Gemeinsamer Bundesausschuss

# Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Sotorasib (lung cancer, non-small cell, KRAS G12C mutation, ≥ 1 prior therapy)

of 4 August 2022

At its session on 4 August 2022, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

**I. Annex XII shall be amended in alphabetical order to include the active ingredient Sotorasib as follows:**

**Sotorasib**

Resolution of: 4 August 2022
Entry into force on: 4 August 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

**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 4 August 2022):**

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.

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 active ingredient of 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 a PD-1/PD-L1 antibody 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 active ingredient of the appropriate comparator 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 | | |

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 | 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. | | |

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

| |
|---|
| 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

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 | | |



## 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

60 - 130 patients

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

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: 20 May 2022):

*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 authorised under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency 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 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Gemcitabine | € 8,218.72 |
| 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 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Paclitaxel | € 17,485.96 |
| 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*[2] | |
| 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 | € 121,016.60 |
| Appropriate comparator therapy: | |
| *Docetaxel (only for patients with PD-L1 negative tumours)* | |
| Docetaxel | € 13,742.17 |
| *Pemetrexed*[3] | |
| Pemetrexed | € 37,075.40 |
| Additionally required SHI costs | € 128.67 - € 177.17 |
| *Nivolumab* | |
| nivolumab | € 76,217.74 |
| *Pembrolizumab* | |

[2] only for patients with ECOG performance status 2 as an alternative to platinum-based combination treatment
[3] 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 |
|---|---|
| Pembrolizumab | € 99,671.38 |
| *Atezolizumab* | |
| Atezolizumab | € 68,139.62 |
| *Docetaxel in combination with nintedanib*[4] | |
| Docetaxel | € 13,742.17 |
| Nintedanib | € 32,010.08 |
| Total | € 45,752.26 |

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

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

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Sotorasib | € 121,016.60 |
| 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 | € 30,935.18 |
| *Pemetrexed* | |
| Pemetrexed | € 37,075.40 |
| Additionally required SHI costs | € 128.67 - € 177.17 |
| *Erlotinib* | |
| Erlotinib | € 9,851.84 |
| *Docetaxel in combination with ramucirumab* | |
| Docetaxel | € 13,742.17 |
| Ramucirumab | € 56,850.15 |
| Total | € 70,592.32 |
| *Docetaxel in combination with nintedanib* | |

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

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Docetaxel | € 13,742.17 |
| Nintedanib | € 32,010.08 |
| Total | € 45,752.26 |
| *Vinorelbine* | |
| Vinorelbine | € 7,509.17 - € 9,373.83 |

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

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 | € 71 | 1 | 17.4 | € 1,235.40 |
| Carboplatin | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 1 | 17.4 | € 1,409.40 |
| Cisplatin | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 1 | 17.4 | € 1,409.40 |
| Docetaxel (monotherapy or combination therapy) | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 1 | 17.4 | € 1,409.40 |
| Gemcitabine (combination therapy) | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 2 | 34.8 | € 2,818.80 |
| Gemcitabine (monotherapy) | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 3 | 39 | € 3,159.00 |
| nab-paclitaxel | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 3 | 52.2 | € 4,228.20 |
| Nivolumab | Surcharge for the preparation of a parenteral | € 71 | 1 | 26.1 | € 1,853.10 |

| Designation of the therapy | Type of service | Costs/ unit | Number/ cycle | Number / patient/ year | Costs/ patient/ year |
|---|---|---|---|---|---|
| | solution containing monoclonal antibodies | | | | |
| Paclitaxel | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 1 | 17.4 | € 1,409.40 |
| Pembrolizumab | Surcharge for the preparation of a parenteral solution containing monoclonal antibodies | € 71 | 1 | 8.7 - 17.4 | € 617.70 - € 1,235.40 |
| Pemetrexed | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 1 | 17.4 | € 1,409.40 |
| Ramucirumab | Surcharge for the preparation of a parenteral solution containing monoclonal antibodies | € 71 | 1 | 17.4 | € 1,235.40 |
| Vinorelbine (combination therapy) | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 2 | 34.8 | € 2,818.80 |
| Vinorelbine (monotherapy) | Surcharge for production of a parenteral preparation containing cytostatic agents | € 81 | 1 | 52.1 | € 4,220.10 |



## II. Entry into force

1. The resolution will enter into force on the day of its publication on the website of the G-BA on 4 August 2022.

2. The period of validity of the resolution is limited in accordance with the following regulations:

The statements made for each of the patient groups

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

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

in numbers 1, 2, 3 and 4 are limited until 1 July 2023.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 4 August 2022

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

Prof. Hecken