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
Seladelpar (primary biliary cholangitis (combination with ursodeoxycholic acid))

of 4 September 2025

At their session on 4 September 2025, 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 Seladelpar as follows:

Seladelpar

Resolution of: 4 September 2025
Entry into force on: 4 September 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 20 February 2025):

Lyvdelzi is indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA alone, or as monotherapy in those unable to tolerate UDCA.

Therapeutic indication of the resolution (resolution of 4 September 2025):

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Seladelpar is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The G-BA determine the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Adults with primary biliary cholangitis (PBC) and inadequate response or intolerance to ursodeoxycholic acid (UDCA)

Extent of the additional benefit and significance of the evidence of seladelpar:

Indication of a minor additional benefit

Study results according to endpoints:[1]

Adults with primary biliary cholangitis (PBC) and inadequate response or intolerance to ursodeoxycholic acid (UDCA)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant differences for the benefit assessment.
Morbidity	↑↑	Advantages in the endpoint of itching
Health-related quality of life	↔	No relevant differences for the benefit assessment.
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		

RESPONSE study (CB8025-32048): double-blind, randomised, controlled phase III study; seladelpar versus placebo over 12 months

Mortality

Endpoint	Seladelpar N = 128	Placebo N = 65	Seladelpar vs placebo
	Patients with event n (%)	*Patients with event n (%)*	*RR [95% CI] p value*
Overall mortality			
Deaths	No deaths occurred.		

[1] Data from the dossier assessment of the G-BA (published on 16. June 2025), and from the amendment to the dossier assessment from 15 August 2025, unless otherwise indicated.

Morbidity

Endpoint	Seladelpar N = 128	Placebo N = 65	Seladelpar vs placebo
	Patients with event n (%)	*Patients with event n (%)*	*RR [95% CI] p value*
Biochemical response[a] *(presented additionally)*			
ALP < 1.67 × ULN and TB ≤ ULN and ALP reduction ≥ 15%	79 (61.7)[b]	13 (20.0)[b]	3.09 [1.87; 5.10] < 0.0001
Clinical events			
Liver transplantation	No events occurred.		
MELD score ≥ 15 at a min. of 2 consecutive visits	No events occurred.		
Ascites requiring treatment	No events occurred.		
Hospitalisation[c] (categorised as "positive" by CERC[d])	1 (0.8)	0 (0)	n.d.

Endpoint	Seladelpar N = 127		Placebo N = 64		Seladelpar vs placebo
	Baseline[f] MV (SD)	*Change from baseline to month 6 LS mean (SE)*	*Baseline[f] MV (SD)*	*Change from baseline to month 6 LS mean (SE)*	*LS mean difference [95% CI] p value Hedges' g[g]*
Itching using Pruritus NRS at month 6					
Pruritus NRS[e] at month 6 (continuous analysis)	3.03 (2.81)	-1.33 (0.14)	3.02 (2.96)	-0.42 (0.19)	-0.90 [-1.35; -0.45]; 0.0001 *-0.58 [-0.89; -0.28]*

Endpoint	Seladelpar N = 127		Placebo N = 64		Seladelpar vs placebo
	Baseline[f] MV (SD)	*Change from baseline to month 12 LS mean (SE)*	*Baseline[f] MV (SD)*	*Change from baseline to month 12 LS mean (SE)*	*LS mean difference [95% CI] p value Hedges' g[g]*
Itching using 5-D Itch at month 12					
5-D Itch[h] total score	11.6 (4.85)	-2.26 (0.33)	11.2 (4.65)	0.05 (0.46)	-2.31 [-3.40; -1.23]; < 0.0001 *-0.62 [-0.93; -0.31]*
- 5-D Itch severity grade	2.26 (1.04)	-0.42 (0.07)	2.24 (0.99)	-0.05 (0.10)	-0.38 [-0.61; -0.15]; 0.002 *-0.47 [-0.77; -0.16]*

- 5-D Itch duration	1.59 (1.11)	-0.32 (0.07)	1.56 (1.08)	0.08 (0.10)	-0.40 [-0.63; -0.16]; 0.001 *-0.49 [-0.79; -0.19]*
- 5-D Itch impairment	2.27 (1.37)	-0.55 (0.09)	2.22 (1.24)	0.05 (0.13)	-0.60 [-0.91; -0.29]; 0.0002 *-0.57 [-0.87; -0.26]*
- 5-D Itch history	3.35 (1.09)	-0.64 (0.13)	3.13 (1.16)	-0.17 (0.18)	-0.47 [-0.90; -0.04]; 0.03 *-0.32 [-0.62; -0.02]*
- 5-D Itch localisation	2.16 (1.29)	-0.25 (0.09)	2.08 (1.20)	0.14 (0.12)	-0.38 [-0.67; -0.10]; 0.009 *-0.39 [-0.69; -0.09]*

