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 and Annex XIIa – Combinations of Medicinal Products with New Active Ingredients according to Section 35a SGB V Encorafenib (new therapeutic indication: non-small cell lung cancer, advanced, BRAF V600E mutation, combination with binimetinib)

of 20 March 2025

Contents

1. Legal basis ... 2

2. Key points of the resolution ... 2

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy ... 3

2.1.1 Approved therapeutic indication of Encorafenib (Braftovi) in accordance with the product information ... 3

2.1.2 Zweckmäßige Vergleichstherapie ... 3

2.1.3 Extent and probability of the additional benefit ... 10

2.1.4 Summary of the assessment ... 11

2.2 Number of patients or demarcation of patient groups eligible for treatment ... 12

2.3 Requirements for a quality-assured application ... 12

2.4 Treatment costs ... 12

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 ... 33

3. Bureaucratic costs calculation ... 37

4. Process sequence ... 37

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 encorafenib (Braftovi) was listed for the first time on 1 October 2018 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 29 August 2024, encorafenib received marketing authorisation for a new therapeutic indication to be 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 23 September 2024, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with

Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient encorafenib with the new therapeutic indication

"Encorafenib in combination with binimetinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 January 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 encorafenib 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 encorafenib.

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 Encorafenib (Braftovi) in accordance with the product information

Encorafenib in combination with binimetinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation.

Therapeutic indication of the resolution (resolution of 20 March 2025):

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) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

Appropriate comparator therapy for encorafenib in combination with binimetinib:

- Dabrafenib in combination with trametinib

  or

- pembrolizumab as monotherapy

  or

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

- atezolizumab as monotherapy

  or

- cemiplimab as monotherapy

  or

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

  or

- pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients without ECOG-PS 0-1)

  or

- atezolizumab in combination with bevacizumab, paclitaxel and carboplatin (only for patients with ECOG-PS 0-1)
- atezolizumab in combination with nab-paclitaxel and carboplatin (only for patients with ECOG-PS 0-1)
- cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)
- durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)

b) <u>Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy</u>

Appropriate comparator therapy for encorafenib in combination with binimetinib:

- Dabrafenib in combination with trametinib

  or

- pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients without ECOG-PS 0-1)

  or

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

  or

- atezolizumab in combination with bevacizumab, paclitaxel and carboplatin (only for patients with ECOG-PS 0-1)

  or

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

  or

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

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

Appropriate comparator therapy for encorafenib in combination with binimetinib:

- Dabrafenib in combination with trametinib

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. In terms of authorisation status, in addition to the medicinal products to be assessed, the cytostatic agents cisplatin, docetaxel, etoposide, gemcitabine, ifosfamide, mitomycin, paclitaxel, nab-paclitaxel, pemetrexed, vindesine, vinorelbine as well as the antibodies atezolizumab, bevacizumab, cemiplimab, ipilimumab, durvalumab, nivolumab, pembrolizumab, ramucirumab, tislelizumab, tremelimumab and the protein kinase inhibitors afatinib, dabrafenib, erlotinib, nintedanib and trametinib are available.

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

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

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

- Afatinib (resolution of 02.10.2016)
- Atezolizumab (resolutions of 16.03.2018, 02.04.2020, 19.11.2021 and 05.01.2023)
- Cemiplimab (resolutions of 20.01.2022 and 19.10.2023)
- Dabrafenib (resolution of 19.10.2017)
- Durvalumab (04.04.2019 and 05.0.2023)
- Ipilimumab (resolution of 03.06.2021)
- Nintedanib (resolution of 18.06.2015)
- Nivolumab (resolutions of 02.10.2016, 03.06.2021 and 01.02.2024)
- Pembrolizumab (resolutions of 03.08.2017, 19.09.2019 and 17.10.2024)
- Trametinib (resolution of 19.10.2017)
- Tremelimumab (resolution of 05.10.2023)
- Ramucirumab (resolutions of 01.09.2016 and 02.08.2020)

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

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

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

There is a joint written statement from the German Society for Haematology and Medical Oncology (DGHO), the Working Group for Internal Oncology of the German Cancer Society (AIO) and the German Respiratory Society (DGP).

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.

For the determination of the appropriate comparator therapy, it is assumed that tumours with BRAF V600 mutation are histologically predominantly adenocarcinomas, which is why therapy options that are explicitly indicated for squamous cell tumour histology are not regularly used in this therapeutic indication. In addition, for the present treatment setting of advanced BRAF V600E mutation-positive NSCLC, it is assumed across therapy lines 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. Furthermore, it is assumed that there is no indication for definitive chemoradiotherapy or local therapy.

First-line treatment

The available evidence shows that the combination therapy of dabrafenib and trametinib is used in the first-line treatment of BRAF V600 mutation-positive NSCLC and that a first-line treatment corresponding to wild-type NSCLC is recommended in addition to this targeted therapy.

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

a) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

   For first-line treatment of metastatic NSCLC with PD-L1 expression ≥ 50% of tumour cells, the guidelines recommend monotherapy with the approved immune checkpoint inhibitors atezolizumab, cemiplimab and pembrolizumab, regardless of histological status. In addition, immunochemotherapies are recommended, whereby a distinction is made between patients with good general condition (ECOG performance status (PS) 0-1) and reduced general condition (ECOG-PS 2) with regard to selection of therapy. As the evidence for patients with ECOG-PS 2 is limited, the therapy recommendations for immunochemotherapies are based on patients with ECOG-PS 0-1. Within this defined framework, pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy, atezolizumab in combination with bevacizumab, paclitaxel and carboplatin or atezolizumab in combination with nab-paclitaxel and carboplatin are used for patients with non-squamous NSCLC.

The combination therapies of nivolumab and ipilimumab and two cycles of platinum-based chemotherapy as well as cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy are also available as histology-independent treatment options.

