Gemeinsamer Bundesausschuss

Justification

for the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Ivosidenib (reassessment of an orphan drug after exceeding the EUR 30 million limit (cholangiocarcinoma with IDH1 R132 mutation, after at least 1 prior therapy))

From 20 August 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical studies the pharmaceutical company have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decide on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient ivosidenib (Tibsovo) was listed for the first time on 15 July 2023 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. Tibsovo for the treatment of cholangiocarcinoma with an IDH1 R132 mutation after at least one prior therapy 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.

At their session on 18 January 2024, the G-BA decided on the benefit assessment of ivosidenib in the therapeutic indication of cholangiocarcinoma with an IDH1 R132 mutation after at least one prior therapy in accordance with Section 35a SGB V.

If the sales of the orphan drug through the statutory health insurance at pharmacy sales prices and outside the scope of SHI-accredited medical care, including value-added tax, exceed an amount of € 30 million in the last twelve calendar months, the pharmaceutical company must

submit evidence in accordance with Chapter 5 Section 5, paragraphs 1 to 6 Rules of Procedure (VerfO) within three months of being requested to do so by the Federal Joint Committee, and in this evidence, must demonstrate the additional benefit compared to the appropriate comparator therapy.

By letter dated 24 November 2025, the pharmaceutical company was requested to submit a dossier for the benefit assessment according to Section 35a SGB V by 1 March 2026, because the EUR 30 million turnover limit was exceeded within the period from September 2024 to August 2025. Pursuant to Section 4, paragraph 3, number 4 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 6 of the Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 27 February 2026.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 June 2026 on the G-BA website at (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of ivosidenib compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods[1] was not used in the benefit assessment of ivosidenib.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made the following assessment:

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

2.1.1 Approved therapeutic indication of ivosidenib (Tibsovo) in accordance with the product information

Tibsovo monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy.

Therapeutic indication of the resolution (resolution of 20.08.2026):

See the approved therapeutic indication

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy

Appropriate comparator therapy:

Individualised therapy with selection of

- folinic acid in combination with 5-fluorouracil and oxaliplatin (FOLFOX; only suitable for patients without FGFR2 fusion, FGFR2 rearrangement, MSI-H and dMMR),
- pemigatinib (only suitable for patients with an FGFR2 fusion or an FGFR2 rearrangement),
- futibatinib (only suitable for patients with an FGFR2 fusion or an FGFR2 rearrangement),
- pembrolizumab (only suitable for patients with MSI-H or dMMR) and
- Best supportive care

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of

medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved for the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved for the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1. In addition to ivosidenib, medicinal products with the active ingredients entrectinib, futibatinib, larotrectinib, pembrolizumab, pemigatinib, repotrectinib, selpercatinib and zanidatamab are approved for this therapeutic indication.

On 2. Non-medicinal treatment is not considered.

On 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Larotrectinib: Resolution of 2 April 2020
- Entrectinib: Resolution of 9 February 2021
- Pemigatinib: Resolution of 7 October 2021
- Pembrolizumab: Resolution of 19 January 2023
- Ivosidenib: Resolution of 18 January 2024
- Futibatinib: Resolution of 22 November 2024
- Selpercatinib (resolution of 7 November 2024)
- Repotrectinib (resolution of 16 October 2025)

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V. A written statement by the Drugs Commission of the German Medical Association (AkdÄ) and a joint written statement by the Working Group for Internal Oncology (AIO) of the German Cancer Society (DKG), the German Society for

Haematology and Medical Oncology (DGHO) and the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS) are available (hereinafter: scientific-medical societies).

Among the approved active ingredients listed under 1.), only certain active ingredients named below will be included in the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of health care provision.

These guidelines recommend various therapy regimens for locally advanced or metastatic cholangiocarcinoma, particularly taking into account molecular genetic alterations.

In addition to ivosidenib for the IDH1 R132 mutation, the active ingredients entrectinib, futibatinib, larotrectinib, pembrolizumab, pemigatinib, repotrectinib, selpercatinib and zanidatamab are approved for sub-populations with corresponding molecular genetic alterations or alterations in gene expression within the therapeutic indication: futibatinib and pemigatinib for FGFR2 fusion or an FGFR2 rearrangement; entrectinib, larotrectinib and repotrectinib in the presence of fusion genes with the neurotrophin receptors TRKA, TRKB and TRKC (NTRK gene fusions), selpercatinib for RET fusion, pembrolizumab for MSI-H or dMMR, and zanidatamab for HER2-positive patients.

