**Sotorasib (lung cancer, non-small cell, KRAS G12C mutation, ≥ 1 prior therapy)**

Resolution of: 4 August 2022/5 January 2023/ 3 August 2023/ 19 October 2023
Entry into force on: 4 August 2022/5.January/ 3 August 2023/ 19 October 2023
Federal Gazette, BAnz AT 07 09 2022 B1/ 10 02 2023 B2/ 06 10 2023 B1/ 11 12 2023 B1

Valid until: unlimited

**Therapeutic indication (according to the marketing authorisation of 6 January 2022):**

LUMYKRAS as monotherapy is indicated for the treatment of adults with advanced non-small cell lung cancer (NSCLC) with KRAS G12C mutation and who have progressed after at least one prior line of systemic therapy.

**Therapeutic indication of the resolution (resolution of 3 August 2023):**

See therapeutic indication according to marketing authorisation.

## 1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

a) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with a PD-1/PD-L1 antibody as monotherapy

**Appropriate comparator therapy:**

- Cisplatin in combination with a third-generation cytostatic drug (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 drug (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

*or*

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

**Extent and probability of the additional benefit of Sotorasib compared to the appropriate comparator therapy:**

An additional benefit is not proven.

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b) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with cytotoxic chemotherapy

**Appropriate comparator therapy:**

- 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 (PD-L1 expression ≥ 1% of tumour cells))

or

- Atezolizumab

or

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

**Extent and probability of the additional benefit of sotorasib compared to the appropriate comparator therapy:**

An additional benefit is not proven.

c) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with an anti-PD-1/PD-L1 in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 and platinum-containing chemotherapy

**Appropriate comparator therapy:**

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.

**Extent and probability of the additional benefit of sotorasib compared to the appropriate comparator therapy:**

c1) Adults for whom docetaxel is the appropriate patient-individual therapy

Hint of a non-quantifiable additional benefit

c2) Adults for whom a therapy other than docetaxel is the appropriate patient-individual therapy

An additional benefit is not proven.

**Study results according to endpoints:[1]**

a) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with an anti-PD-1/PD-L1 as monotherapy

No adequate data are available to allow an assessment of the additional benefit.

**Summary of results for relevant clinical endpoints**

| Endpoint category | Direction of effect/ risk of bias | Summary |
|---|---|---|
| Mortality | n.a. | There are no assessable data. |
| Morbidity | n.a. | There are no assessable data. |
| Health-related quality of life | n.a. | There are no assessable data. |
| Side effects | n.a. | There are no assessable data. |
| Explanations:<br>↑: statistically significant and relevant positive effect with low/unclear reliability of data<br>↓: statistically significant and relevant negative effect with low/unclear reliability of data<br>↑↑: statistically significant and relevant positive effect with high reliability of data<br>↓↓: statistically significant and relevant negative effect with high reliability of data<br>↔: no statistically significant or relevant difference<br>∅: There are no usable data for the benefit assessment.<br>n.a.: not assessable | | |

**Study results according to endpoints:[2]**

b) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with cytotoxic chemotherapy

No adequate data are available to allow an assessment of the additional benefit.

**Summary of results for relevant clinical endpoints**

| Endpoint category | Direction of effect/ risk of bias | Summary |
|---|---|---|
| Mortality | ∅ | No data available. |
| Morbidity | ∅ | No data available. |
| Health-related quality of life | ∅ | No data available. |
| Side effects | ∅ | No data available. |
| Explanations:<br>↑: statistically significant and relevant positive effect with low/unclear reliability of data<br>↓: statistically significant and relevant negative effect with low/unclear reliability of data<br>↑↑: statistically significant and relevant positive effect with high reliability of data | | |

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-28) unless otherwise indicated.
[2] Data from the dossier assessment of the IQWiG (A23-06) and from the addendum (A23-53), unless otherwise indicated.