Immunochemotherapy with the immune checkpoint inhibitor tislelizumab in combination with pemetrexed and platinum-containing chemotherapy is a new treatment option in this therapeutic indication. The active ingredient was only recently approved (marketing authorisation on 08.07.2024). Based on the generally accepted state of medical knowledge, tislelizumab in combination with pemetrexed and platinum-containing chemotherapy is not identified to be an appropriate comparator therapy for the present resolution.

In summary, the G-BA considers it appropriate on the available body of evidence to determine immune checkpoint inhibitors as monotherapies and in combination with platinum-containing chemotherapy as appropriate comparator therapies in addition to dabrafenib in combination with trametinib, whereby the immunochemotherapies are restricted to patients with an ECOG-PS of 0-1. In this context, individual therapy options only represent a comparator therapy for the part of the patient population that has the patient and disease characteristics specified in brackets. The therapeutic alternatives are only to be considered equally appropriate in the therapeutic indication, where the patient populations have the same characteristics.

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

b) <u>Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy</u>

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

The combination therapies of nivolumab and ipilimumab and two cycles of platinum-based chemotherapy as well as cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy are also available as histology-independent treatment options.

Immunochemotherapy with the immune checkpoint inhibitor tislelizumab in combination with pemetrexed and platinum-containing chemotherapy is a new treatment option in this therapeutic indication. The active ingredient was only recently approved (marketing authorisation on 08.07.2024). Based on the generally

accepted state of medical knowledge, tislelizumab in combination with pemetrexed and platinum-containing chemotherapy is not identified to be an appropriate comparator therapy for the present resolution.

In summary, the G-BA considers it appropriate on the basis of the available body of evidence to determine dabrafenib in combination with trametinib, atezolizumab as monotherapy and the immune checkpoint inhibitors in combination with platinum-containing chemotherapy as appropriate comparator therapies, whereby the combination immunochemotherapies are restricted to patients with an ECOG-PS of 0-1. In this context, individual therapy options only represent a comparator therapy for the part of the patient population that has the patient and disease characteristics specified in brackets. The therapeutic alternatives are only to be considered equally appropriate in the therapeutic indication, where the patient populations have the same characteristics.

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

Treatment after first-line therapy

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

For patients who have already been treated with a BRAF/MEK inhibitor in previous therapy, the available evidence does not recommend re-therapy with a BRAF/MEK inhibitor. Accordingly, no patients who have already been treated with a BRAF/MEK inhibitor in the previous therapy are taken as a basis for determining the appropriate comparator therapy. On the basis of the available evidence, the combination therapy of dabrafenib and trametinib is derived for the so defined treatment setting of BRAF V600 mutation-positive NSCLC after prior therapy without a BRAF/MEK inhibitor.

Overall, the G-BA therefore considers it appropriate to determine dabrafenib alone in combination with trametinib as appropriate comparator therapies for the patient group of adults with advanced NSCLC with a BRAF V600E mutation after first-line therapy.

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

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

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

Change of the appropriate comparator therapy

Compared to the originally determined appropriate comparator therapy, this is supplemented in the present resolution for patient groups a) and b) with "cemiplimab

in combination with platinum-based chemotherapy" and "durvalumab in combination with tremelimumab and platinum-based chemotherapy".

According to current evidence, immunochemotherapies should be offered for first-line treatment of metastatic NSCLC for patients with a good general condition (ECOG-PS 0-1), regardless of histological status and regardless of PD-L1 status. For patients with non-squamous NSCLC, cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy were also unanimously named in addition to pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy, atezolizumab in combination with bevacizumab, paclitaxel and carboplatin as well as atezolizumab in combination with nab-paclitaxel and carboplatin. The use of cemiplimab in combination with platinum-based chemotherapy and durvalumab in combination with tremelimumab and platinum-based chemotherapy is independent of NSCLC histology.

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

The present assessment of the additional benefit of encorafenib in combination with binimetinib remains unaffected.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of encorafenib in combination with binimetinib is assessed as follows:

a) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

An additional benefit is not proven.

b) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy

An additional benefit is not proven.

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

An additional benefit is not proven.

Justification:

About the PHAROS study

The pharmaceutical company presented results from the single-arm PHAROS study to prove the additional benefit.

Patients with metastatic NSCLC with a BRAF V600 mutation were enrolled in the ongoing, open-label, multicentre, single-arm phase II PHAROS study - 59 patients in the first-line and 39 pretreated patients. Pretreatment included platinum-based chemotherapy or an anti-PD-1 inhibitor or anti-PD-L1 inhibitor alone or in combination with platinum-based chemotherapy or an anti-PD-1 inhibitor or anti-PD-L1 inhibitor in combination with immunotherapy (such as ipilimumab) with or without platinum-based chemotherapy. The primary endpoint was the

objective response rate, secondary endpoints were overall survival, duration of response and progression-free survival.

No suitable data for an indirect comparison could be identified by the pharmaceutical company, which is why the pharmaceutical company decided not to present an indirect comparison in the dossier for the benefit assessment.

No assessable data are available as the single-arm PHAROS study does not allow a comparison with the appropriate comparator therapy in any of the three patient groups.

Conclusion

The G-BA therefore concluded that an additional benefit of encorafenib in combination with binimetinib in the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation is not proven.

2.1.4 Summary of the assessment

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

"Encorafenib in combination with binimetinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation."

In the therapeutic indication to be considered, three patient groups were distinguished:

a) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

b) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

The G-BA determined the appropriate comparator therapy to be various immunologically effective active ingredients - for first-line therapy in patient groups a) and b) - as monotherapy or in combination with chemotherapy as well as the combination of dabrafenib and trametinib, which is used specifically for BRAF V600 mutations. For patient group c), the G-BA determined dabrafenib in combination with trametinib as the appropriate comparator therapy.