The guidelines consider futibatinib, pemigatinib, ivosidenib and pembrolizumab to be indicated for patients with the relevant molecular genetic alteration. In their written statement, the scientific-medical societies regard the active ingredient ivosidenib as the standard therapy in this therapeutic indication. However, ivosidenib itself is excluded as an appropriate comparator therapy with regard to the research question of the benefit assessment since the present case concerns the determination of the appropriate comparator therapy for ivosidenib.

As part of the written statement procedure carried out here, the same scientific-medical societies state that the aforementioned aberrations almost never occur in conjunction with an IDH1 mutation. However, the guidelines do not contain any relevant statements or figures on the frequency of such aberrations. In the overall assessment, the G-BA did not exclude the targeted active ingredients per se when determining the appropriate comparator therapy for the present resolution.

In the benefit assessment for orphan drugs, a hint of a non-quantifiable additional benefit of pemigatinib (G-BA resolution of 7 October 2021) was identified since the scientific data does not allow quantification. In the benefit assessments for pembrolizumab (resolution of 19 January 2023) and futibatinib (resolution of 22 November 2024), no additional benefit was identified in either case compared with the appropriate comparator therapy, as no suitable data were available.

There are no corresponding recommendations for the tumour-agnostic approved active ingredients targeting NTRK gene fusions and RET fusions. From the G-BA's perspective, an overall analysis showed that these active ingredients assume secondary importance in this therapeutic indication; consequently, entrectinib, larotrectinib,

repotrectinib and selpercatinib are not considered to be the appropriate comparator therapy.

The active ingredient zanidatamab represents a new treatment option for patients with HER2-positive (IHC 3+) cholangiocarcinoma in this therapeutic indication. Although the active ingredient was approved as early as June 2025, it has only recently become available on the German market (since 15.05.2026). According to the generally recognised state of medical knowledge, zanidatamab is not determined as an appropriate comparator therapy for the present resolution.

Evidence-based guideline recommendations and the written statement by the AkdÄ recommend treatment with FOLFOX (folinic acid in combination with 5-fluorouracil and oxaliplatin) for patients who do not exhibit any of the aforementioned molecular genetic alterations. However, the combination therapy FOLFOX is not approved for the present therapeutic indication. Accordingly, the use of FOLFOX in this therapeutic indication constitutes off-label use. At their session on 22 November 2024, the G-BA, drawing in particular on the findings of Lamarca et al. 2021[2], decided to commission the Expert Group on Off-Label Use in accordance with Section 35c paragraph 1 SGB V to assess the current state of scientific knowledge on FOLFOX in the treatment of patients with locally advanced or metastatic biliary carcinoma who were previously treated by at least one prior line of systemic therapy.

Apart from the approved active ingredient ivosidenib, there are no other approved therapy options for patients who do not have any of the aforementioned molecular genetic alterations in addition to the IDH1 R132 mutation. It is therefore appropriate to determine the off-label use of FOLFOX as the appropriate comparator therapy for this patient population in accordance with Section 6, paragraph 2, sentence 3, number 3 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV).

Best supportive care as part of individualised therapy is a suitable treatment for patients within the therapeutic indication for whom further standard systemic antineoplastic therapy is not an option. "Best supportive care" (BSC) is understood as the therapy that ensures the best possible, patient-individually optimised, supportive treatment to alleviate symptoms and improve quality of life.

Overall, the evidence suggests that the treatment is selected, particularly taking into account molecular genetic alterations (FGFR2 fusion, FGFR2 rearrangement, MSI-H, dMMR) and suitability for further antineoplastic therapy; consequently, the G-BA especially consider these criteria when determining an individualised therapy with selection of FOLFOX, pemigatinib, futibatinib, pembrolizumab, and best supportive care (BSC).

Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

[2] Lamarca A, Palmer DH, Wasan HS, et al. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomised, controlled trial. Lancet Oncol 2021; 22: 690–701

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of ivosidenib is assessed as follows:

An additional benefit is not proven.