Health-related quality of life

Endpoint	**Seladelpar N = 126**		**Placebo N = 63**		**Seladelpar vs placebo**
	Baseline[f] MV (SD)	*Change from baseline to month 12 LS mean (SE)*	*Baseline[f] MV (SD)*	*Change from baseline to month 12 LS mean (SE)*	*LS mean difference [95% CI] p value*
Domains Questionnaire PBC-40[i] at month 12					
- Itching	5.14 (3.85)	-1.31 (0.26)	5.60 (3.97)	-0.48 (0.36)	-0.83 (-1.68; 0.02); 0.054
- General symptoms	15.1 (4.56)	-0.10 (0.30)	15.7 (5.46)	-0.19 (0.41)	0.09 (-0.87; 1.06); 0.85
- Fatigue	27.6 (10.0)	-1.97 (0.67)	27.4 (10.6)	-1.50 (0.92)	-0.47 (-2.66; 1.71); 0.67
- Cognitive functioning	13.2 (5.51)	-0.55 (0.33)	12.8 (4.88)	-0.42 (0.44)	-0.13 (-1.20; 0.94); 0.81
- Emotional functioning	7.79 (2.89)	-0.70 (0.20)	7.72 (3.15)	-0.95 (0.27)	0.25 (-0.40; 0.90); 0.45
- Social functioning	22.9 (8.44)	-0.67 (0.47)	22.2 (8.32)	-1.72 (0.64)	1.05 (-0.47; 2.56); 0.17

Side effects

Endpoint **MedDRA system organ classes/ preferred terms/ AEs of special interest**	**Seladelpar N = 128**	**Placebo N = 65**	**Seladelpar vs placebo**
	Patients with event n (%)	*Patients with event n (%)*	*RR [95% CI] p value*
Total adverse events (presented additionally)	111 (86.7)	55 (84.6)	-

Serious adverse events (SAE)	9 (7.0)	4 (6.2)	1.14 [0.37; 3.57]; 0.82
Severe adverse events (CTCAE grade 3 or 4)	14 (10.9)	5 (7.7)	1.42 [0.54; 3.78]; 0.48
Therapy discontinuation due to adverse events	4 (3.1)	3 (4.6)	0.68 [0.16; 2.94]; 0.60
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)			
- No significant differences			
SAEs according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)			
- No significant differences			
Adverse events of special interest (with statistically significant difference between the treatment arms)			
Pruritus-related AE (regardless of severity grade)	7 (5.5)	10 (15.4)	0.36 [0.14; 0.89]; 0.03

a. Primary endpoint of the Response study. Subjects were categorised as responders if all 3 of the following conditions were met: ALP < 1.67 × ULN; ALP reduction from baseline by ≥ 15%; total bilirubin ≤ 1.0 × ULN.
b. A total of 14 subjects in the seladelpar arm and 8 subjects in the placebo arm had missing values at month 12 and were therefore imputed as non-responders.
c. Hospitalisations due to a new occurrence or recurrence of: variceal haemorrhage, hepatic encephalopathy or spontaneous bacterial peritonitis were collected.
d. CERC members assessed whether the definitions of clinical PBC events were met in a blinded, independent vote. They were categorised as "positive" (i.e. event is present), "negative" (event is absent) or "undetermined".
e. Intensity of the worst itching within the last 24 hours on an 11-point scale from 0 (= no itching) to 10 (= worst perceivable itching) (self-report).
f. Baseline was defined as the arithmetic mean of all available measurements at screening, during the run-in phase (approx. 2 weeks before day 1), on day 1 and during unplanned visits before or on day 1.
g. Hedges' g, calculated post-hoc.
h. The total score to be achieved is between 5 and 25 points. Each domain can achieve a value of 1 to 5 points. Higher points indicate more severe itching.
i. Survey of health-related quality of life in participants with PBC, consisting of 40 items in 6 domains. Depending on the number of items in the individual domains, there are different ranges of values for the scores of the domains, which range from 3 to 55 points. Higher scores reflect a deterioration, while lower scores indicate an improvement.

Abbreviations used:
ALP = alkaline phosphatase; CERC = Clinical Event Review Committee; CTCAE = Common Terminology Criteria for Adverse Events; n.d.: no data available; CI = confidence interval; LS = least squares; MELD = Model for End-Stage Liver Disease; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; NRS = numerical rating scale; PBC = primary biliary cholangitis; RR = relative risk; SD = standard deviation; SE = standard error; (S)AE = (serious) adverse event. TB = total bilirubin; ULN = upper limit of normal; vs = versus

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

Adults with primary biliary cholangitis (PBC) and inadequate response or intolerance to ursodeoxycholic acid (UDCA)

Approx. 6,000 to 13,000 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 Gilead's seladelpar (active ingredient: seladelpar) at the following publicly accessible link (last access: 26 August 2025):

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

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 will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

4. Treatment costs

Annual treatment costs:

Adults with primary biliary cholangitis (PBC) and inadequate response or intolerance to ursodeoxycholic acid (UDCA)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Seladelpar	€ 63,796.08
+ ursodeoxycholic acid (UDCA) Total:	€ 520.49 € 64,316.57

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 August 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 with primary biliary cholangitis (PBC) and inadequate response or intolerance to ursodeoxycholic acid (UDCA)

- No medicinal product with new active ingredients that can be used in a combination therapy that fulfils 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.

6. Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Lyvdelzi is a medicinal product placed on the market from 1 January 2025.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5% of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant extent within the scope of SGB V.

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 September 2025.

2. The period of validity of the resolution is limited to 1 March 2031.

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

Berlin, 4 September 2025

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

Prof. Hecken