Results from the ongoing single-arm PHAROS study were presented for the assessment. No suitable data for an indirect comparison could be identified by the pharmaceutical company, which is why the pharmaceutical company decided not to present an indirect comparison in the dossier for the benefit assessment.

No assessable data are available as the single-arm PHAROS study does not allow a comparison with the appropriate comparator therapy in any of the three patient groups.

The G-BA therefore concluded that an additional benefit of encorafenib in combination with binimetinib in the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation is not proven.

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

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

The G-BA bases its resolution on the information provided by the pharmaceutical company.

It should be noted that the upper limit for patient groups a) and b) is underestimated due to a potentially higher percentage of BRAF V600E mutations.

The numbers for patient group c) are subject to uncertainty due to potential prior therapy with a BRAF/MEK inhibitor.

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 Braftovi (active ingredient: encorafenib) at the following publicly accessible link (last access: 2 December 2024):

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

Treatment with encorafenib 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 pulmonary medicine and other doctors from specialist groups participating in the Oncology Agreement.

If the use of encorafenib in combination with binimetinib is being considered, the BRAF V600E mutation must be determined using a validated test procedure.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 1 March 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.

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

During the subcutaneous administration of atezolizumab in combination with bevacizumab, paclitaxel and carboplatin, atezolizumab (SC) is initially administered in an induction phase lasting four or six cycles in combination with bevacizumab, paclitaxel and carboplatin every three weeks, followed by a maintenance phase in combination with bevacizumab every three weeks.

During subcutaneous administration of atezolizumab in combination with nab-paclitaxel and carboplatin, atezolizumab (SC) is administered in an induction phase lasting four or six cycles in combination with carboplatin and nab-paclitaxel every three weeks, followed by the maintenance phase with atezolizumab monotherapy every three weeks.

According to the product information, cisplatin is dosed differently depending on the concomitant active ingredient - in combination with pemetrexed, the product information specifies a dosage of 75 mg/m^2.

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

For nivolumab, the recommended dose is 360 mg every 3 weeks in combination with 1 mg/kg ipilimumab every 6 weeks and platinum-based chemotherapy every 3 weeks, whereby treatment with 360 mg nivolumab intravenously every 3 weeks in combination with 1 mg/kg ipilimumab intravenously every 6 weeks continues after 2 cycles of chemotherapy.

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

Treatment period:

a) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Encorafenib + binimetinib				
Binimetinib	Continuously, 2 x daily	365	1	365
Encorafenib	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Monotherapies with immune checkpoint inhibitors				
Atezolizumab	1 x per 21-day cycle	17.4	1	17.4
Cemiplimab	1 x per 21-day cycle	17.4	1	17.4
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Dabrafenib + trametinib				
Dabrafenib	Continuously, 2 x daily	365	1	365
Trametinib	Continuously, 1 x daily	365	1	365
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[2]				
Nivolumab	1 x per 21-day cycle	17.4	1	17.4
Ipilimumab	1 x per 42-day cycle	8.7	1	8.7
Cisplatin	1 x per 21-day cycle	2	1	2.0
Carboplatin	1 x per 21-day cycle	2	1	2.0
Pemetrexed	1 x per 21-day cycle	2	1	2.0
Atezolizumab + bevacizumab + paclitaxel + carboplatin (only for patients with ECOG-PS 0-1)				
Induction therapy				
Atezolizumab	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Bevacizumab	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Paclitaxel	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Carboplatin	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Maintenance treatment				
Atezolizumab	1 x per 21-day cycle	11.4 - 13.4	1	11.4 - 13.4
Bevacizumab	1 x per 21-day cycle	11.4 - 13.4	1	11.4 - 13.4
Atezolizumab + carboplatin + nab-paclitaxel (only for patients with ECOG-PS 0-1)				
Induction therapy				
Atezolizumab	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Carboplatin	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0

2 Paclitaxel is not considered here as a concomitant active ingredient, as tumours with BRAF V600E mutation are histologically predominantly adenocarcinomas and this combination with paclitaxel is explicitly indicated for squamous cell tumour histology.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
nab-paclitaxel	3 x per 21-day cycle	4 - 6	3	12.0 - 18.0
Maintenance treatment				
Atezolizumab	1 x per 21-day cycle	11.4 - 13.4	1	11.4 - 13.4
Pembrolizumab + pemetrexed + platinum-containing chemotherapy (only for patients with ECOG-PS 0-1)				
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7
Pemetrexed	1 x per 21-day cycle	17.4	1	17.4
Cisplatin	1 x per 21-day cycle	17.4	1	17.4
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[3]				
Cemiplimab	1 x per 21-day cycle	17.4	1	17.4
Carboplatin				
Cisplatin				
Paclitaxel				
Pemetrexed				
Durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[4]				
Durvalumab	1 x per 21-day cycle	4	1	4.0
Tremelimumab	1 x per 21-day cycle	4	1	4.0
Carboplatin	1 x per 21-day cycle	4	1	4.0
Cisplatin	1 x per 21-day cycle	4	1	4.0
nab-paclitaxel	3 x per 21-day cycle	4	3	12.0

3 The treatment options for platinum-based chemotherapy were carboplatin or cisplatin in combination with paclitaxel or pemetrexed.