Justification:

The pharmaceutical company has submitted data from the pivotal, randomised, double-blind, placebo-controlled phase III ClarIDHy study for benefit assessment. This study, which compared ivosidenib with placebo, permitted additional supportive measures as part of best supportive care (BSC) in both study arms.

Adult patients with unresectable or metastatic cholangiocarcinoma with an IDH1 R132 mutation and proven disease progression after at least one but no more than two prior lines of systemic therapy for advanced cholangiocarcinoma were enrolled in the study, with the condition that at least one previous therapy regimen must have included gemcitabine or 5-fluorouracil (5-FU). Furthermore, patients had to have a good health status, corresponding to an Eastern Cooperative Oncology Group Performance Status (ECOG-PS) ≤ 1. It was randomised in a ratio of 2:1 to the study arms ivosidenib + BSC (intervention arm, N = 124) and placebo + BSC (control arm, N = 61), stratified by the number of prior lines of systemic therapy (1 vs 2). After the first data cut-off, 2 more subjects were enrolled in the study and randomised into the intervention arm.

Treatment in the study arms was initially double-blind. After confirmed disease progression, the blinding could be cancelled at the principal investigator's request and participants from the control arm could switch to treatment with ivosidenib (crossover).

The patients were recruited between 2017 and 2019 from study sites in the USA, South Korea and Europe. The primary endpoint of the study that ended in 2021 was progression-free survival (PFS), additional endpoints were collected on mortality, symptomatology, health-related quality of life and adverse events.

The pharmaceutical company reported a total of three data cut-offs for the ClarIDHy study in the dossier (from 31 January 2019, 31 May 2020 and 21 June 2021).

Assessment:

The appropriate comparator therapy was determined as an individualised therapy with selection of FOLFOX, pemigatinib, futibatinib, pembrolizumab and BSC, taking into account molecular genetic alterations (FGFR2 fusion, FGFR2 rearrangement, MSI-H, dMMR) and suitability for further antineoplastic therapy. The phase III ClarIDHy study presented by the pharmaceutical company is a single-comparator study in which treatment with placebo plus

BSC was the only option in the comparator arm. It was therefore not possible for the principal investigator to make a patient-individualised treatment decision.

It cannot be concluded from the available information that BSC represents the most appropriate individualised therapy for a significant percentage of patients in the comparator arm.

Because it is not possible to determine the exact number of patients with a therapeutically relevant molecular genetic alteration (FGFR2 fusion, FGFR2 rearrangement, MSI-H, or dMMR) based on data from the ClarIDHy study, the number of patients in the comparator arm of the study who would have been eligible for targeted therapy with pemigatinib, futibatinib, or pembrolizumab remains unclear.

Furthermore, given the good general condition (ECOG-PS ≤ 1) of the enrolled patients, it is assumed that treatment with FOLFOX – the recommended second-line medicinal therapy – is the most appropriate patient-individualised therapy for most of those who have only received one line of systemic therapy (54% of the patients in the study). This is supported by the data from the pharmaceutical company's statement regarding previous cancer treatments in the total population of the ClarIDHy study. Accordingly, based in particular on the data relating to the individual components of FOLFOX, an estimated 9 (4.9%) patients received FOLFOX in the 1st line of therapy (including 2 patients in the comparator arm) and 31 (16.8%) patients had received prior therapy with FOLFOX in the 2nd line of therapy (including about 5 to 8 patients in the comparator arm). It can therefore be concluded that a new FOLFOX therapy would not be indicated in only about 10 (16%) patients due to their pretreatment.

Regardless of this, the pharmaceutical company did not provide any justification or further information as to why BSC constitutes the appropriate comparator therapy for the enrolled patients.

Conclusion:

The data from the single-comparator ClarIDHy study are unsuitable for the assessment of the additional benefit. The presented study neither allowed for a comparison with an individualised therapy due to a lack of choice, nor was it suitable, for the aforementioned reasons, for drawing conclusions for patients for whom BSC represents the most appropriate therapy option among those offered by the individualised therapy (designated as the appropriate comparator therapy). Therefore, an additional benefit of ivosidenib for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy is not proven.

