Gemeinsamer Bundesausschuss

Justification

of 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)
Futibatinib (cholangiocarcinoma, with FGFR2 fusion or FGFR2 rearrangement, after at least 1 prior therapy)

of 22 November 2024

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses 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 trials the pharmaceutical company has 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 decides 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 relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient futibatinib on 1 June 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 1 VerfO on 28 May 2024.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 September 2024 on the G-BA website (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 futibatinib 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 has 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 futibatinib.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to 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 Futibatinib (Lytgobi) in accordance with the product information

Lytgobi monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy.

Therapeutic indication of the resolution (resolution of 22 November 2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or FGFR2 rearrangement; after at least one prior line of systemic therapy

Appropriate comparator therapy for futibatinib as monotherapy:

Pemigatinib

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 in accordance with 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.

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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 it determines 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 in 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 in 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.

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

On 1. With regard to the authorisation status, the active ingredients pemigatinib, ivosidenib and pembrolizumab are available in addition to futibatinib in 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:
- Pembrolizumab: resolution of 19 January 2023
- Pemigatinib: resolution of 7 October 2021

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.

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 care.

In addition to futibatinib, pemigatinib, ivosidenib and pembrolizumab are also approved for the treatment of patients with cholangiocarcinoma after at least one prior line of systemic therapy.

Ivosidenib is indicated here for the treatment of tumours with an IDH1 R132 mutation and pembrolizumab for the treatment of tumours with MSI-H or with a dMMR.

Pemigatinib, in contrast, is explicitly approved for the treatment of patients with FGFR2 fusion or FGFR2 rearrangement. The guidelines recommend treatment with pemigatinib for patients whose tumours have an FGFR2 fusion or an FGFR2 rearrangement and who have progressed after at least one systemic therapy.

By resolution of 7 October 2021, a hint for a non-quantifiable additional benefit was identified in the benefit assessment of pemigatinib, which was approved as an orphan drug.

The guidelines and the statements of the scientific-medical societies - Working Group for Internal Oncology of the German Cancer Society (AIO), German Society for Haematology and Medical Oncology (DGHO) and German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS) - describe pemigatinib as the current sole standard therapy for patients with biliary carcinoma and evidence of FGFR2 gene fusion after at least one prior systemic therapy.

For the above-mentioned reasons, pemigatinib is determined to be the appropriate comparator therapy.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

<u>Adults with locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or FGFR2 rearrangement; after at least one prior line of systemic therapy</u>

An additional benefit is not proven.

Justification:

In the absence of direct comparator studies of futibatinib versus the appropriate comparator therapy, the pharmaceutical company demonstrated the additional benefit using the phase II FOENIX-CCA2 study for the intervention and the FIGHT-202 study for the appropriate comparator therapy.

Description of the FOENIX-CCA2 study

The FOENIX-CCA2 study is a single-arm, open-label, multicentre phase I/II study investigating the efficacy and safety of futibatinib. In the phase II of the study, 103 adults with locally advanced or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements, who had received prior therapy and had disease progression, were enrolled. The study was conducted between July 2014 and May 2021 in 48 study sites in Australia, Asia, Europe and North America. The patients enrolled in the study come mainly from North America and Europe.

Description of the FIGHT-202 study

The FIGHT-202 study is a single-arm, open-label, multicentre phase II study to investigate the efficacy and safety of pemigatinib in adults with locally advanced or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements who have received prior therapy and have disease progression.

Between January 2017 and March 2019, 146 patients were enrolled in the study at 146 study sites, mainly in Europe and the USA.

For the proof of an additional benefit of futibatinib, the pharmaceutical company used the results of the FOENIX-CCA2 study. They also presented a naïve comparison as well as Matching-Adjusted Indirect Comparison (MAIC) analyses without a bridge comparator for the indirect comparison of treatment with futibatinib versus pemigatinib of individual arms based on the FOENIX-CCA2 and FIGHT-202 studies.

Due to the single-arm study design, the FOENIX-CCA2 study presented by the pharmaceutical company does not allow a comparison with the appropriate comparator therapy pemigatinib and is therefore unsuitable for the assessment of the additional benefit.

MAIC analyses without a bridge comparator are not considered an adequate option for confounder adjustment. The performance of MAIC analyses for only one endpoint (here: overall survival) is also considered inappropriate.

Conclusion:

The pharmaceutical company used the results of the single-arm FOENIX-CCA2 study for assessment of the additional benefit of futibatinib. For an indirect comparison of treatment with futibatinib versus pemigatinib, the pharmaceutical company submitted a naïve comparison and MAIC analyses without bridge comparator of individual arms based on the FOENIX-CCA2 and FIGHT-202 studies. The results of the single-arm study are unsuitable for assessment of the additional benefit as they do not allow a comparison with the appropriate comparator therapy. Overall, the indirect comparisons are unsuitable to prove an additional benefit compared to the appropriate comparator therapy.