4 The treatment options for platinum-based chemotherapy were pemetrexed + cisplatin or pemetrexed + carboplatin for squamous NSCLC, and nab-paclitaxel + carboplatin, regardless of tumour histology. Gemcitabine is not considered here as a concomitant active ingredient, as tumours with BRAF V600E mutation are histologically predominantly adenocarcinomas and these combinations with gemcitabine are explicitly indicated for squamous cell tumour histology.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Pemetrexed	1 x per 21-day cycle	4	1	4.0
Antibody maintenance treatment and histology-based maintenance treatment with pemetrexed				
Durvalumab	1 x per 28-day cycle	10		10.0
Tremelimumab	1 x in week 16	1		1.0
Pemetrexed	1 x per 28-day cycle	10		10.0

b) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Encorafenib + binimetinib				
Binimetinib	Continuously, 2 x daily	365	1	365
Encorafenib	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Monotherapy with immune checkpoint inhibitor				
Atezolizumab	1 x per 21-day cycle	17.4	1	17.4
Dabrafenib + trametinib				
Dabrafenib	Continuously, 2 x daily	365	1	365
Trametinib	Continuously, 1 x daily	365	1	365
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
(only for patients with ECOG-PS 0-1)[5]				
Nivolumab	1 x per 21-day cycle	17.4	1	17.4
Ipilimumab	1 x per 42-day cycle	8.7	1	8.7
Cisplatin	1 x per 21-day cycle	2	1	2.0
Carboplatin	1 x per 21-day cycle	2	1	2.0
Pemetrexed	1 x per 21-day cycle	2	1	2.0
Atezolizumab + bevacizumab + paclitaxel + carboplatin (only for patients with ECOG-PS 0-1)				
Induction therapy				
Atezolizumab	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Bevacizumab	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Paclitaxel	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Carboplatin	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Maintenance treatment				
Atezolizumab	1 x per 21-day cycle	11.4 - 13.4	1	11.4 - 13.4
Bevacizumab	1 x per 21-day cycle	11.4 - 13.4	1	11.4 - 13.4
Atezolizumab + carboplatin + nab-paclitaxel (only for patients with ECOG-PS 0-1)				
Induction therapy				
Atezolizumab	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
Carboplatin	1 x per 21-day cycle	4 - 6	1	4.0 - 6.0
nab-paclitaxel	3 x per 21-day cycle	4 - 6	3	12.0 - 18.0
Maintenance treatment				
Atezolizumab	1 x per 21-day cycle	11.4 - 13.4	1	11.4 - 13.4
Pembrolizumab + pemetrexed + platinum-containing chemotherapy (only for patients with ECOG-PS 0-1)				

5 *Paclitaxel is not considered here as a concomitant active ingredient, as tumours with BRAF V600E mutation are histologically predominantly adenocarcinomas and this combination with paclitaxel is explicitly indicated in patients with squamous cell tumour histology.*

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7
Pemetrexed	1 x per 21-day cycle	17.4	1	17.4
Cisplatin	1 x per 21-day cycle	17.4	1	17.4
Carboplatin	1 x per 21-day cycle	17.4	1	17.4
Cemiplimab in combination with platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[3]				
Cemiplimab	1 x per 21-day cycle	17.4	1	17.4
Carboplatin				
Cisplatin				
Paclitaxel				
Pemetrexed				
Durvalumab in combination with tremelimumab and platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[4]				
Durvalumab	1 x per 21-day cycle	4	1	4.0
Tremelimumab	1 x per 21-day cycle	4	1	4.0
Carboplatin	1 x per 21-day cycle	4	1	4.0
Cisplatin	1 x per 21-day cycle	4	1	4.0
nab-paclitaxel	3 x per 21-day cycle	4	3	12.0
Pemetrexed	1 x per 21-day cycle	4	1	4.0
Antibody maintenance treatment and histology-based maintenance treatment with pemetrexed				
Durvalumab	1 x per 28-day cycle	10		10.0
Tremelimumab	1 x in week 16	1		1.0
Pemetrexed	1 x per 28-day cycle	10		10.0

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Encorafenib + binimetinib				
Binimetinib	Continuously, 2 x daily	365	1	365
Encorafenib	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Dabrafenib + trametinib				
Dabrafenib	Continuously, 2 x daily	365	1	365
Trametinib	Continuously, 1 x daily	365	1	365

Consumption:

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements of the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg). This results in a body surface area of 1.91 m² (calculated according to Du Bois 1916).[6]

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

a) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Medicinal product to be assessed					
Encorafenib + binimetinib					

