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
Selpercatinib (reassessment after the deadline: thyroid cancer, RET-mutated, monotherapy, 12 years and older)

of 20 November 2025

At their session on 20 November 2025, the Federal Joint Committee (G-BA) resolved not 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. **In Annex XII, after No. 5 on the benefit assessment of Selpercatinib in the version of the resolution of 7 November 2024 on the therapeutic indication "for the treatment of advanced RET fusion-positive solid tumours, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted", the information on the active ingredient selpercatinib in the version of the resolution of 16.03.2023 (BAnz AT 19.05.2023 B9) is replaced by the following information:**

Selpercatinib

Resolution of: 20 November 2025
Entry into force on: 20 November 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 2 September 2022):

Retsevmo as monotherapy is indicated for the treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC).

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

Retsevmo as monotherapy is indicated for the treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC), first-line therapy.

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

Adults and adolescents 12 years and older with advanced medullary RET receptor tyrosine kinase (rearranged during transfection - RET)-mutant thyroid cancer; first-line therapy

Appropriate comparator therapy:

– Vandetanib

or

– cabozantinib

Extent and probability of the additional benefit of selpercatinib as monotherapy compared to cabozantinib or vandetanib:

Indication of a major additional benefit.

Study results according to endpoints:[1]

Adults and adolescents 12 years and older with advanced medullary RET receptor tyrosine kinase (rearranged during transfection - RET)-mutant thyroid cancer; first-line therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival
Morbidity	↑	Advantages in fatigue, nausea and vomiting, pain, insomnia, appetite loss, diarrhoea and health status
Health-related quality of life	↑	Advantages in all functional scales of the EORTC QLQ-C30 physical functioning
Side effects	↑↑	Advantages in the endpoints of severe, serious AEs and therapy discontinuation due to AEs, as well as in detail mainly advantages for specific AEs.
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		

LIBRETTO-531 study

- Comparison: Selpercatinib versus cabozantinib or vandetanib
- Study design: open-label, randomised, controlled phase III study
- Results based on the data cut-off from 11.03.2024

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A25-71) unless otherwise indicated.

Mortality

Endpoint	Selpercatinib		Cabozantinib or vandetanib		Intervention vs control
	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 (%)*	Hazard ratio [95% CI] p value [a] Absolute difference (AD) [b]
Mortality					
Overall survival	193	n.r. 10 (5.2)	98	n.r. 16 (16.3)	0.28 [0.12; 0.61] < 0.001

Morbidity

Progression-free survival (PFS) [c]					
PFS according to BICR	193	n.r. [35.78; n.c.] 34 (17.6)	98	13.9 [12.25; 19.55] 47 (48.0)	0.20 [0.13; 0.32] < 0.001
Symptomatology					
EORTC QLQ-C30 (time to first deterioration) [d]					
Fatigue	193	4.6 [2.73; 7.46] 128 (66.3)	98	1.2 [0.99; 1.91] 68 (69.4)	0.56 [0.41; 0.76] < 0.001 AD: + 3.4 months
Nausea and vomiting	193	19.4 [11.01; 24.87] 97 (50.3)	98	2.2 [1.81; 4.63] 56 (57.1)	0.44 [0.32; 0.62] < 0.001 AD: + 17.2 months
Pain	193	5.7 [2.89; 11.07] 115 (59.6)	98	1.9 [1.12; 2.63] 65 (66.3)	0.54 [0.39; 0.74] < 0.001 AD: + 3.8 months
Dyspnoea	193	27.4 [10.15; n.c.] 94 (48.7)	98	10.6 [6.47; 22.60] 44 (44.9)	0.79 [0.55; 1.13] 0.195
Insomnia	193	n.r. [16.62; n.c.] 79 (40.9)	98	2.8 [2.10; 19.42] 51 (52.0)	0.55 [0.39; 0.79] < 0.001
Appetite loss	193	35.9 [19.35; n.c.] 82 (42.5)	98	2.0 [1.87; 3.71] 64 (65.3)	0.28 [0.20; 0.39] < 0.001 AD: + 33.9 months

