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
Avapritinib (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit (indolent systemic mastocytosis (ISM)))

dated 7 May 2026

At their session on 7 May 2026, 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. In Annex XII, the information on the active ingredient Avapritinib in the version of the resolution of 20 June 2024 (Federal Gazette, BAnz AT 31.07.2024 B2) shall be replaced by the following information:

Avapritinib

Resolution of: 7 May 2026
Entry into force on: 7 May 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 11 December 2023):

AYVAKYT is indicated for the treatment of adult patients with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment.

Therapeutic indication of the resolution (resolution of 7 May 2026):

See therapeutic indication according to marketing authorisation.

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

Adults with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment

Appropriate comparator therapy:

- Best supportive care

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

Hint for a minor additional benefit.

Study results according to endpoints:[1]

Adults with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↑↑	Advantages in the ISM-SAF endpoints (skin domain and most severe cardinal domain/ symptom cluster), PGIS and EQ-5D VAS
Health-related quality of life	↑↑	Advantages in the MC-QoL endpoints (total score, symptoms, social life/ functioning and emotions) and the PCS of the SF-12

[1] Data from the dossier assessment of the IQWiG (A25-136) and from the addendum (A26-28), unless otherwise indicated.

Side effects	↔	No relevant differences for the benefit assessment.
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		

PIONEER study, part 2

- Multicentre phase II study with double-blind, randomised, controlled study phase (part 2; 24 weeks)
- Avapritinib + best supportive care vs placebo + best supportive care
- Population: Patients with confirmed systemic mastocytosis and moderate to severe symptoms based on a mean ISM-SAF TSS ≥ 28 despite symptomatic therapy in the screening phase.

Mortality

Endpoint	**Avapritinib + BSC**		**Placebo + BSC**		**Avapritinib + BSC vs Placebo + BSC**
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[a]
Overall survival[b]					
No deaths occurred.					

Morbidity

Endpoint	Avapritinib + BSC		Placebo + BSC		Avapritinib + BSC vs Placebo + BSC
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[a]
Symptomatology					
ISM-SAF – Improvement at week 24[c]					
Total symptom score	141	54 (38.3)	71	19 (26.8)	1.47 [0.94; 2.27] 0.088
Gastrointestinal domain	141	45 (31.9)	71	25 (35.2)	0.94 [0.64; 1.38] > 0.999 [d]
Skin domain	141	70 (51.1)	71	19 (26.8)	1.94 [1.27; 2.96] 0.002 [d]
Neurocognitive domain	141	49 (34.8)	71	20 (28.2)	1.26 [0.82; 1.93] 0.294 [d]
PGIS – Improvement at week 24[e]					
	141	72 (51.1)	71	24 (33.8)	1.54 [1.07; 2.21] 0.020
Health status					
EQ-5D VAS – Improvement at week 24[f]					
	141	40 (28.4)	71	7 (9.9)	2.88 [1.36; 6.12] 0.006
PGIC– Improvement at week 24 [d, g]					
	141	11 (7.8)	71	1 (1.4)	5.81 [0.64; 53.03] 0.119

Endpoint	Avapritinib + BSC				Placebo + BSC				Avapritinib + BSC vs Placebo + BSC
	Values at the start of study		Change at week 24		Values at the start of the study		Change at week 24		Mean difference [95% CI] p value
	N	MV (SD)	N	MV (SD)	N	MV (SD)	N	MV (SD)	Hedges' g [95% CI]
Cardinal symptom and cardinal domain using ISM-SAF [d]									
(most severe) cardinal symptom	139	7.66 (1.693)	131	-2.19 (0.223)	71	7.91 (1.679)	66	-1.38 (0.29)	-0.81 [-1.46; -0.17] 0.014 -0.32 [-0.63; -0.03]
(most severe) cardinal domain/ symptom cluster	139	17.51 (6.033)	131	-6.18 (0.570)	71	18.58 (6.397)	66	-2.90 (0.749)	-3.27 [-4.93; -1.62] < 0.001 -0.51 [-0.82; -0.21]