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Binimetinib	45 mg	90 mg	6 x 15 mg	365	2,190 x 15 mg
Encorafenib	450 mg	450 mg	6 x 75 mg	365	2,190 x 15 mg
Appropriate comparator therapy					
Monotherapies with immune checkpoint inhibitors					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	17.4	17.4 x 1875 mg
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 x 350 mg
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Dabrafenib + trametinib					
Dabrafenib	150 mg	300 mg	4 x 75 mg	365	1,460 x 75 mg
Trametinib	2 mg	2 mg	1 x 2 mg	365	365 x 2 mg
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[2]					
Nivolumab	360 mg	360 mg	3 x 120 mg	17.4	52.2 x 120 mg
Ipilimumab	1 mg/kg = 77.7 mg	77.7 mg	2 x 50 mg	8.7	17.4 x 50 mg
Cisplatin	75 mg/m2 = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	2.0	2 x 50 mg + 2 x 100 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 450 mg + 1 x 600 mg	2.0	2 x 450 mg + 2 x 600 mg
Pemetrexed	500 mg/m^2 = 955 mg	955 mg	1 x 1,000 mg	2.0	2 x 1,000 mg
Atezolizumab + bevacizumab + paclitaxel + carboplatin (only for patients with ECOG-PS 0-1)					
Induction therapy					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	4.0 – 6.0	4.0 x 1,875 mg or 6.0 x 1,875 mg
Bevacizumab	7.5 mg/kg = 582.8 mg	582.8 mg	1 x 400 mg + 2 x 100 mg – 1 x 400 mg + 2 x 100 mg	4.0 – 6.0	4.0 x 400 mg + 8.0 x 100 mg – 6.0 x 400 mg + 12.0 x 100 mg
	or				
	15 mg/kg = 1,165.5 mg	1,165.5 mg	3 x 400 mg	4.0 – 6.0	12.0 x 400 mg – 18.0 x 400 mg
Paclitaxel	175 mg/m² = 334.3 mg	334.3 mg	1 x 150 mg + 2 x 100 mg – 1 x 150 mg + 2 x 100 mg	4.0 – 6.0	4.0 x 150 mg + 8.0 x 100 mg – 6.0 x 150 mg + 12.0 x 100 mg
Carboplatin	500 mg/m² = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg – 1 x 600 mg + 1 x 450 mg	4.0 – 6.0	4.0 x 600 mg + 4.0 x 450 mg – 6.0 x 600 mg + 6.0 x 450 mg
Maintenance treatment					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	11.4 – 13.4	11.4 x 1,875 mg – 13.4 x 1,875 mg
Bevacizumab	7.5 mg/kg = 582.8 mg	582.8 mg	1 x 400 mg + 2 x 100 mg	11.4 – 13.4	11.4 x 400 mg + 22.8 x 100 mg – 13.4 x 400 mg + 26.8 x 100 mg
	or				
	15 mg/kg = 1,165.5 mg	1,165.5 mg	3 x 400 mg	11.4 – 13.4	34.2 x 400 mg – 40.2 x 400 mg
Atezolizumab + carboplatin + nab-paclitaxel (only for patients with ECOG-PS 0-1)					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Induction					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	4.0 – 6.0	4.0 x 1,875 mg – 6.0 x 1,875 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	4.0 – 6.0	4.0 x 600 mg + 4.0 x 450 mg – 6.0 x 600 mg + 6.0 x 450 mg
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	12 – 18	24 x 100 mg – 36 x 100 mg
Maintenance					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	11.4 – 13.4	11.4 x 1,875 mg – 13.4 x 1,875 mg
Pembrolizumab + pemetrexed + platinum-containing chemotherapy (only for patients with ECOG-PS 0-1)					
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Pemetrexed	500 mg/m^2 = 955 mg	955 mg	1 x 1,000 mg	17.4	17.4 x 1,000 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 450 mg + 1 x 600 mg	17.4	17.4 x 450 mg + 17.4 x 600 mg
Cisplatin	75 mg/m^2 = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	17.4	17.4 x 50 mg + 17.4 x 100 mg
Cemiplimab + platinum-based chemotherapy[3]					
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 x 350 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	17.4	17.4 x 600 mg + 17.4 x 450 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	17.4	17.4 x 50 mg + 17.4 x 100 mg
	80 mg/m² = 152.8 mg	152.8 mg	1 x 10 mg + 1 x 50 mg + 1 x 100 mg	17.4	17.4 x 10 mg + 17.4 x 50 mg + 17.4 x 100 mg
Paclitaxel	175 mg/m² = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
Pemetrexed	500 mg/m² = 955 mg	955 mg	1 x 1,000 mg	17.4	17.4 x 1,000 mg
Durvalumab + tremelimumab + platinum-basedchemotherapy[4]					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	4.0	12.0 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	4.0	12.0 x 25 mg
Carboplatin	500 mg/m² = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	4.0	4.0 x 600 mg + 4.0 x 450 mg
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	4.0	4.0 x 50 mg + 4.0 x 100 mg
nab-paclitaxel	100 mg/m² = 191 mg	191 mg	2 x 100 mg	12.0	24.0 x 100 mg
Pemetrexed	500 mg/m² = 955 mg	955 mg	1 x 1,000 mg	4.0	4.0 x 1,000 mg
Antibody maintenance treatment and histology-based maintenance treatment with pemetrexed					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	10.0	30.0 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	1.0	3.0 x 25 mg
Pemetrexed	500 mg/m² = 955 mg	955 mg	1 x 1,000 mg	10.0	10.0 x 1,000 mg

b) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Medicinal product to be assessed					
Encorafenib + binimetinib					
Binimetinib	45 mg	90 mg	6 x 15 mg	365	2,190 x 15 mg
Encorafenib	450 mg	450 mg	6 x 75 mg	365	2,190 x 15 mg
Appropriate comparator therapy					
Monotherapy with immune checkpoint inhibitors					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	17.4	17.4 x 1875 mg
Dabrafenib + trametinib					
Dabrafenib	150 mg	300 mg	4 x 75 mg	365	1,460 x 75 mg
Trametinib	2 mg	2 mg	1 x 2 mg	365	365 x 2 mg
Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy (only for patients with ECOG-PS 0-1)[2]					
Nivolumab	360 mg	360 mg	3 x 120 mg	17.4	52.2 x 120 mg
Ipilimumab	1 mg/kg = 77.7 mg	77.7 mg	2 x 50 mg	8.7	17.4 x 50 mg
Cisplatin	75 mg/m2 = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	2.0	2 x 50 mg + 2 x 100 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 450 mg + 1 x 600 mg	2.0	2 x 450 mg + 2 x 600 mg
Pemetrexed	500 mg/m^2 = 955 mg	955 mg	1 x 1,000 mg	2.0	2 x 1,000 mg
Atezolizumab + bevacizumab + paclitaxel + carboplatin (only for patients with ECOG-PS 0-1)					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Induction therapy					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	4.0 – 6.0	4.0 x 1,875 mg or 6.0 x 1,875 mg
Bevacizumab	7.5 mg/kg = 582.8 mg	582.8 mg	1 x 400 mg + 2 x 100 mg – 1 x 400 mg + 2 x 100 mg	4.0 – 6.0	4.0 x 400 mg + 8.0 x 100 mg – 6.0 x 400 mg + 12.0 x 100 mg
	or				
	15 mg/kg = 1,165.5 mg	1,165.5 mg	3 x 400 mg	4.0 – 6.0	12.0 x 400 mg – 18.0 x 400 mg
Paclitaxel	175 mg/m^2 = 334.3 mg	334.3 mg	1 x 150 mg + 2 x 100 mg – 1 x 150 mg + 2 x 100 mg	4.0 – 6.0	4.0 x 150 mg + 8.0 x 100 mg – 6.0 x 150 mg + 12.0 x 100 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg – 1 x 600 mg + 1 x 450 mg	4.0 – 6.0	4.0 x 600 mg + 4.0 x 450 mg – 6.0 x 600 mg + 6.0 x 450 mg
Maintenance treatment					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	11.4 – 13.4	11.4 x 1,875 mg – 13.4 x 1,875 mg
Bevacizumab	7.5 mg/kg = 582.8 mg	582.8 mg	1 x 400 mg + 2 x 100 mg	11.4 – 13.4	11.4 x 400 mg + 22.8 x 100 mg – 13.4 x 400 mg + 26.8 x 100 mg
	or				
	15 mg/kg = 1,165.5 mg	1,165.5 mg	3 x 400 mg	11.4 – 13.4	34.2 x 400 mg – 40.2 x 400 mg
Atezolizumab + carboplatin + nab-paclitaxel					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
(only for patients with ECOG-PS 0-1)					
Induction					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	4.0 – 6.0	4.0 x 1,875 mg – 6.0 x 1,875 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	4.0 – 6.0	4.0 x 600 mg + 4.0 x 450 mg – 6.0 x 600 mg + 6.0 x 450 mg
nab-paclitaxel	100 mg/m^2 = 191 mg	191 mg	2 x 100 mg	12 – 18	24 x 100 mg – 36 x 100 mg
Maintenance					
Atezolizumab	1,875 mg	1,875 mg	1 x 1,875 mg	11.4 – 13.4	11.4 x 1,875 mg – 13.4 x 1,875 mg
Pembrolizumab + pemetrexed + platinum-containing chemotherapy (only for patients with ECOG-PS 0-1)					
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Pemetrexed	500 mg/m^2 = 955 mg	955 mg	1 x 1,000 mg	17.4	17.4 x 1,000 mg
Carboplatin	500 mg/m^2 = 955 mg	955 mg	1 x 450 mg + 1 x 600 mg	17.4	17.4 x 450 mg + 17.4 x 600 mg
Cisplatin	75 mg/m^2 = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	17.4	17.4 x 50 mg + 17.4 x 100 mg
Cemiplimab + platinum-based chemotherapy[3]					
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 x 350 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Carboplatin	500 mg/m² = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	17.4	17.4 x 600 mg + 17.4 x 450 mg
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	17.4	17.4 x 50 mg + 17.4 x 100 mg
	80 mg/m² = 152.8 mg	152.8 mg	1 x 10 mg + 1 x 50 mg + 1 x 100 mg	17.4	17.4 x 10 mg + 17.4 x 50 mg + 17.4 x 100 mg
Paclitaxel	175 mg/m² = 334.3 mg	334.3 mg	2 x 100 mg + 1 x 150 mg	17.4	34.8 x 100 mg + 17.4 x 150 mg
Pemetrexed	500 mg/m² = 955 mg	955 mg	1 x 1,000 mg	17.4	17.4 x 1,000 mg
Durvalumab + tremelimumab + platinum-basedchemotherapy[4]					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	4.0	12.0 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	4.0	12.0 x 25 mg
Carboplatin	500 mg/m² = 955 mg	955 mg	1 x 600 mg + 1 x 450 mg	4.0	4.0 x 600 mg + 4.0 x 450 mg
Cisplatin	75 mg/m² = 143.3 mg	143.3 mg	1 x 50 mg + 1 x 100 mg	4.0	4.0 x 50 mg + 4.0 x 100 mg
nab-paclitaxel	100 mg/m² = 191 mg	191 mg	2 x 100 mg	12.0	24.0 x 100 mg
Pemetrexed	500 mg/m² = 955 mg	955 mg	1 x 1,000 mg	4.0	4.0 x 1,000 mg
Antibody maintenance treatment and histology-based maintenance treatment with pemetrexed					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	10.0	30.0 x 500 mg
Tremelimumab	75 mg	75 mg	3 x 25 mg	1.0	3.0 x 25 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Pemetrexed	500 mg/m^2 = 955 mg	955 mg	1 x 1,000 mg	10.0	10.0 x 1,000 mg

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Encorafenib + binimetinib					
Binimetinib	45 mg	90 mg	6 x 15 mg	365	2,190 x 15 mg
Encorafenib	450 mg	450 mg	6 x 75 mg	365	2,190 x 15 mg
Appropriate comparator therapy					
Dabrafenib + trametinib					
Dabrafenib	150 mg	300 mg	4 x 75 mg	365	1,460 x 75 mg
Trametinib	2 mg	2 mg	1 x 2 mg	365	365 x 2 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 Sections 130 and 130 a 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					
Binimetinib 15 mg	168 FCT	€ 3,061.36	€ 1.77	€ 171.54	€ 2,888.05
Encorafenib 75 mg	168 HC	€ 6,235.18	€ 1.77	€ 0.00	€ 6,233.41
Appropriate comparator therapy					
Atezolizumab 1,875 mg	1 SFI	€ 4,129.23	€ 1.77	€ 232.53	€ 3,894.93
Bevacizumab 100 mg	1 CIS	€ 200.97	€ 1.77	€ 9.00	€ 190.20
Bevacizumab 400 mg	1 CIS	€ 769.91	€ 1.77	€ 36.00	€ 732.14
Carboplatin 450 mg	1 CIS	€ 228.24	€ 1.77	€ 10.29	€ 216.18
Carboplatin 600 mg	1 CIS	€ 300.84	€ 1.77	€ 13.74	€ 285.33
Cemiplimab 350 mg	1 CIS	€ 4,326.55	€ 1.77	€ 243.80	€ 4,080.98
Cisplatin 50 mg	1 CIS	€ 47.71	€ 1.77	€ 1.73	€ 44.21
Cisplatin 100 mg	1 CIS	€ 76.59	€ 1.77	€ 3.10	€ 71.72
Dabrafenib 75 mg	120 HC	€ 5,831.99	€ 1.77	€ 0.00	€ 5,830.22
Durvalumab 500 mg	1 CIS	€ 2,105.19	€ 1.77	€ 116.94	€ 1,986.48
Ipilimumab 50 mg	1 CIS	€ 3,489.23	€ 1.77	€ 195.98	€ 3,291.48
Nab-paclitaxel 100 mg	1 PIS	€ 429.36	€ 1.77	€ 19.84	€ 407.75
Nivolumab 120 mg	1 CIS	€ 1,546.96	€ 1.77	€ 85.05	€ 1,460.14
Paclitaxel 100 mg	1 CIS	€ 289.47	€ 1.77	€ 13.20	€ 274.50
Paclitaxel 150 mg	1 CIS	€ 428.97	€ 1.77	€ 19.82	€ 407.38
Pembrolizumab 100 mg	1 CIS	€ 2,743.07	€ 1.77	€ 153.37	€ 2,587.93
Pemetrexed 1,000 mg	1 CIS	€ 1,124.81	€ 1.77	€ 52.84	€ 1,070.20
Trametinib 2 mg	30 FCT	€ 4,367.62	€ 1.77	€ 0.00	€ 4,365.85
Tremelimumab 25 mg	1 CIS	€ 1,779.95	€ 1.77	€ 98.36	€ 1,679.82
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PIS = powder for the preparation of an infusion suspension					