Constipation	193	2.9 [2.14; 4.47] 131 (67.9)	98	3.7 [1.91; 14.03] 51 (52.0)	1.04 [0.75; 1.45]; 0.795
Diarrhoea	193	n.r. [10.81; n.c.] 85 (44.0)	98	2.0 [1.45; 3.25] 58 (59.2)	0.39 [0.28; 0.55] < 0.001
Pain (Worst Pain NRS) (time to first deterioration) [e]					
	193	n.r. 44 (22.8)	98	9.1 [1.71; n.c.] 40 (40.8)	0.42 [0.27; 0.65] < 0.001
Health status					
EQ-5D VAS - time to first deterioration [f]					
	193	38.7 [24.87; n.c.] 72 (37.3)	98	3.7 [2.43; 7.98] 53 (54.1)	0.40 [0.28; 0.58] < 0.001 AD: + 35 months

Health-related quality of life

EORTC QLQ-C30 (time to first deterioration) [g]					
Global health status	193	5.4 [3.71; 7.39] 123 (63.7)	98	1.8 [0.99; 1.91] 66 (67.3)	0.53 [0.39; 0.72] < 0.001 AD: + 4 months
Physical functioning	193	27.6 [11.60; n.c.] 87 (45.1)	98	2.7 [1.87; 3.68] 61 (62.2)	0.35 [0.25; 0.50] < 0.001 AD: + 24.9 months
Role functioning	193	5.8 [3.75; 12.94] 114 (59.1)	98	1.9 [1.02; 2.96] 66 (67.3)	0.49 [0.36; 0.66] < 0.001 AD: + 3.9 months
Emotional functioning	193	29.1 [20.30; n.c.] 81 (42.0)	98	5.2 [2.79; 9.26] 48 (49.0)	0.51 [0.35; 0.74] < 0.001 AD: + 23.9 months
Cognitive functioning	193	5.6 [4.21; 9.40] 123 (63.7)	98	4.4 [2.00; 6.47] 59 (60.2)	0.73 [0.53; 0.99] 0.046 AD: + 1.2 months
Social functioning	193	9.0	98	2.2	0.53 [0.38; 0.72]

		[4.70; 14.65] 110 (57.0)		[1.81; 3.68] 61(62.2)	< 0.001 AD: + 6.8 months

Side effects

Total adverse events (presented additionally)					
	193	0.3 [0.26; 0.30] 192 (99.5)	97	0.2 [0.13; 0.23] 96 (99.0)	–
Serious adverse events (SAE)					
	193	n.r. [33.12; n.c.] 59 (30.6)	97	30.3 [22.05; n.c.] 33 (34.0)	0.59 [0.38; 0.92] 0.017
Severe adverse events (CTCAE grade ≥ 3)					
	193	10.1 [5.06; 12.39] 119 (61.7)	97	1.9 [1.12; 4.60] 79 (81.4)	0.54 [0.40; 0.73] < 0.001 AD: + 8.2 months
Therapy discontinuation due to adverse events					
	193	n.r. 11 (5.7)	97	n.r. [18.17; n.c.] 31 (32.0)	0.11 [0.05; 0.23] < 0.001
Specific adverse events					
PRO-CTCAE	No suitable data [h]				
Gastrointestinal disorders (SOC, AEs)	193	2.3 [1.25; 3.65] 135 (69.9)	97	0.5 [0.30; 0.92] 82 (84.5)	0.53 [0.40; 0.71] < 0.001 AD: + 1.8 months
Dry mouth (PT, AEs)	193	n.r. 70 (36.3)	97	n.r. 10 (10.3)	3.65 [1.88; 7.09] < 0.001
Diarrhoea (PT, AEs)	193	n.r. 54 (28.0)	97	3.0 [1.84; 5.26] 61 (62.9)	0.27 [0.19; 0.40] < 0.001
Nausea (PT, AEs)	193	n.r. 22 (11.4)	97	n.r. [13.73; n.c.] 34 (35.1)	0.22 [0.12; 0.38] < 0.001
Vomiting (PT, AEs)	193	n.r. 19 (9.8)	97	40.0 [n.c.] 25 (25.8)	0.26 [0.14; 0.47] < 0.001
Stomatitis (PT, AEs)	193	n.r. 7 (3.6)	97	n.r. 19 (19.6)	0.14 [0.06; 0.33] < 0.001