Health-related quality of life

Endpoint	Avapritinib + BSC		Placebo + BSC		Avapritinib + BSC vs Placebo + BSC
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[a]
Health-related quality of life					
MC-QoL – Improvement at week 24[h]					
Total score	141	93 (66.0)	71	31 (43.7)	1.54 [1.15; 2.08] 0.004
Symptoms	141	102 (72.3)	71	38 (53.5)	1.37 [1.08; 1.74] 0.010[d]
Social life/ functioning	141	97 (68.8)	71	35 (49.3)	1.42 [1.09; 1.84] 0.008 [d]
Emotions	141	101 (71.6)	71	37 (52.1)	1.41 [1.10; 1.80] 0.006[d]
Skin	141	99 (70.2)	71	50 (70.4)	1.01 [0.84; 1.22] 0.904[d]

Endpoint	Avapritinib + BSC		Placebo + BSC		Avapritinib + BSC vs Placebo + BSC
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[a]
SF-12v2 – Improvement at week 24					
Physical Component Summary (PCS) score[i]	141	71 (50.4)	71	25 (35.2)	1.43 [1.01; 2.03] 0.042
Mental Component Summary (MCS) score[j]	141	70 (49.6)	71	30 (42.3)	1.19 [0.87; 1.63] 0.285

Side effects

Endpoint	Avapritinib + BSC		Placebo + BSC		Avapritinib + BSC vs Placebo + BSC
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[a]
Adverse events in total					
	141	128 (90.8)	71	66 (93.0)	-
Serious adverse events (SAEs)					
	141	7 (5.0)	71	8 (11.3)	0.44 [0.17; 1.17] 0.101[k]
Severe adverse events (CTCAE grade 3 or 4)					
	141	30 (21.3)	71	15 (21.1)	1.01 [0.58; 1.75] > 0.999[k]
Therapy discontinuation due to adverse events					
	141	3 (2.1)	71	1 (1.4)	1.51 [0.16; 14.26] 0.790[k]
Specific adverse events					
No specific adverse events were identified.					

a. Asymptotic normal approximation of the logarithmic Mantel-Haenszel estimate, stratified by the stratification factors serum tryptase (< 20 ng/ml vs ≥ 20 ng/ml) and baseline ISM status (moderate vs severe)
b. The results on overall mortality are based on the data on fatal AEs.
c. A decrease by ≥ 16.5 points (ISM-SAF total score) compared to the start of the study is considered as clinically relevant improvement (scale range: ISM-SAF total score: 0 to 110; gastrointestinal, skin and neurocognitive domains: 0 to 30).
d. Results from the pharmaceutical company's dossier.
e. A decrease in the PGIS score by ≥ 1 point compared to the start of the study is considered as clinically relevant improvement (scale range: 0 to 4).
f. An increase in the EQ-5D VAS score by ≥ 15 points compared to the start of the study is considered as clinically relevant improvement (scale range: 0 to 100).
g. A decrease in the PGIC score by ≥ 1.5 points compared to the start of the study is considered as clinically relevant improvement (scale range: 0 to 10).
h. An increase by ≥ 15 points compared to the start of the study is considered as clinically relevant improvement (scale range: MC-QoL total score and individual domains: 0 to 100).
i. An increase in the PCS score by ≥ 9.1 points compared to the start of the study is considered as clinically relevant improvement (scale range: 11.1 to 71.8 determined using the 2009 normative sample).
j. An increase in the MCS score by ≥ 8.5 points compared to the start of the study is considered as clinically relevant improvement (scale range: 11.3 to 68.2 determined using the 2009 normative sample).
k. Own calculation

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; ISM = indolent systemic mastocytosis; SAF = Standard Assessment Form; CI = confidence interval; MC-QoL = Mastocytosis Quality of Life Questionnaire; MCS = Mental Component Summary; N = number of patients evaluated; n = number of patients with (at least one) event; PCS = Physical Component Summary; PGIS = Patients' Global Impression of Symptom Severity; SF-12v2 = Short Form-12 Health Survey Version 2; VAS = visual analogue scale; vs = versus

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

Adults with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment

Approx. 715 to 1,000 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 Ayvakyt (active ingredient: avapritinib) at the following publicly accessible link (last access: 29 January 2026):

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

Treatment with avapritinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of indolent systemic mastocytosis.

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 assess new information on this medicinal product at least annually and update the product information where necessary.

4. Treatment costs

Annual treatment costs:

Adults with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Avapritinib	€ 173,780.88
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 February 2026)

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 with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment

- No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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.

II. The resolution will enter into force on the day of its publication on the G-BA website on 7 May 2026.

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

Berlin, 7 May 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken