlotinib and afatinib being named as treatment options.

The recommendation of further therapy with a (different) PD-1/ PD-L1 antibody does not emerge from the available evidence.

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).

For ramucirumab in combination with docetaxel, no additional benefit was shown in the benefit assessment compared to docetaxel (resolution of 1 September 2016). The benefit assessment showed no additional benefit for afatinib for the treatment of adults with squamous cell histology compared to the appropriate comparator therapy docetaxel (resolution of 20 October 2016). With regard to the above-mentioned benefit assessments, however, it should be noted that they were based on the treatment setting of a second-line therapy after prior platinum-containing chemotherapy and thus, on an indication that deviated from the present treatment setting with regard to the prior therapy.

Overall, in view of the limited evidence for the present treatment setting, the G-BA determined a patient-individual therapy as the appropriate comparator therapy, taking into account the prior therapy and histology, selecting afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab and docetaxel in combination with nintedanib as well as vinorelbine.

The specific appropriate comparator therapy comprises a selection of different active ingredients and combinations of active ingredients that can be considered for the present therapeutic indication according to the authorisation status of the medicinal products and the recommendations in the guidelines.

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

Courtesy translation – only the German version is legally binding.

2.1.3 Extent and probability of the additional benefit

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

a) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

An additional benefit is not proven.

b) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a platinum-containing chemotherapy

An additional benefit is not proven.

c) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-based chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy

An additional benefit is not proven.

Justification:

Data basis

VISION study

No relevant randomised clinical studies for a direct or adjusted indirect comparison that allow a comparison of tepotinib with the appropriate comparator therapy were identified by the pharmaceutical company.

The pharmaceutical company presents results from the still ongoing, open-label, 2-part, uncontrolled, multicentre phase II VISION study for the proof of additional benefit of tepotinib for the treatment of adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping, who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

The study enrolled adult patients with locally advanced or metastatic NSCLC with proven alterations leading to METex14 skipping who were therapy-naïve or had received up to 2 prior advanced therapies. Furthermore, patients had to be in good general condition at the start of the study, corresponding to an Eastern Cooperative Oncology Group - Performance Status (ECOG-PS) of 0 or 1.

In the first part of the study, patients were enrolled based on the mutation present and divided into 2 cohorts, cohort A (alterations leading to METex14 skipping) or cohort B (MET amplification). In the subsequent, second part of the study, patients harbouring alterations

Courtesy translation – only the German version is legally binding.

leading to METex14 skipping were enrolled in confirmatory cohort C after completion of cohort A recruitment. These two cohorts A and C were evaluated together as the METex14 skipping cohort by the pharmaceutical company for the benefit assessment.

In addition to the objective response rate according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 as the primary endpoint, overall survival, health-related quality of life, morbidity and adverse events in particular were collected as patient-relevant secondary endpoints.

As the VISION study is a 1-arm study, the pharmaceutical company classifies the results of the VISION study using the results, based on the 0015 and 0035 studies, from everyday care by comparing individual endpoints descriptively.

0015 and 0035 studies

These two studies are 2 retrospective, non-interventional studies by the pharmaceutical company based on electronic health records of oncology practices from the USA (0015 study) and patient records from several oncology study sites (0035 study). In this study, the efficacy of therapies was investigated on the basis of overall survival and tumour response in patients with advanced NSCLC (stage IIIB to IV) with alterations leading to METex14 skipping. Inclusion criterion for both studies was the index diagnosis of advanced NSCLC with alterations leading to METex14 skipping or MET amplifications, with no exclusion criteria defined in each case. A total of 54 (0015 study) and 70 (0035 study) patients were included in the analysis, of whom only 5 (0015 study) and 44 (0035 study) met the inclusion and exclusion criteria of the VISION study.

Overall assessment

The evaluations presented by the pharmaceutical company are a purely descriptive comparison of individual endpoints from different studies.

The results of the VISION study presented alone are not suitable for assessing the additional benefit of tepotinib as they do not allow a comparison with the appropriate comparator therapy.

In order to classify an additional benefit of tepotinib, the pharmaceutical company made a purely descriptive comparison between the results of individual endpoints from the VISION study and the 2 non-interventional studies, based on health or patient records (0015 and 0035). In this context, the pharmaceutical company neither conducted an information procurement for the appropriate comparator therapy nor a systematic review of the cohorts of 0015 and 0035 studies presented by them. The data presented by the pharmaceutical company to classify the results from their 1-arm study are therefore not suitable for assessing the additional benefit of tepotinib compared to the appropriate comparator therapy.

Overall, there are therefore no data for the assessment of the additional benefit of tepotinib compared to the appropriate comparator therapy. Therefore, an additional benefit is not proven for all 3 patient groups.

In the present therapeutic indication, tepotinib may represent a relevant treatment option for individual patients.

Courtesy translation – only the German version is legally binding.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Tepmetko with the active ingredient tepotinib.

The active ingredient tepotinib is approved for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with alterations leading to METex14 skipping (exon 14 skipping in the mesenchymal-epithelial transition factor gene) who require systemic therapy after platinum-based chemotherapy and/or treatment with immunotherapy.

In the therapeutic indication under consideration, 3 patient groups were distinguished and the appropriate comparator therapy was determined as follows (abbreviated version):

a) Adults after first-line therapy with a PD-1/PD-L1 antibody as monotherapy

   The appropriate comparator therapy includes platinum-based (cisplatin/ carboplatin) chemotherapy. For adults with an ECOG performance status of 2, monochemotherapy may be considered as an alternative.

b) Adults after first-line therapy with a cytotoxic chemotherapy

   The appropriate comparator therapy includes different chemotherapies without platinum (cisplatin/ carboplatin) as well as treatment with an immune checkpoint inhibitor as monotherapy.

c) Adults after first-line therapy with a PD-1/PD-L1 antibody in combination with platinum-containing chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and platinum-containing chemotherapy.

   The appropriate comparator therapy includes several active ingredients as monotherapy as well as in combination therapies, which are available for a patient-individual treatment decision, taking into account prior therapy and histology.

For the benefit assessment, the pharmaceutical company submitted the results from the VISION study for the treatment with tepotinib. This is a non-controlled study that does not include a comparator group and therefore does not allow a comparison with the appropriate comparator therapy.

For the classification of the results in everyday care, the pharmaceutical company presents 2 non-interventional studies based on health or patient records (0015 and 0035). This is a purely descriptive comparison of individual endpoints.

Overall, the data presented are unsuitable for the assessment of the additional benefit, which is why an additional benefit of tepotinib compared to the appropriate comparator therapy is not proven.

In the present therapeutic indication, tepotinib may represent a relevant treatment option for individual patients.

Courtesy translation – only the German version is legally binding.

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

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

For the number of German patients with lung cancer, the projected incidence for 2021 (60,333 patients) is used as the basis for the calculations.

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

1. The percentage of lung cancer patients with NSCLC is between 73.6% and 83.6% (44,405 to 50,439 patients).

2. Of these, 51.8% to 61.6% of patients are in stage IIIB and IV at initial diagnosis (23,002 to 31,070 patients). The number of patients in stage I and IIA who have progressed to stage IV in 2021 is 5,866 to 8,364 patients. The total number of patients in tumour stage IIIB and IV is 28,868 to 39,434.

3. First-line therapy is given in 76.9% to 96.1% of cases (22,199 - 37,896 patients).

4. The percentage of patients with alterations leading to METex14 skipping is 2.7% (599 to 1,023 patients).

5. Of these, as first-line treatment

   5a. 14.3% (86 to 146 patients) received monotherapy with a PD-1/PD-L1 antibody,

   5b. 10.7% (64 to 110 patients) received chemotherapy or

   5c. 75% (449 to 767 patients) received a PD-1/PD-L1 antibody in combination with platinum-containing chemotherapy.