Asthenia (PT, AEs)	193	n.r. 26 (13.5)	97	n.r. [33.08; n.c.] 27 (27.8)	0.37 [0.21; 0.63] < 0.001
Mucosa inflammation (PT, AEs)	193	n.r. 14 (7.3)	97	n.r. 24 (24.7)	0.23 [0.12; 0.45] < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)	193	n.r. [19.61; n.c.] 84 (43.5)	97	1.0 [0.59; 0.99] 78 (80.4)	0.27 [0.20; 0.37] < 0.001
Palmar-plantar erythrodysesthesia syndrome (PT, AEs)	193	n.r. 7 (3.6)	97	n.r. [2.53; n.c.] 42 (43.3)	0.06 [0.03; 0.13] < 0.001
Alanine aminotransferase elevated (PT, severe AEs) [i]	193	n.r. 21 (10.9)	97	n.r. 2 (2.1)	5.16 [1.21; 22.07] 0.014
Metabolism and nutrition disorder (SOC, severe AEs)[i]	193	n.r. 12 (6.2)	97	n.r. [30.29; n.c.] 19 (19.6)	0.19 [0.09; 0.41] < 0.001
Nervous system disorders (SOC, severe AEs) [i]	193	n.r. 5 (2.6)	97	n.r. 7 (7.2)	0.29 [0.09; 0.93] 0.027
Blood and lymphatic system disorders (SOC, severe AEs) [i]	193	n.r. 4 (2.1)	97	n.r. 7 (7.2)	0.17 [0.05; 0.60] 0.002
Respiratory, thoracic and mediastinal disorders (SOC, severe AEs) [i]	193	n.r. 3 (1.6)	97	n.r. 5 (5.2)	0.17 [0.04; 0.74] 0.008

[a] Cox model with stratification variables RET mutation and indicated therapy; p value: stratified log-rank test
[b] Data on absolute difference (AD) only in the case of statistically significant difference; own calculation
[c] Information from the dossier of the pharmaceutical company
[d] An increase in EORTC QLQ-C30 score by ≥ 10 points compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 100)
[e] An increase in pain (Worst Pain NRS) score by ≥ 2 points compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 10)
[f] A decrease in EQ-5D VAS score by ≥ 15 points compared to the start of study is considered as clinically relevant deterioration (scale range: 0 to 100)
[g] A decrease in EORTC QLQ-C30 score by ≥ 10 points compared to the baseline is considered as clinically relevant deterioration (scale range: 0 to 100)
[h] No suitable data available; for justification, see section I 4.1 of the present dossier assessment
[i] Operationalised as CTCAE grade ≥ 3

Abbreviations used:

AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR = hazard ratio; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; NRS = numerical rating scale; PRO: Patient Reported Outcome; PT = preferred term; QLQ-C30 = Quality of Life Questionnaire - Core 30; RET = Rearranged During Transfection; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

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

Adults and adolescents 12 years and older with advanced medullary RET receptor tyrosine kinase (rearranged during transfection - RET)-mutant thyroid cancer; first-line therapy

Approx. 40 – 170 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 Retsevmo (active ingredient: selpercatinib) at the following publicly accessible link (last access: 20 August 2025):

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

Treatment with selpercatinib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology, specialists in internal medicine, endocrinology and diabetology, specialists in paediatrics and adolescent medicine, all of whom are experienced in the treatment of patients with thyroid cancer, as well as other doctors from other specialist groups participating in the Oncology Agreement.

This medicinal product received a conditional marketing authorisation. 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.

RET testing

The presence of an RET gene fusion (NSCLC and non-medullary thyroid cancer) or mutation (MTC) should be confirmed by a validated test prior to starting treatment with Retsevmo.

4. Treatment costs

Annual treatment costs:

Adults and adolescents 12 years and older with advanced medullary RET receptor tyrosine kinase (rearranged during transfection - RET)-mutant thyroid cancer; first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Selpercatinib	€ 35,099.71 - € 46,718.70
Appropriate comparator therapy:	
Cabozantinib[2]	€ 67,650.66
Vandetanib	First year of treatment: € 52,868.61 - € 55,322.77 Subsequent year: € 54,612.52 - € 55,292.39

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 September 2025)

Costs for additionally required SHI services: not applicable

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

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Adults and adolescents 12 years and older with advanced medullary RET receptor tyrosine kinase (rearranged during transfection - RET)-mutant thyroid cancer; first-line therapy

- 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.

[2] Patients ≥ 18 years.

II. **The resolution will enter into force on the day of its publication on the website of the G-BA on 20 November 2025.**

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

Berlin, 20 November 2025

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

Prof. Hecken