| |
|---|
| ↓↓: statistically significant and relevant negative effect with high reliability of data<br>↔: no statistically significant or relevant difference<br>∅: No data available.<br>n.a.: not assessable |

c) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with an anti-PD-1/PD-L1 in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 and platinum-containing chemotherapy

c1) Adults for whom docetaxel is the appropriate patient-individual therapy

**Summary of results for relevant clinical endpoints**

| Endpoint category | Direction of effect/ risk of bias | Summary |
|---|---|---|
| Mortality | ↔ | No relevant difference for the benefit assessment. |
| Morbidity | ↑ | Advantages in symptomatology and health status. |
| Health-related quality of life | n.a. | There are no assessable data. |
| Side effects | ↔ | No relevant difference for the benefit assessment. |
| Explanations:<br>↑: statistically significant and relevant positive effect with low/unclear reliability of data<br>↓: statistically significant and relevant negative effect with low/unclear reliability of data<br>↑↑: statistically significant and relevant positive effect with high reliability of data<br>↓↓: statistically significant and relevant negative effect with high reliability of data<br>↔: no statistically significant or relevant difference<br>∅: No data available.<br>n.a.: not assessable | | |

CodeBreak 200 study: Sotorasib **vs** docetaxel

Study design: randomised, open-label, parallel

Data cut-off: 2 August 2022

**Mortality**

| Endpoint | Sotorasib | | Docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| **Overall survival** | | | | | |
| | 171 | 10.64 [8.94; 13.96] *109 (63.7)* | 174 | 11.30 [9.00; 14.85] *94 (54.0)* | 1.010 [0.77; 1.33] 0.94 |

**Morbidity**

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| **Progression-free survival (PFS)[b]** | | | | | |
| | 171 | 5.62 [4.27; 7.75] *122 (71.3)* | 174 | 4.47 [3.02; 5.68] *101 (58.0)* | 0.663 [0.509; 0.864] 0.003 AD = 1.15 |
| **Symptomatology (EORTC QLQ-C30) [b]** | | | | | |
| Fatigue | 160 | 3.0 [2.1; 4.3] *104 (65.0)* | 130 | 1.4 [0.8; 1.4] *105 (80.8)* | 0.47 [0.35; 0.63] <0.0001 |
| Nausea / vomiting | 160 | 9.1 [5.5; 16.6] *69 (43.1)* | 130 | 5.6 [3.9; 9.9] *56 (43.1)* | 0.76 [0.53; 1.11] 0.1583 |
| Pain | 160 | 2.8 [2.1; 4.2] *106 (66.2)* | 130 | 2.1 [1.4; 2.3] *91 (70.0)* | 0.77 [0.57; 1.03] 0.0809 |
| Dyspnoea | 160 | 8.3 [5.6; 13.7] *72 (45.0)* | 130 | 3.5 [2.3; 5.0] *68 (52.3)* | 0.64 [0.45; 0.91] 0.0113 |
| Insomnia | 160 | 5.9 [4.2; 10.4] *78 (48.8)* | 130 | 3.7 [3.0; 5.6] *66 (50.8)* | 0.79 [0.56; 1.11] 0.1739 |
| Loss of appetite | 160 | 5.9 [3.5; 9.2] | 130 | 3.5 [2.1; 4.2] | 0.68 |