6. Taking into account a percentage of SHI-insured patients of 88.3%, step 5a-c results in 529 to 903 patients after prior therapy with a PD-1/PD-L1 antibody and/or chemotherapy, of which

   6a. 80 to 130 patients with a PD-1/PD-L1 antibody as first-line treatment (patient population a),

   6b. 60 to 100 patients with chemotherapy as first-line treatment (patient population b) and

   6c. 400 to 680 patients with a PD-1/PD-L1 antibody and platinum-containing chemotherapy as first-line treatment

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

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Tepmetko (active ingredient: tepotinib) at the following publicly accessible link (last access: 16 August 2022):

Courtesy translation – only the German version is legally binding.

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

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

METex14 skipping test
Prior to treatment with Tepmetko, the presence of alterations leading to METex14 skipping must be confirmed by a validated test method.

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: 15 August 2022).

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				
Tepotinib	1 x daily	365	1	365
Appropriate comparator therapy				
Patient population a)				
Cisplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed)[2]				
Cisplatin	1 x per 21-day cycle	17.4	1	17.4
Vinorelbine	2 x per 21-day cycle	17.4	2	34.8
Gemcitabine	2 x per 21-day cycle	17.4	2	34.8
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
Pemetrexed	1 x per 21-day cycle	17.4	1	17.4
Carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed)[2]				
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Vinorelbine	2 x per 21-day cycle	17.4	2	34.8

[2] except in the case of predominantly squamous histology

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Gemcitabine	2 x per 21-day cycle	17.4	2	34.8
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Paclitaxel	1 x per 21-day cycle	17.4	1	17.4
Pemetrexed	1 x per 21-day cycle	17.4	1	17.4
Carboplatin in combination with nab-paclitaxel				
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
nab-paclitaxel	3 x per 21-day cycle	17.4	3	52.2
Monotherapy with gemcitabine or vinorelbine[3]				
Gemcitabine	on day 1, 8 and 15 of a 28-day cycle	13.0	3	39
Vinorelbine	1 x every 7 days	52.1	1	52.1
Patient population b)				
Docetaxel (only for patients with PD-L1 negative tumours)				
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Pemetrexed[4]				
Pemetrexed	1 x per 21-day cycle	17.4	1	17.4
Nivolumab				
Nivolumab	1 x per 14-day cycle	26.1	1	26.1
Pembrolizumab[5]				
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7
Atezolizumab				
Atezolizumab	1 x per 21-day cycle	17.4	1	17.4
Docetaxel in combination with nintedanib[6]				
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Nintedanib	2 x on day 2-21 of a 21-day cycle	17.4	20	348

[3] only for patients with ECOG performance status 2 as an alternative to platinum-based combination treatment

[4] only for patients with PD-L1 negative tumours and except in the case of predominantly squamous cell histology

[5] only for patients with PD-L1 expressing tumours, Tumour Proportion Score (TPS) ≥ 1%

[6] only for patients with PD-L1 negative tumours and adenocarcinoma histology

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Patient population c)				
Patient-individual therapy, taking into account previous therapy and histology with selection of afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab, docetaxel in combination with nintedanib and vinorelbine				
Afatinib				
Afatinib	1 x daily	365	1	365
Pemetrexed				
Pemetrexed	1 x per 21-day cycle	17.4	1	17.4
Erlotinib				
Erlotinib	1 x daily	365	1	365
Docetaxel				
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Docetaxel in combination with ramucirumab				
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Ramucirumab	1 x per 21-day cycle	17.4	1	17.4
Docetaxel in combination with nintedanib[6]				
Docetaxel	1 x per 21-day cycle	17.4	1	17.4
Nintedanib	2 x on day 2-21 of a 21-day cycle	17.4	20	348
Vinorelbine				
Vinorelbine	1 x every 7 days	52.1	1	52.1

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 comorbidities) are not taken into account when calculating the annual treatment costs.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

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

Courtesy translation – only the German version is legally binding.

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements were applied (average height: 1,72 m; average body weight: 77 kg). This results in a body surface area of 1.90 m² (calculated according to Du Bois 1916)[7].

Cisplatin is dosed differently, depending on the concomitant active ingredient. According to the product information of the concomitant medicinal products, the single dose of cisplatin in combination with vinorelbine or gemcitabine is 75 - 100 mg/m², in combination with docetaxel, pemetrexed and pembrolizumab 75 mg/m² and in combination with paclitaxel 80 mg/m².