LAUER-TAXE® last revised: 1 March 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 need to be taken into account.

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Medicinal product to be assessed							
Appropriate comparator therapy							
Pemetrexed							
2 cycles *Nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy* *(only for patients with ECOG-PS 0-1)*							
Dexamethasone[7] 2 x 4 mg	20 x 4 mg TAB	€ 24.61	€ 1.77	€ 1.05	€ 21.79	6	€ 21.79
Folic acid[8] 350 – 1,000 µg/day	30 x 400 µg TAB	€ 3.42	€ 0.00	€ 0.00	€ 3.42	70	€ 10.26 - € 17.10
Vitamin B12[7] 1,000 µg/day, every 3 cycles	5 x 1,000 µg ILO	€ 4.95	€ 0.25	€ 0.22	€ 4.48	1	€ 4.48
17.4 cycles *(pembrolizumab + pemetrexed + platinum-containing chemotherapy)*							
Dexamethasone[7] 2 x 4 mg	100 x 4 mg TAB	€ 79.54	€ 1.77	€ 5.40	€ 72.37	52.2	€ 75.55
Folic acid[8] 350 – 1,000 µg/day	30 x 400 µg TAB	€ 3.42	€ 0.00	€ 0.00	€ 3.42	365	€ 41.61 - € 83.22
Vitamin B12[7] 1,000 µg/day, every 3 cycles	10 x 1,000 µg ILO	€ 7.40	€ 0.37	€ 0.32	€ 6.71	5.8	€ 3.89
4 cycles of 21 days each *(durvalumab + tremelimumab + platinum-based chemotherapy; induction phase)*							

[7] Fixed reimbursement rate

[8] The cost calculation for folic acid is based on the single dose of 400 µg of the non-divisible tablets available for cost calculation related to a dose range of 400 - 800 µg per day, even if a dose range of 350 - 1,000 µg is given in the product information.

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Dexamethasone[7] 2 x 4 mg	100 x 4 mg TAB	€ 79.54	€ 1.77	€ 5.40	€ 72.37	12	€ 17.36
Folic acid[8] 350 – 1,000 µg/day	30 x 400 µg TAB	€ 3.42	€ 0.00	€ 0.00	€ 3.42	84	€ 9.58 - € 19.15
Vitamin B12[7] 1,000 µg/day, every 3 cycles	10 x 1,000 µg ILO	€ 7.40	€ 0.37	€ 0.32	€ 6.71	2	€ 1.34
10 cycles of 28 days each *Maintenance treatment with durvalumab + tremelimumab including histology-based maintenance treatment with pemetrexed)*							
Dexamethasone[7] 2 x 4 mg	100 x 4 mg TAB	€ 79.54	€ 1.77	€ 5.40	€ 72.37	30	€ 43.42
Folic acid[8] 350 – 1,000 µg/day	30 x 400 µg TAB	€ 3.42	€ 0.00	€ 0.00	€ 3.42	281	€ 32.03 - € 64.07
Vitamin B12[7] 1,000 µg/day, every 3 cycles	10 x 1,000 µg ILO	€ 7.40	€ 0.37	€ 0.32	€ 6.71	3	€ 2.01
Paclitaxel							
4 - 6 cycles *Atezolizumab + bevacizumab + paclitaxel + carboplatin* *(only for patients with ECOG-PS 0-1)*							
Dexamethasone[7] 2 x 20 mg	10 x 20 mg TAB	€ 32.42	€ 1.77	€ 0.00	€ 30.65	4 - 6	€ 30.65 - € 52.32
	20 x 20 mg TAB	€ 54.09	€ 1.77	€ 0.00	€ 52.32		
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 x 4 mg SFI	€ 26.24	€ 1.77	€ 7.02	€ 17.45	4 - 6	€ 34.90 - € 52.35
Cimetidine[7] 300 mg IV	10 x 200 mg AMP	€ 19.80	€ 1.77	€ 0.40	€ 17.63	4 - 6	€ 17.63 - € 35.26
17.4 cycles *(pembrolizumab + carboplatin + paclitaxel* *as well as* cemiplimab in combination with platinum-based chemotherapy)							
Dexamethasone[7] 2 x 20 mg	50 x 20 mg TAB	€ 118.88	€ 1.77	€ 0.00	€ 117.11	17.4	€ 81.51
Dimetindene IV 1 mg/ 10 kg = 7.7 mg	5 x 4 mg SFI	€ 26.24	€ 1.77	€ 7.02	€ 17.45	17.4	€ 121.45