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| | | *84 (52.5)* | | *67 (51.5)* | [0.49; 0.96] 0.0279 |
| Constipation | 160 | 12.8 [6.2; n.r.] *63 (39.4)* | 130 | 2.8 [1.5; 4.9] *73 (56.2)* | 0.52 [0.36; 0.74] 0.0002 |
| Diarrhoea | 160 | 2.7 [2.1; 3.5] *94 (58.8)* | 130 | 4.4 [2.1; 9.9] *64 (49.2)* | 1.13 [0.81; 1.56] 0.4681 |
| **Symptomatology (EORTC QLQ-LC13)** [b] | | | | | |
| Dyspnoea | 158 | 3.6 [2.8; 6.2] *93 (58.9)* | 124 | 1.5 [1.4; 2.1] *92 (74.2)* | 0.55 [0.40; 0.75] 0.0001 |
| Cough | 158 | 16.6 [11.9; n.r.] *52 (32.9)* | 124 | 4.6 [2.8; n.r.] *52 (41.9)* | 0.50 [0.33; 0.76] 0.0010 |
| Haemoptysis | 158 | n.r. [n.r.; n.r.] *18 (11.4)* | 124 | n.r. [9.9; n.r.] *21 (16.9)* | 0.39 [0.20; 0.78] 0.0058 |
| Chest pain | 158 | 13.1 [6.4; n.c.] *59 (37.3)* | 124 | 7.3 [5.6; n.r.] *48 (38.7)* | 0.80 [0.54; 1.18] 0.2592 |
| Pain in arm / shoulder | 158 | 5.2 [4.0; 9.0] *85 (53.8)* | 124 | 14.1 [3.7; 14.1] *49 (39.5)* | 1.11 [0.77; 1.61] 0.5632 |
| Other pain | 158 | 4.2 [2.8; 7.8] *90 (57.0)* | 124 | 3.0 [2.3; 4.0] *68 (54.8)* | 0.82 [0.59; 1.15] 0.2514 |
| Painkiller use | 137 | 11.0 [7.6; n.r.] *48 (35.0)* | 101 | n.r. [3.5; n.r.] *32 (31.7)* | 0.86 [0.53; 1.39] 0.5322 |
| Alopecia | 158 | n.r. [19.4; n.r.] *32 (20.3)* | 124 | 0.7 [0.7; 0.8] *110 (88.7)* | 0.07 [0.05; 0.12] < 0.0001 |
| Peripheral neuropathy | 158 | 10.3 [5.5; n.r.] *65 (41.1)* | 124 | 3.5 [2.8; 5.6] *66 (53.2)* | 0.61 [0.42; 0.87] 0.0063 |
| Wounded mouth | 158 | n.r. [14.5; n.r.] *42 (26.6)* | 124 | 4.4 [2.8; n.r.] *57 (46.0)* | 0.39 [0.26; 0.60] |

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| | | | | | < 0.0001 |
| Dysphagia | 158 | n.r. [18.7; n.r.] *45 (28.5)* | 124 | 6.9 [4.7; n.r.] *46 (37.1)* | 0.61 [0.40; 0.93] 0.0210 |
| **BPI-SF** [b] | | | | | |
| Worst pain | 163 | 2.2 [1.4; 3.4] *113 (69.3)* | 128 | 1.5 [1.4; 2.2] *94 (73.4)* | 0.76 [0.57; 1.01] 0.0605 |
| Medium pain intensity | 163 | 5.4 [4.2; 8.3] *87 (53.4)* | 128 | 3.5 [2.7; 7.6] *65 (50.8)* | 0.88 [0.63; 1.23] 0.4651 |
| Impairment due to pain | 163 | 7.5 [4.2; 9.8] *83 (50.9)* | 128 | 4.3 [2.8; 7.6] *60 (46.9)* | 0.80 [0.57; 1.13] 0.2119 |
| **Burden due to therapy (FACT-G GP5)** | | | | | |
| | 163 | 2.8 [2.2; 3.6] *92 (56.4)* | 128 | 1.4 [0.8; 1.4] *96 (75.0)* | 0.52 [0.38; 0.70] < 0.0001 |
| **Health status (PGI-C)** | | | | | |
| Cough | 143 | n.r. [3.5; n.r.] *5 (3.5)* | 110 | 4.4 [3.3; n.r.] *19 (17.3)* | 0.24 [0.09; 0.66] 0.0028 |
| Shortness of breath | 143 | n.r. [n.r.; n.r.] *9 (6.3)* | 110 | 4.4 [3.0; n.r.] *28 (25.5)* | 0.26 [0.12; 0.56] 0.0002 |
| Chest pain | 143 | n.r. [n.r.; n.r.] *4 (2.8)* | 110 | n.r. [n.r.; n.r.] *7 (6.4)* | 0.52 [0.14; 1.84] 0.2999 |
| **Health status (EQ-5D VAS)**[d] | | | | | |
| | 160 | 5.2 [3.6; 10.4] *83 (51.9)* | 138 | 1.6 [1.0; 3.3] *83 (60.1)* | 0.55 [0.40; 0.76] <0.001 AD = 3.6 |

**Health-related quality of life**

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| **Functional scales (EORTC QLQ-C30)** | | | | | |
| No suitable data[c] | | | | | |