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

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					
Tepotinib	450 mg	450 mg	2 x 225 mg	365	730 x 225 mg
Appropriate comparator therapy					
Patient population a)					
Cisplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed)[2]					
Cisplatin	75 mg/m² = 142.5 mg	142.5 mg	1 x 100 mg + 1 x 50 mg	17.4	17.4 x 100 mg + 17.4 x 50 mg
	80 mg/m² = 152 mg	152 mg	1 x 100 mg + 1 x 50 mg + 1 x 10 mg	17.4	17.4 x 100 mg + 17.4 x 50 mg + 17.4 x 10 mg
	100 mg/m² = 190 mg	190 mg	2 x 100 mg	17.4	34.8 x 100 mg
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg
Gemcitabine	1,250 mg/m² = 2,375 mg	2,375 mg	1 x 2,000 mg x 2 x 200 mg	34.8	34.8 x 2,000 mg + 69.6 x 200 mg
Paclitaxel	175 mg/m² = 332.5 mg	332.5 mg	2 x 100 + 1 x 150 mg	17.4	17.4 x 150 mg + 34.8 x 100 mg

[7] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Pemetrexed	500 mg/m² = 950 mg	950 mg	2 x 500 mg	17.4	34.8 x 500 mg
Vinorelbine	25 mg/m² = 47.5 mg - 30 mg/m² = 57 mg	47.5 mg - 57 mg	1 x 50 mg - 1 x 50 mg + 1 x 10 mg	34.8	34.8 x 50 mg - 34.8 x 50 mg + 34.8 x 10 mg
Carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed)[2]					
Carboplatin	500 mg/m² = 950 mg	950 mg	2 x 450 mg + 1 x 50 mg	17.4	34.8 x 450 mg + 17.4 x 50 mg
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg
Gemcitabine	1,250 mg/m² = 2,375 mg	2,375 mg	1 x 2,000 mg + 2 x 200 mg	34.8	34.8 x 2,000 mg + 69.6 x 200 mg
Paclitaxel	175 mg/m² = 332.5 mg	332.5 mg	2 x 100 + 1 x 150 mg	17.4	17.4 x 150 mg + 34.8 x 100 mg
Pemetrexed	500 mg/m² = 950 mg	950 mg	2 x 500 mg	17.4	34.8 x 500 mg
Vinorelbine	25 mg/m² = 47.5 mg - 30 mg/m² = 57 mg	47.5 mg - 57 mg	1 x 50 mg - 1 x 50 mg + 1 x 10 mg	34.8	34.8 x 50 mg - 34.8 x 50 mg + 34.8 x 10 mg
Carboplatin in combination with nab-paclitaxel					
Carboplatin	500 mg/m² = 950 mg	950 mg	2 x 450 mg + 1 x 50 mg	17.4	34.8 x 450 mg + 17.4 x 50 mg
nab-paclitaxel	100 mg/m² = 190 mg	190 mg	2 x 100 mg	52.2	104.4 x 100 mg
Monotherapy with gemcitabine or vinorelbine[3]					
Gemcitabine	1,000 mg/ m² = 1,900 mg	1,900 mg	1 x 2,000 mg	39	39 x 2,000 mg
Vinorelbine	25 mg/m² = 47.5 mg - 30 mg/mg² = 57 mg	47.5 mg – 57 mg	1 x 50 mg - 1 x 50 mg + 1 x 10 mg	52.1	52.1 x 50 mg - 52.1 x 50 mg + 52.1 x 10 mg
Patient population b)					