2.1.4 Summary of the assessment

The present assessment is the new benefit assessment of the active ingredient ivosidenib because its EUR 30 million turnover limit was exceeded. Ivosidenib was approved as an orphan drug. The therapeutic indication assessed here is as follows:

"Tibsovo monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy."

The appropriate comparator therapy was determined as an individualised therapy with selection of FOLFOX, pemigatinib, futibatinib, pembrolizumab and BSC, taking into account molecular genetic alterations (FGFR2 fusion, FGFR2 rearrangement, MSI-H, dMMR) and suitability for further antineoplastic therapy.

The pharmaceutical company presented the results of the completed double-blind, placebo-controlled phase III ClarIDHy study, which compared ivosidenib with placebo; in both study arms, supportive measures as part of BSC in accordance with the requirements of the respective study site were permitted. The data from this single-comparator study are unsuitable for the assessment of the additional benefit. The presented study neither allowed for a comparison with an individualised therapy due to a lack of choice, nor was it suitable for drawing conclusions for patients for whom BSC represents the most appropriate therapy option among those offered by the individualised therapy (designated as the appropriate comparator therapy). Therefore, an additional benefit of ivosidenib for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy is not proven.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The present resolution is based on the patient numbers from the resolution on ivosidenib (resolution of 18 February 2024)[3] in order to allow for consistent analysis of the patient numbers, taking into account the resolutions adopted on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V.

The uncertainties from the previous procedure due to methodological limitations remain.

2.3 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 Tibsovo (active ingredient: ivosidenib) at the following publicly accessible link (last access: 18 June 2026):

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

Treatment with ivosidenib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with cholangiocarcinoma, as well as specialists in internal medicine and gastroenterology, and other doctors from other specialist groups participating in the Oncology Agreement.

An electrocardiogram (ECG) must be performed before start of treatment and at least once a week during the first 3 weeks of therapy.

[3] Benefit assessment procedure D-955 ivosidenib; https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/972/

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 June 2026).

The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is different from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

The annual treatment costs shown refer to the first year of treatment.

Treatment period:

Adults with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Ivosidenib				
Ivosidenib	Continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
Folinic acid in combination with 5-fluorouracil and oxaliplatin				
(FOLFOX; only suitable for patients without FGFR2 fusion, FGFR2 rearrangement, MSI-H and dMMR)[4,5,6]				
Folinic acid	1 x per 14-day cycle	26.1	1	26.1
5-fluorouracil	1 x per 14-day cycle	26.1	2	26.1

[4] S3 Guideline on the Diagnosis and Treatment of Hepatocellular Carcinoma and Biliary Tract Carcinomas, Version 5.2 - June 2025, AWMF registry number: 032/053OL

[5] EASL-ILCA Clinical Practice Guidelines on the Management of Intrahepatic Cholangiocarcinoma; European Association for the Study of the Liver, 2023

[6] Lamarca A, Palmer DH, Wasan HS, et al. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomised, controlled trial. Lancet Oncol 2021; 22: 690–701

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Oxaliplatin	1 x per 14-day cycle	26.1	1	26.1
Pemigatinib (only suitable for patients with an FGFR2 fusion or an FGFR2 rearrangement)				
Pemigatinib	1 x daily on day 1-14 of a 21-day cycle	17.4	14	243.6
Futibatinib (only suitable for patients with an FGFR2 fusion or an FGFR2 rearrangement)				
Futibatinib	Continuously, 1 x daily	365	1	365
Pembrolizumab (only suitable for patients with MSI-H or dMMR)				
Pembrolizumab	1 x per 21-day cycle	17.4	1	17.4
	or			
	1 x per 42-day cycle	8.7	1	8.7
Best supportive care				
Best supportive care[7]	Different from patient to patient			

Consumption:

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

The (daily) doses recommended in the product information were used as the calculation basis.

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "2025 Microcensus – body measurements of the population" were applied (average body height: 1.73 m; average body weight: 78.3 kg). This results in a body surface area of 1.92 m² (calculated according to Du Bois 1916)[8].

[7] When comparing ivosidenib versus best supportive care, the costs of best supportive care must also be additionally considered for the medicinal product to be assessed.