**Side effects**

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| **Total adverse events (presented additionally)**[e] | | | | | |
| | 169 | 0.72 [0.49; 0.82] *165 (97.6)* | 151 | 0.16 [0.13; 0.20] *148 (98.0)* | - |
| **Serious adverse events (SAE)**[e] | | | | | |
| | 169 | 9.86 [7.29; 15.34] *82 (48.5)* | 151 | 7.10 [3.68; n.r.] *66 (43.7)* | 0.73 [0.52; 1.01] 0.061 |
| **Severe adverse events (CTCAE grade ≥ 3)**[e] | | | | | |
| | 169 | 3.35 [2.53; 4.73] *114 (67.5)* | 151 | 2.96 [1.38; 4.14] *90 (59.6)* | 0.80 [0.61; 1.06] 0.13 |
| **Discontinuation due to AEs** | | | | | |
| | 169 | n.r. *28 (16.6)* | 151 | n.r. [13.40; n.c.] *24 (15.9)* | 0.79 [0.45; 1.39] 0.40 |
| **Specific adverse events** | | | | | |
| Diseases of the liver (SMQ[g], severe AEs[f]) | 169 | n.r. *33 (19.5)* | 151 | n.r. *2 (1.3)* | 13.92 [3.3; 58.76] < 0.001 |

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |
| Interstitial lung disease (SMQ[g], severe AEs[f]) | 169 | n.r. *2 (1.2)* | 151 | n.r. *4 (2.6)* | 0.31 [0.06; 1.55] 0.17 |
| Stomatitis (PT, AE) | 169 | n.r. *3 (1.8)* | 151 | n.r. *19 (12.6)* | 0.13 [0.04; 0.41] < 0.001 |
| Chest pain (PT, AE) | 169 | n.r. *15 (8.9)* | 151 | n.r. *2 (1.3)* | 4.3 [0.91; 20.30] 0.038 |
| Peripheral oedema (PT, AE) | 169 | n.r. *5 (3.0)* | 151 | n.r. [16.53: n.r.] *19 (12.6)* | 0.14 [0.05; 0.40] < 0.001 |
| Fever (PT, AE) | 169 | n.r. *11 (6.5)* | 151 | n.r. *20 (13.2)* | 0.32 [0.15; 0.67] 0.002 |
| Peripheral neuropathy (PT, AE) | 169 | n.r. *1 (0.6)* | 151 | n.r. *16 (10.6)* | 0.03 [0; 0.29] < 0.001 |
| Alopecia (PT, AE) | 169 | n.r. *3 (1.8)* | 151 | n.r. *35 (23.2)* | 0.06 [0.02; 0.21] < 0.001 |
| Blood and lymphatic system disorders (SOC, severe AEs[e]) | 169 | n.r. *10 (5.9)* | 151 | n.r. *27 (17.9)* | 0.25 [0.13; 0.50] < 0.001 |
| Infections and infestations (SOC, severe AEs[f]) | 169 | n.r. *10 (5.9)* | 151 | 18.37 [18.37; n.r.] *27 (17.9)* | 0.20 [0.10; 0.40] < 0.001 |
| Diarrhoea (PT, severe AEs:[f]) | 169 | n.r. *23 (13.6)* | 151 | n.r. *4 (2.6)* | 4.75 [1.65; 13.69] 0.002 |
| Fatigue (PT, severe AEs:[f]) | 169 | n.r. *4 (2.4)* | 151 | n.r. *9 (6.0)* | 0.31 [0.10; 1.05] 0.043 |

[a] Indication of absolute difference (AD) only in case of statistically significant difference; own calculation

| Endpoint | Sotorasib | | docetaxel | | Sotorasib vs docetaxel |
|---|---|---|---|---|---|
| | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | N | **Median time to event in months [95% CI]** *Patients with event n (%)* | Effect estimator [95% CI] p value Absolute difference (AD)[a] |

[b] Information from the dossier of the pharmaceutical company
[c] Weighing the extent of the difference between the treatment arms in terms of the percentage of patients included in the analysis and the magnitude of the effects on the quality of life endpoints.
[d] Time to deterioration by ≥ 15 points (without death)
[e] excluding events deemed by the pharmaceutical company to be progression of the underlying disease (any PTs containing the terms metastasis / metastases, tumour pain, NSCLC / non-small cell lung cancer or adenocarcinoma of the lung)
[f] Operationalised as CTCAE grade ≥ 3
[g] SMQ broad scope