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Cimetidine[7] 300 mg IV	10 x 200 mg AMP	€ 19.80	€ 1.77	€ 0.40	€ 17.63	17.4	€ 61.35
Cisplatin							
Antiemetic treatment: In clinical practice, an appropriate antiemetic treatment is established before and/or after administration of cisplatin. The product information for cisplatin does not provide any specific information on this, which is why the necessary costs cannot be quantified.							
Hydration and forced diuresis *2 cycles* *(nivolumab + ipilimumab + 2 cycles of platinum-based chemotherapy)*							
Mannitol 10% Inf. sol., 37.5 g/day	10 x 250 ml INF	€ 87.05	€ 4.35	€ 7.94	€ 74.76	2	€ 74.76
Sodium chloride 0.9% Inf. sol., 3 - 4.4 l/day	6 x 1,000 ml INF	€ 25.09	€ 1.25	€ 2.05	€ 21.79	2	€ 21.79 - € 32.58
	10 x 1,000 ml INF	€ 35.47	€ 1.77	€ 1.12	€ 32.58		
Hydration and forced diuresis *4 cycles* (durvalumab in combination with tremelimumab and platinum-based chemotherapy)							
Mannitol 10% Inf. sol., 37.5 g/day	10 x 250 ml INF	€ 87.05	€ 4.35	€ 7.94	€ 74.76	4	€ 74.76
Sodium chloride 0.9% Inf. sol., 3 - 4.4 l/day	6 x 1,000 ml INF	€ 25.09	€ 1.25	€ 2.05	€ 21.79	4	€ 54.37 - € 65.16
	10 x 1,000 ml INF	€ 35.47	€ 1.77	€ 1.12	€ 32.58		
Hydration and forced diuresis *17.4 cycles* *(*cemiplimab in combination with platinum-based chemotherapy *as well as pembrolizumab + pemetrexed + platinum-containing chemotherapy)*							
Mannitol 10% Inf. sol., 37.5 g/day	10 x 250 ml INF	€ 87.05	€ 4.35	€ 7.94	€ 74.76	17.4	€ 260.17
Sodium chloride 0.9% Inf. sol., 3 - 4.4 l/day	10 x 1,000 ml INF	€ 35.47	€ 1.77	€ 1.12	€ 32.58	17.4	€ 170.07 - € 247.05
	10 x 500 ml INF	€ 13.28	€ 0.66	€ 0.96	€ 11.66		

Other SHI services:

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

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

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

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the

procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

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

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

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

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

Concomitant active ingredient

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

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

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

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

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

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

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

Designation

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

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

Exception to the designation

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

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

Legal effects of the designation

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

framework of Section 35a, paragraph 3, sentence 4 SGB V.

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

Justification for the findings on designation in the present resolution:

a) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% and a BRAF V600E mutation; first-line therapy

Each of the designated medicinal products is an active ingredient that is specifically named as a concomitant active ingredient in the product information for the assessed medicinal product. Corresponding text extract from the product information for the assessed medicinal product: "Encorafenib in combination with binimetinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation."

For the designated medicinal products, the requirements of Section 35a, paragraph 3, sentence 4 SGB V are also fulfilled.

References:
Product information for encorafenib (Braftovi); Braftovi 50 mg hard capsules; Braftovi 75 mg hard capsules; last revised: December 2024

b) Adults with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% and a BRAF V600E mutation; first-line therapy

Each of the designated medicinal products is an active ingredient that is specifically named as a concomitant active ingredient in the product information for the assessed medicinal product. Corresponding text extract from the product information for the assessed medicinal product: "Encorafenib in combination with binimetinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation."

For the designated medicinal products, the requirements of Section 35a, paragraph 3, sentence 4 SGB V are also fulfilled.

References:
Product information for encorafenib (Braftovi); Braftovi 50 mg hard capsules; Braftovi 75 mg hard capsules; last revised: December 2024

c) Adults with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation; after first-line therapy

Each of the designated medicinal products is an active ingredient that is specifically named as a concomitant active ingredient in the product information for the assessed medicinal product. Corresponding text extract from the product information for the assessed medicinal product: "Encorafenib in combination with binimetinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation."

For the designated medicinal products, the requirements of Section 35a, paragraph 3, sentence 4 SGB V are also fulfilled.

References:
Product information for encorafenib (Braftovi); Braftovi 50 mg hard capsules; Braftovi 75 mg hard capsules; last revised: December 2024

Supplement to Annex XIIa of the Pharmaceuticals Directive

Since the resolution under I.5 mentions medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V, which can be used in a combination therapy with the assessed active ingredient in the therapeutic indication of the resolution, the information on this designation is to be added to Annex XIIa of the Pharmaceuticals Directive and provided with patient-group-related information on the period of validity of the designation.

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 26 September 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 its session on 27 August 2024.

On 23 September 2024, the pharmaceutical company submitted a dossier for the benefit assessment of encorafenib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 26 September 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 encorafenib.

The dossier assessment by the IQWiG was submitted to the G-BA on 20 December 2024, and the written statement procedure was initiated with publication on the G-BA website on 2 January 2025. The deadline for submitting statements was 23 January 2025.

The oral hearing was held on 10 February 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 March 2025, and the proposed draft resolution was approved.

At its session on 20 March 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	26 September 2023	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	27 August 2024	New determination of the appropriate comparator therapy
Working group Section 35a	4 February 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 February 2025	Conduct of the oral hearing, if applicable: commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	18 February 2025 4 March 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 March 2025	Concluding discussion of the draft resolution
Plenum	20 March 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 March 2025

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

Prof. Hecken