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
Zanidatamab
(biliary tract cancer, HER2+ [IHC3+], pretreated)

From 6 August 2026

At their session on 6 August 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, information on the active ingredient zanidatamab shall be added in alphabetical order as follows:

Zanidatamab

Resolution of: 6 August 2026
Entry into force on: 6 August 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 27 June 2025):

Ziihera as monotherapy is indicated for the treatment of adults with unresectable locally advanced or metastatic HER2-positive (IHC3+) biliary tract cancer (BTC) previously treated with at least one prior line of systemic therapy.

Therapeutic indication of the resolution (resolution of 6 August 2026):

See therapeutic indication according to marketing authorisation

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

Zanidatamab is approved as a medicinal product for the treatment of rare diseases under 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 unresectable locally advanced or metastatic HER2-positive (IHC 3+) biliary tract cancer previously treated with at least one prior line of systemic therapy

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

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Adults with unresectable locally advanced or metastatic HER2-positive (IHC 3+) biliary tract cancer previously treated with at least one prior line of systemic therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	The data are not assessable.
Morbidity	n.a.	The data are not assessable.
Health-related quality of life	∅	No data available.
Side effects	n.a.	The data are not assessable.

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

HERIZON-BTC-01

- open-label, single-arm phase IIb study
- Relevant sub-population: Sub-population of cohort 1 with HER2 expression of IHC 3+
- data cut-off: 2nd data cut-off from 28 July 2024

Mortality

Endpoint	Zanidatamab	
	N	Patients with event n (%)
Overall survival		
Deaths	62	45 (72.6)
		Kaplan-Meier estimator (%) [95% CI]
At month 12	62	65.0 [51.6; 75.6]
Endpoint	N	Median survival time in months [95% CI]
	62	18.1 [12.2; 22.9]

[1]Data from the dossier assessment of the G-BA (published on 15 May 2026), unless otherwise indicated.

Morbidity

Endpoint	Zanidatamab	
	N	Patients with event n (%) Median PFS (IRC) in months [95% CI]
Progression-free survival (PFS)[2] as defined by the IRC according to the RECIST criteria		
	62	44 (71.0) 7.16 [5.36; 9.43]
		Patients with event n (%) [95% CI]
Confirmed objective response rate (cORR)[3] as defined by the IRC according to RECIST criteria (presented additionally)		
	62	32 (51.6) [38.6; 64.5]
		Patients with event n (%)
Pain assessment using BPI-sf[a] (deterioration by ≥ 15% at the end of treatment)		
Pain intensity (items 3 to 6)	62	8 (18.6)
Impairments due to pain (items 9a to 9g)	62	19 (30.6)
		Patients with event n (%)
Health status as measured by the EQ-5D-VAS[b] (deterioration by ≤ 15 points at the end of treatment)		
	62	9 (14.5)

Health-related quality of life

Endpoint	Zanidatamab	
	N	
		No data available.

[2] Data from the dossier of the pharmaceutical company (Module 4); data cut-off from 28.07.2024
[3] Primary endpoint of the HERIZON-BTC study; data cut-off from 28.07.2024

Side effects

Endpoint	Zanidatamab	
	N	Patients with event n (%)
Total adverse events (presented additionally)		
	62	61 (98.4)
Serious adverse events (SAEs)		
	62	33 (53.2)
Severe adverse events (CTCAE grade ≥ 3)		
	62	40 (64.5)
Therapy discontinuation due to adverse events		
	62	2 (3.2)
Severe adverse events (CTCAE grade ≥ 3) by MedDRA system organ class (SOC) (with an incidence ≥ 10%)		
Gastrointestinal disorders	62	15 (24.2)
Hepatobiliary disorders	62	12 (19.4)
Investigations	62	14 (22.6)
Infections and infestations	62	12 (19.4)
Blood and lymphatic system disorders	62	11 (17.7)
Vascular disorders	62	7 (11.3)
SAEs by MedDRA system organ class (SOC) (with an incidence ≥ 10%)		
Hepatobiliary disorders	62	12 (19.4)
Gastrointestinal disorders	62	11 (17.7)
Infections and infestations	62	12 (19.4)

a. An increase in score by ≥ 15% compared to the start of the study is considered a clinically relevant deterioration (scale range: 0 to 10).
b. A decrease in score by ≥ 15% compared to the start of the study is considered a clinically relevant deterioration (scale range: 0 to 100).

Abbreviations used:
BPI-sf = Brief Pain Inventory – short form; cORR = confirmed objective response rate; CTCAE = Common Terminology Criteria for Adverse Events; IRC = Independent Review Committee; CI = confidence interval; MedDRA = Medical Dictionary for
Regulatory Activities; N = number of patients evaluated; n = number of patients with (at least one) event; PFS = progression-free survival; SOC = system organ class (MedDRA); SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale

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

Adults with unresectable locally advanced or metastatic HER2-positive (IHC 3+) biliary tract cancer previously treated with at least one prior line of systemic therapy

Approx. 30 to 160 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 Ziihera (active ingredient: zanidatamab) at the following publicly accessible link (last access: 20 July 2026):

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

Treatment with zanidatamab should only be initiated and monitored by specialists in internal medicine, haematology and oncology as well as specialists in internal medicine and gastroenterology and other specialists from other specialist groups participating in the Oncology Agreement, all of whom are experienced in the treatment of patients with biliary tract cancer.

This medicinal product was approved under "exceptional circumstances". 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 unresectable locally advanced or metastatic HER2-positive (IHC 3+) biliary tract cancer previously treated with at least one prior line of systemic therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Zanidatamab	€ 620,464.86
Additionally required SHI costs	€ 124.84
Total:	€ 620,589.70

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 June 2026)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed:					
Zanidatamab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	26.1	€ 2,610

II. The resolution will enter into force on the day of its publication on the G-BA website on 6 August 2026.

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

Berlin, 6 August 2026

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

Dr Optendrenk