Abbreviations used:
AD = absolute difference; BPI-SF = Brief Pain Inventory - Short Form; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; QLQ C30 = Quality-of-life Questionnaire Core 30; QLQ-LC13 = Quality-of-life Questionnaire Core 13; FACT-G GP5 = Functional Assessment of Cancer Therapy Tool General form General Population 5; HR = hazard ratio; CI = confidence interval; MedDRA = Medical Dictionary of Drug Regulatory Activities; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PGIC = Patient Global Impression of Change; PT = preferred term; RCT = randomised controlled trial; SMQ = standardised MedDRA query; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

c2) Adults for whom a therapy other than docetaxel is the appropriate patient-individual therapy

No adequate data are available to allow an assessment of the additional benefit.

**Summary of results for relevant clinical endpoints**

| Endpoint category | Direction of effect/ risk of bias | Summary |
|---|---|---|
| Mortality | ∅ | No data available. |
| Morbidity | ∅ | No data available. |
| Health-related quality of life | ∅ | No data available. |
| Side effects | ∅ | No data available. |

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference
∅: No data available.
n.a.: not assessable

## 2. Number of patients or demarcation of patient groups eligible for treatment

a) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with a PD-1/PD-L1 antibody as monotherapy

80 - 170 patients

b) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with cytotoxic chemotherapy

approx. 60 - 130 patients

c) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with an anti-PD-1/PD-L1 in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 and platinum-containing chemotherapy

approx. 420 - 910 patients

## 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 Lumykras (active ingredient: sotorasib) at the following publicly accessible link (last access: 15 May 2023):

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

Treatment with sotorasib 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.

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency EMA will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

*Testing KRAS G12C mutation*

The presence of a KRAS G12C mutation must be confirmed by a validated test prior to start of therapy.

## 4. Treatment costs

**Annual treatment costs:**

a) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with aPD-1/PD-L1 antibody as monotherapy

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Sotorasib | € 121,016.60 |
| Appropriate comparator therapy: | |
| *Cisplatin in combination with a third-generation cytostatic drug (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed)* | |
| *Cisplatin + vinorelbine* | |
| Cisplatin | € 2,015.79 - € 2,494.46 |
| Vinorelbine | € 5,015.72 - € 6,261.22 |
| Total | € 7,031.51 - € 8,755.68 |
| Additionally required SHI costs | € 328.58 - € 421.62 |
| *Cisplatin + gemcitabine* | |
| Cisplatin | € 2,015.79 - € 2,494.46 |
| Gemcitabine | € 8,218.72 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Total | € 10,234.51 - € 10,713.18 |
| Additionally required SHI costs | € 328.58 - € 421.62 |
| *Cisplatin + docetaxel* | |
| Cisplatin | € 2,015.79 |
| Docetaxel | € 13,742.17 |
| Total | € 15,757.96 |
| Additionally required SHI costs | € 328.58 - € 421.62 |
| *Cisplatin + paclitaxel* | |
| Cisplatin | € 2,284.10 |
| Paclitaxel | € 17,485.96 |
| Total | € 19,770.05 |
| Additionally required SHI costs | € 537.20 - € 630.24 |
| *Cisplatin + pemetrexed* | |
| Cisplatin | € 2,015.79 |
| Pemetrexed | € 37,075.40 |
| Total | € 39,091.19 |
| Additionally required SHI costs | € 457.25 - € 598.79 |
| *Carboplatin in combination with a third-generation cytostatic drug (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed)* | |
| *Carboplatin + vinorelbine* | |
| Carboplatin | € 8,074.47 |
| Vinorelbine | € 5,015.72 - € 6,261.22 |
| Total | € 13,090.19 - € 14,335.69 |
| *Carboplatin + gemcitabine* | |
| Carboplatin | € 8,074.47 |
| Gemcitabine | € 8,218.72 |
| Total | € 16,293.19 |
| *Carboplatin + docetaxel* | |
| Carboplatin | € 8,074.47 |
| Docetaxel | € 13,742.17 |
| Total | € 21,816.64 |
| *Carboplatin + paclitaxel* | |
| Carboplatin | € 8,074.47 |
| Paclitaxel | € 17,485.96 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Total | € 25,560.43 |
| Additionally required SHI costs | € 208.62 |
| *Carboplatin + pemetrexed* | |
| Carboplatin | € 8,074.47 |
| Pemetrexed | € 37,075.40 |
| Total | € 45,149.87 |
| Additionally required SHI costs | € 128.67 - € 177.17 |
| *Carboplatin in combination with nab-paclitaxel* | |
| Carboplatin | € 8,074.47 |
| nab-paclitaxel | € 39,113.46 |
| Total | € 47,187.93 |
| *Monotherapy with gemcitabine or vinorelbine*[3] | |
| Gemcitabine | € 7,166.25 |
| Vinorelbine | € 7,509.17 - € 9,373.83 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2022)

b) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with cytotoxic chemotherapy

