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
Bulevirtide (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit (hepatitis delta virus (HDV) infection, HDV-RNA positive, ≥ 3 years, ≥ 10 kg BW))

of 19 February 2026

At their session on 19 February 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 Bulevirtide in the version of the resolution of 18 February 2021 (Federal Gazette, BAnz AT 09.04.2021 B3) shall be replaced by the following information:

Bulevirtide

Resolution of: 19 February 2026
Entry into force on: 19 February 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 26 November 2024):

Hepcludex is indicated for the treatment of chronic hepatitis delta virus (HDV) infection in plasma (or serum) HDV-RNA positive adult and paediatric patients 3 years of age and older weighing at least 10 kg with compensated liver disease.

Therapeutic indication of the resolution (resolution of 19 February 2026):

See therapeutic indication according to marketing authorisation.

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

a) Adults with chronic hepatitis D infection with compensated liver disease

Appropriate comparator therapy:

Best supportive care

Extent and probability of the additional benefit of bulevirtide compared to best supportive care:

An additional benefit is not proven.

b) Children and adolescents 3 to < 18 years of age with chronic hepatitis D infection and compensated liver disease

Appropriate comparator therapy:

Best supportive care

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

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with chronic hepatitis D infection with compensated liver disease

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↔	No relevant differences for the benefit assessment.
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		

MYR301 study: Bulevirtide (relevant study arm with a dosage of 2 mg/d) versus no treatment of HDV infection

Study design: randomised, open-label, relevant observation period is the comparative phase of 48 weeks

Mortality

Endpoint	Bulevirtide		Best supportive care		Bulevirtide vs Best supportive care
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator
Overall mortality	49	0 (0)	51	0 (0)	–

[1] Data from IQWiG's dossier assessment (A25-113).

Morbidity

Endpoint	Bulevirtide		Best supportive care		Bulevirtide vs Best supportive care
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[a]
Liver-related events[b]	49	0 (0)	51	0 (0)	–
Fatigue (FSS improvement at week 48[c])	49	20 (40.8)	51	13 (25.5)	1.60 [0.90; 2.85]; 0.121
Health status (EQ-5D-VAS improvement at week 48[c])	49	17 (34.7)	51	13 (25.5)	1.36 [0.74; 2.50]; 0.364
Virological response (*presented additionally*)					
Virological response[d]	49	36 (73.5)	51	2 (3.9)	18.73 [4.77; 73.64]; < 0.001
Undetectable HDV-RNA	49	6 (12.2)	51	0 (0)	13.52 [0.78; 233.76]; 0.073
Decrease in viral load by ≥ 2 $\log_{10}$ (IU/ml)	49	36 (73.5)	51	2 (3.9)	18.73 [4.77; 73.64]; < 0.001

Health-related quality of life

Endpoint	Bulevirtide		Best supportive care		Bulevirtide vs Best supportive care
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
HQLQ[e] (SF-36 – improvement at week 48[f])					
Physical Component Summary (PCS) score	49	4 (8.2)	51	3 (5.9)	1.39 [0.33; 5.88] 0.717
Mental Component Summary (MCS) score	49	13 (26.5)	51	8 (15.7)	1.69 [0.77; 3.72] 0.222
Physical functioning	49	11 (22.4)	51	10 (19.6)	1.14 [0.53; 2.45]

Endpoint	Bulevirtide		Best supportive care		Bulevirtide vs Best supportive care
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Physical role functioning	49	15 (30.6)	51	8 (15.7)	1.95 [0.91; 4.19]
Physical pain	49	14 (28.6)	51	14 (27.5)	1.04 [0.56; 1.95]
General health perception	49	16 (32.7)	51	15 (29.4)	1.11 [0.62; 1.99]
Vitality	49	14 (28.6)	51	10 (19.6)	1.46 [0.72; 2.97]
Social functioning	49	12 (24.5)	51	6 (11.8)	2.08 [0.85; 5.11]
Emotional role functioning	49	19 (38.8)	51	16 (31.4)	1.24 [0.72; 2.11]
Psychological well-being	49	18 (36.7)	51	15 (29.4)	1.25 [0.71; 2.19]
HQLQ[e] (hepatitis-specific questions – improvement at week 48[c])					
Health issues	49	24 (49.0)	51	18 (35.3)	1.39 [0.87; 2.22]; 0.222
Positive well-being	49	11 (22.4)	51	11 (21.6)	1.04 [0.50; 2.18]; 0.948
Hepatitis-specific health issues	49	28 (57.1)	51	23 (45.1)	1.27 [0.86; 1.87]; 0.250
Hepatitis-specific limitations	49	16 (32.7)	51	8 (15.7)	2.08 [0.98; 4.42]; 0.057