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Docetaxel (only for patients with PD-L1 negative tumours)					
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg
Pemetrexed[4]					
Pemetrexed	500 mg/m² = 950 mg	950 mg	2 x 500 mg	17.4	34.8 x 500 mg
Nivolumab					
Nivolumab	240 mg	240 mg	2 x 120 mg	26.1	52.2 x 120 mg
Pembrolizumab[5]					
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	1,200 mg	1,200 mg	1 x 1,200 mg	17.4	17.4 x 1,200 mg
Docetaxel in combination with nintedanib[6]					
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg
Nintedanib	200 mg	400 mg	4 x 100 mg	348	1,392 x 100 mg
Patient population c)					
Patient-individual therapy, taking into account previous therapy and histology with selection of afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab, docetaxel in combination with nintedanib and vinorelbine.					
Afatinib					
Afatinib	40 mg	40 mg	1 x 40 mg	365	365 x 40 mg
Pemetrexed					
Pemetrexed	500 mg/m² = 950 mg	950 mg	2 x 500 mg	17.4	34.8 x 500 mg
Erlotinib					
Erlotinib	150 mg	150 mg	1 x 150 mg	365	365 x 150 mg
Docetaxel					
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg

Courtesy translation – only the German version is legally binding.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Docetaxel in combination with ramucirumab					
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg
Ramucirumab	10 mg/kg = 770 mg	770 mg	1 x 500 mg + 3 x 100 mg	17.4	17.4 x 500 mg + 52.2 x 100 mg
Docetaxel in combination with nintedanib					
Docetaxel	75 mg/m² = 142.5 mg	142.5 mg	2 x 80 mg	17.4	34.8 x 80 mg
Nintedanib	200 mg	400 mg	4 x 100 mg	348	1,392 x 100 mg
Vinorelbine					
Vinorelbine	25 mg/m² = 47.5 mg - 30 mg/m² = 57 mg	47.5 mg - 57 mg	1 x 50 mg - 1 x 50 mg + 1 x 10 mg	52.1	52.1 x 50 mg - 52.1 x 50 mg + 52.1 x 10 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.

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					
Tepotinib 225 mg	60 FCT	€ 10,476.07	€ 1.77	€ 595.00	€ 9,879.30
Appropriate comparator therapy					
Atezolizumab 1,200 mg	1 CIS	€ 4,151.65	€ 1.77	€ 233.81	€ 3,916.07
Afatinib 40 mg	28 FCT	€ 2,515.23	€ 1.77	€ 140.35	€ 2,373.11

Courtesy translation – only the German version is legally binding.

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
Carboplatin 450 mg	1 CIS	€ 228.21	€ 1.77	€ 10.29	€ 216.15
Carboplatin 50 mg	1 CIS	€ 34.63	€ 1.77	€ 1.11	€ 31.75
Cisplatin 100 mg	1 CIS	€ 76.55	€ 1.77	€ 3.10	€ 71.68
Cisplatin 50 mg	1 CIS	€ 47.67	€ 1.77	€ 1.73	€ 44.17
Cisplatin 10 mg	1 CIS	€ 17.49	€ 1.77	€ 0.30	€ 15.42
Docetaxel 80 mg	1 CIS	€ 415.86	€ 1.77	€ 19.20	€ 394.89
Erlotinib 150 mg[8]	30 FCT	€ 880.24	€ 1.77	€ 68.73	€ 809.74
Gemcitabine 200 mg	1 CIS	€ 28.81	€ 1.77	€ 0.83	€ 26.21
Gemcitabine 2,000 mg	1 CIS	€ 194.20	€ 1.77	€ 8.68	€ 183.75
nab-paclitaxel 100 mg	1 PIS	€ 429.33	€ 1.77	€ 52.91	€ 374.65
Nintedanib 100 mg	120 SC	€ 2,761.26	€ 1.77	€ 0.00	€ 2,759.49
Nivolumab 120 mg	1 CIS	€ 1,546.93	€ 1.77	€ 85.05	€ 1,460.11
Paclitaxel 100 mg	1 CIS	€ 304.03	€ 1.77	€ 13.89	€ 288.37
Paclitaxel 150 mg	1 CIS	€ 450.83	€ 1.77	€ 20.86	€ 428.20
Pembrolizumab 100 mg	1 CIS	€ 3,035.99	€ 1.77	€ 170.10	€ 2,864.12
Pemetrexed 500 mg	1 PCI	€ 266.85	€ 1.77	€ 12.13	€ 252.95
Ramucirumab 100 mg	1 CIS	€ 441.14	€ 1.77	€ 23.80	€ 415.57
Ramucirumab 500 mg	1 CIS	€ 2,141.31	€ 1.77	€ 119.00	€ 2,020.54
Vinorelbine 10 mg	1 CIS	€ 41.63	€ 1.77	€ 3.84	€ 36.02
Vinorelbine 50 mg	1 CIS	€ 156.68	€ 1.77	€ 18.40	€ 136.51
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; PIS = powder for the preparation of an infusion suspension; PCI = powder for a concentrate for the preparation of a solution for infusion; SC = soft capsules					