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Sotorasib | € 52,955.42 |
| Appropriate comparator therapy: | |
| *Docetaxel (only for patients with PD-L1 negative tumours)* | |
| docetaxel | € 8,522.69 |
| *Pemetrexed*[4] | |
| Pemetrexed | € 18,931.20 |
| Additionally required SHI costs | € 129.97 - € 180.78 |
| *Nivolumab* | |
| Nivolumab | € 73,034.06 |
| *Pembrolizumab* | |
| Pembrolizumab | € 93,514.21 |

[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

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| *Atezolizumab* | |
| Atezolizumab | € 67,863.65 - € 71,692.26 |
| *Docetaxel in combination with nintedanib*[5] | |
| docetaxel | € 8,522.69 |
| Nintedanib | € 30,728.05 |
| Total | € 39,250.75 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2023)

c) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with an anti-PD-1/PD-L1 in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 and platinum-containing chemotherapy

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Sotorasib | € 52,955.42 |
| Appropriate comparator therapy: | |
| *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 | € 29,625.23 |
| *Pemetrexed* | |
| Pemetrexed | € 18,931.20 |
| Additionally required SHI costs | € 129.97 - € 180.78 |
| *Erlotinib* | |
| Erlotinib | € 9,849.04 |
| *Docetaxel in combination with ramucirumab* | |
| docetaxel | € 8,522.69 |
| Ramucirumab | € 54,467.74 |
| Total | € 62,990.44 |
| *Docetaxel in combination with nintedanib* | |
| docetaxel | € 8,522.69 |

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

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Nintedanib | € 30,728.05 |
| Total | € 39,250.75 |
| *Vinorelbine* | |
| Vinorelbine | € 7,061.95 - € 8,513.24 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2023)

Other SHI services:

| Designation of the therapy | Type of service | Costs/ unit | Number/ cycle | Number/ patient/ year | Costs/ patient/ year |
|---|---|---|---|---|---|
| Appropriate comparator therapy: | | | | | |
| Atezolizumab | Surcharge for the preparation of a parenteral solution containing monoclonal antibodies | € 100 | 1 | 13.0 - 26.1 | € 1,300 - € 2,610 |
| Docetaxel (monotherapy or combination therapy) | Surcharge for production of a parenteral preparation containing cytostatic agents | € 100 | 1 | 17.4 | € 1,740 |
| Nivolumab | Surcharge for the preparation of a parenteral solution containing monoclonal antibodies | € 100 | 1 | 26.1 | € 2,610 |
| Pembrolizumab | Surcharge for the preparation of a parenteral solution containing monoclonal antibodies | € 100 | 1 | 8.7 - 17.4 | € 870 - € 1,740 |
| Pemetrexed | Surcharge for production of a parenteral preparation containing cytostatic agents | € 100 | 1 | 17.4 | € 1,740 |
| Ramucirumab | Surcharge for the preparation of a parenteral solution containing monoclonal antibodies | € 100 | 1 | 17.4 | € 1,740 |
| Vinorelbine | Surcharge for production of a parenteral preparation containing cytostatic agents | € 100 | 1 | 52.1 | € 5,210 |

## 5. 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 Sotorasib

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with sotorasib for the treatment of adults with advanced non-small cell lung cancer (NSCLC) with KRAS G12C mutation in whom disease progression has been identified after at least one prior systemic therapy:

b) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with cytotoxic chemotherapy

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

c) Adults with advanced non-small cell lung cancer (NSCLC) with KRAS p.G12C mutation after first-line therapy with an anti-PD-1/PD-L1 in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 and platinum-containing chemotherapy

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. 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.