Side effects

Endpoint	Bulevirtide		Best supportive care		Bulevirtide vs Best supportive care
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Adverse events in total					
	49	41 (83.7)	51	41 (80.4)	–
Serious adverse events (SAEs)					
	49	2 (4.1)	51	1 (2.0)	2.08 [0.19; 22.23]; 0.598
Severe adverse events (CTCAE ≥ grade 3)					
	49	5 (10.2)	51	4 (7.8)	1.30 [0.37; 4.56]; 0.771
Therapy discontinuation due to adverse events					
	49	0 (0)	51	0 (0)	–
Specific adverse events					
Symptomatic increase in bile salts		No suitable data			
General disorders and administration site conditions (SOC, AE)	49	15 (30.6)	51	2 (3.9)	7.81 [1.88; 32.37]; < 0.001
Nervous system disorders (SOC, AE)[h]	49	11 (22.4)	51	0 (0)	23.92 [1.45; 395.20]; < 0.001

a. IQWiG calculation of RR, CI (asymptotic) and p value (unconditional exact test, CSZ method; normal approximation of the combined response (Wald method)) In the case of 0 events in one study arm, the correction factor 0.5 was used in both study arms when calculating effect and CI.
b. Defined as the development of cirrhosis, the development or deterioration of jaundice, coagulation disorders, ascites, hepatic encephalopathy or bleeding from oesophageal varices, the development of hepatocellular carcinoma, the occurrence of liver transplantation, liver-related hospitalisations or liver-related death

c. An increase in score by ≥ 15% of the scale range compared to the start of the study is considered as clinically relevant improvement.
d. Defined as the simultaneous occurrence of virological response (undetectable HDV-RNA [LOD = 6 IU/ml] or a decrease in HDV-RNA by ≥ 2 $\log_{10}$ IU/ml compared to the start of the study) and biochemical response (normalisation of ALT, depending on the central laboratory [Russian sites: ≤ 31 U/l for women and ≤ 41 U/l for men; all other sites: ≤ 34 U/l for women and ≤ 49 U/l for men]).
e. Comprising the SF-36 and 15 additional hepatitis-specific questions
f. An increase in the PCS by ≥ 9.45 points or the MCS by ≥ 9.6 points compared to the start of the study is considered as clinically relevant improvement (scale range: 7.3 to 70.1 for PCS and 5.8 to 69.9 for MCS; determined using the 2009 normative sample).
g. This effect is largely determined by the difference in PT headache (9 vs 0).

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; HQLQ: Hepatitis Quality of Life Questionnaire; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; RR = relative risk; (S)AE = (serious) adverse event; vs = versus

b) Children and adolescents 3 to < 18 years of age with chronic hepatitis D infection and compensated liver disease

No data available.

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
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↔: 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 chronic hepatitis D infection with compensated liver disease

Approx. 400 – 3,200 patients

b) Children and adolescents 3 to < 18 years of age with chronic hepatitis D infection and compensated liver disease

Approx. 0 – 2 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 Hepcludex (active ingredient: bulevirtide) at the following publicly accessible link (last access: 14 January 2026):

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

Treatment with bulevirtide should only be initiated and monitored by specialists who are experienced in the treatment of patients with HDV infection.

4. Treatment costs

Annual treatment costs:

a) Adults with chronic hepatitis D infection with compensated liver disease

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Bulevirtide	€ 72,751.07
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 December 2025)

b) Children and adolescents 3 to < 18 years of age with chronic hepatitis D infection and compensated liver disease

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Bulevirtide	€ 72,751.07
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 December 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:

a) Adults with chronic hepatitis D infection with compensated liver disease

- No medicinal product with new active ingredients that can be used in a combination therapy, for which the requirements of Section 35a, paragraph 3, sentence 4 SGB V are fulfilled.

b) Children and adolescents 3 to < 18 years of age with chronic hepatitis D infection and compensated liver disease

- No medicinal product with new active ingredients that can be used in a combination therapy, for which the requirements of Section 35a, paragraph 3, sentence 4 SGB V are fulfilled.

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 website of the G-BA on 19 February 2026.

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

Berlin, 19 February 2026

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

Prof. Hecken