[8] Federal Health Reporting. Average body measurements of the population (2025, both sexes), www.gbe-bund.de

Adults with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Ivosidenib					
Ivosidenib	500 mg	500 mg	2 x 250 mg	365.0	730 x 250 mg
Appropriate comparator therapy					
Folinic acid in combination with 5-fluorouracil and oxaliplatin (FOLFOX; only suitable for patients without FGFR2 fusion, FGFR2 rearrangement, MSI-H and dMMR) [4,5,6]					
Folinic acid	350 mg	350 mg	1 x 400 mg	26.1	26.1 x 400 mg
5-fluorouracil	400 mg/m² = 768 mg	768 mg	1 x 1,000 mg	26.1	26.1 x 1,000 mg
	2,400 mg/m² = 4,608 mg	4,608 mg	2 x 2,500 mg	26.1	52.2 x 2,500 mg
Oxaliplatin	85 mg/m² = 163.2 mg	163.2 mg	1 x 200 mg	26.1	26.1 x 200 mg
Pemigatinib (only suitable for patients with an FGFR2 fusion or an FGFR2 rearrangement)					
Pemigatinib	13.5 mg	13.5 mg	1 x 13.5 mg	243.6	243.6 x 13.5 mg
Futibatinib (only suitable for patients with an FGFR2 fusion or an FGFR2 rearrangement)					
Futibatinib	20 mg	20 mg	5 x 4 mg	365.0	1,825.0 x 4 mg
Pembrolizumab (only suitable for patients with MSI-H or dMMR)					
Pembrolizumab	200 mg	200 mg	2 x 100 mg	17.4	34.8 x 100 mg
	or				
	400 mg	400 mg	4 x 100 mg	8.7	34.8 x 100 mg
Best supportive care					
Best supportive care	Different from patient to patient				

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment

costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Adults with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Ivosidenib 250 mg	60 FCT	€ 13,036.43	€ 1.77	€ 0.00	€ 13,034.66
Appropriate comparator therapy					
Calcium folinate 400 mg[9]	5 SFI	€ 1,184.28	€ 1.77	€ 92.77	€ 1,089.74
Fluorouracil 1,000 mg[9]	1 SFI	€ 16.67	€ 1.77	€ 0.42	€ 14.48
Fluorouracil 2,500 mg[9]	1 SFI	€ 23.60	€ 1.77	€ 0.97	€ 20.86
Futibatinib 4 mg	35 FCT	€ 2,104.86	€ 1.77	€ 0.00	€ 2,103.09
Oxaliplatin 200 mg	1 CIS	€ 395.68	€ 1.77	€ 18.24	€ 375.67
Pembrolizumab 100 mg	2 CIS	€ 4,853.26	€ 1.77	€ 273.88	€ 4,577.61
Pemigatinib 13.5 mg	14 TAB	€ 7,467.32	€ 1.77	€ 423.17	€ 7,042.38
Best supportive care	Different from patient to patient				
Abbreviations: FCT = film-coated tablets; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; TAB = tablets					

LAUER-TAXE® last revised: 15 June 2026

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5aSGB V, when a non-prescription medicinal product is dispensed and invoiced in accordance with Section 300, a medicinal product dispensing

[9] Fixed reimbursement rate

price in the amount of the dispensing price of the pharmaceutical company plus the surcharges in accordance with Sections 2 and 3 of the Pharmaceutical Price Ordinance in the version valid on 31 December 2003 applies to the insured.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-apply unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At their session on 27 January 2026, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 27 February 2026, the pharmaceutical company submitted a dossier for the benefit assessment of ivosidenib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 6 VerfO.

By letter dated 2 March 2026 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient ivosidenib.

The dossier assessment by the IQWiG was submitted to the G-BA on 27 May 2026, and the written statement procedure was initiated with publication on the G-BA website on 1 June 2026. The deadline for submitting written statements was 22 June 2026.

The oral hearing was held on 6 July 2026.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI

umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing were discussed at the Subcommittee's session on 11 August 2026, and deliberation of the draft resolution was concluded.

At their session on 20 August 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	27 January 2026	Determination of the appropriate comparator therapy
Working group Section 35a	30 June 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	6 July 2026	Conduct of the oral hearing
Working group Section 35a	14 July 2026 4 August 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 August 2026	Concluding discussion of the draft resolution
Plenum	20 August 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 August 2026

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

Dr Optendrenk