LAUER-TAXE® last revised: 15 August 2022

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 to the Pharmaceuticals Directive (so-called OTC

[8] Fixed reimbursement rate

Courtesy translation – only the German version is legally binding.

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.

In clinical practice, an appropriate antiemetic treatment is established before and/or after administration of cisplatin. The product information for cisplatin does not provide any specific information on this, which is why the necessary costs cannot be quantified.

Type of service	Cost/ pack (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Cost/ service	Treatment days/ year	Cost/ patient/ year
Medicinal product to be assessed: tepotinib							
Not applicable							
Appropriate comparator therapy							
Cisplatin							
Mannitol 10% infusion solution, 37.5 g/day, 10 x 500 ml INF	€ 106.22	€ 5.31	€ 9.81	€ 91.10	€ 9.11	17.4	€ 158.51
Sodium chloride 0.9% infusion solution, 3 - 4.4 l/day, 10 x 500 ml INF/ 10 x 1,000 ml INF	€ 22.72	€ 1.14	€ 0.69	€ 20.89	€ 15.12	17.4	€ 263.11 -
	€ 35.47	€ 1.77	€ 1.12	€ 32.58	€ 9.55	17.4	€ 170.07
Paclitaxel							
Dexamethasone 20 mg[8], 50 TAB	€ 118.85	€ 1.77	€ 0.00	€ 117.08	€ 4.68	17.4	€ 40.74
Dimetindene IV 1 ml/ 10 kg, 5 x 4 mg SFI	€ 23.67	€ 1.77	€ 5.58	€ 16.32	€ 6.53	17.4	€ 113.59
Cimetidine 300 mg IV, 10 CIS x 200 mg	€ 19.77	€ 1.77	€ 0.00	€ 18.00	€ 3.60	17.4	€ 62.64
Pemetrexed							
Dexamethasone	€ 79.50	€ 1.77	€ 5.40	€ 72.33	€ 1.45	52.2	€ 75.51

Courtesy translation – only the German version is legally binding.

Type of service	Cost/ pack (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Cost/ service	Treatment days/ year	Cost/ patient/ year
2 x 4 mg[8, 9], 100 TAB							
Folic acid 350 – 1,000 µg/day, 100 TAB	€ 16.70	€ 0.84	€ 2.41	€ 13.45	€ 0.13 - € 0.27	365	€ 49.09 - € 98.19
Vitamin B12[8] 1,000 µg/day, every 3 cycles, 10 SFI	€ 7.40	€ 0.37	€ 0.33	€ 6.70	€ 0.67	5.8	€ 3.89
Abbreviations: CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; INF = infusion solution; TAB = tablets							

Other SHI services:

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

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic drugs a maximum amount of € 81 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 71 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.

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.

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

Courtesy translation – only the German version is legally binding.

4. Process sequence

At its session on 10 November 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 22 February 2022, the pharmaceutical company submitted a dossier for the benefit assessment of tepotinib to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 28 February 2022 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient tepotinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 30 May 2022, and the written statement procedure was initiated with publication on the website of the G-BA on 1 June 2022. The deadline for submitting written statements was 22 June 2022.

The oral hearing was held on 11 July 2022.

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 23 August 2022, and the proposed resolution was approved.

At its session on 1 September 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	10 November 2020	Determination of the appropriate comparator therapy
Working group Section 35a	5 July 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	11 July 2022	Conduct of the oral hearing
Working group Section 35a	19 July 2022 2 August 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal products	23 August 2022	Concluding discussion of the draft resolution

Courtesy translation – only the German version is legally binding.

Plenum	1 September 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 1 September 2022

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

Prof. Hecken

Courtesy translation – only the German version is legally binding.