Therefore, an additional benefit of futibatinib as monotherapy for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or FGFR2 rearrangement that has progressed after at least one prior line of systemic therapy is not proven.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Lytgobi with the active ingredient futibatinib. Lytgobi received a conditional marketing authorisation.

The therapeutic indication assessed here is as follows:

Lytgobi monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy.

The G-BA determined a therapy with pemigatinib as the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company submitted the results of the single-arm FOENIX-CCA2 study. The results of the single-arm study are unsuitable for assessment of the additional benefit as they do not allow a comparison with the appropriate comparator therapy. In addition, for an indirect comparison with pemigatinib, the pharmaceutical company presented a naïve comparison as well as MAIC analyses without bridge comparator of individual arms based on the FOENIX-CCA2 and FIGHT-202 studies. Overall, these indirect comparisons are unsuitable to prove an additional benefit compared to the appropriate comparator therapy. An additional benefit of futibatinib as monotherapy for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or FGFR2 rearrangement that has progressed after at least one prior line of systemic therapy is therefore 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 resolution is based on the information from the addendum of IQWiG (addendum of 28 October 2024).

These patient numbers also represent a better estimate compared to the resolution figures for pemigatinib (resolution of 7 October 2021) with 35 to 300 patients in the SHI target population, as the present procedure was based especially on study-based percentage values for the receipt of first-line chemotherapy, whereas a flat rate of 100% was assumed in this step when deriving the target population for pemigatinib.

In the overall analysis, the newly presented derivation is methodologically more suitable for deriving the patient number in the SHI target population than the one from the dossier. However, according to IQWiG's assessment (addendum of 28 October 2024), more suitable percentage values or percentage ranges can be determined for some derivation steps. In the addendum of 28 October 2024, IQWiG partly recalculated with these more suitable percentage values. The patient number in the SHI target population calculated in this way is used as the basis for this resolution. This number is of comparable magnitude to that of the pharmaceutical company.

The patient number in the SHI target population is subject to uncertainty due to the following aspects:

- The range for the percentage of patients with unresectable or metastatic disease (59 – 80.5%) is subject to uncertainty with regard to transferability to the present therapeutic indication, as the lower limit is generally based on "malignant neoplasm

of the liver and intrahepatic bile ducts" and it is unclear whether the upper limit refers to the time of initial diagnosis. Conversely, the range for the percentage of patients with resectable disease is also subject to uncertainty with regard to transferability.

- With regard to patients with a relapse after surgery, it remains questionable whether each relapse can be assigned to the locally advanced or metastatic stage of cholangiocarcinoma relevant for the therapeutic indication.
- With regard to the percentage of patients with FGFR2 fusion or rearrangement in intrahepatic cholangiocarcinoma, it cannot be ruled out that the percentage may be higher (cf. pemigatinib, resolution of 7 October 2021).
- In general, the information relates to patients without restriction to specific stages of the disease or treatment settings. Therefore, the transferability to the patient population to be specifically considered in this therapeutic indication remains questionable.
- In addition, there is uncertainty due to the omission of patients for the receipt of second-line chemotherapy who are generally eligible for treatment with futibatinib as well as a potentially lower upper limit of the percentage range for patients with extrahepatic cholangiocarcinoma and FGFR2 fusion or FGFR2 rearrangement.

There are approximately 27 – 229 patients in this therapeutic indication.

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 Lytgobi (active ingredient: futibatinib) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 30 October 2024):

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

Treatment with futibatinib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology, internal medicine and gastroenterology, and specialists participating in the Oncology Agreement experienced in the treatment of adults with cholangiocarcinoma.

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.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 October 2024).

Treatment period:

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 varies 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 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.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Futibatinib	daily	365	1.0	365.0
Appropriate comparator therapy				
Pemigatinib	1x daily on days 1 - 14 of a 21-day cycle	17.4 cycles	14	243.6

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Futibatinib	20 mg	20 mg	5 x 4 mg	365.0	1825 x 4 mg
Appropriate comparator therapy					
Pemigatinib	13.5 mg	13.5 mg	1 x 13.5 mg	243.6	243.6 x 13.5 mg

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 Sections 130 and 130 a 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.

Costs of the medicinal products:

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					
Futibatinib	35 FCT	€ 2,971.72	€ 2.00	€ 169.12	€ 2,800.60
Appropriate comparator therapy					
Pemigatinib	14 TAB	€ 7,467.32	€ 2.00	€ 423.17	€ 7,042.15
Abbreviations: FCT = film-coated tablets; TAB = tablet					

LAUER-TAXE® last revised: 15 October 2024

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.

Because there are no 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, no costs for additionally required SHI services need to be taken into account.

2.5 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

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication)

and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be

attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit

had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

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.

Justification for the findings on designation in the present resolution:

Adults with locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or FGFR2 rearrangement; after at least one prior line of systemic therapy

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

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 its session on 12 November 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at its session on 12 September 2023.

On 28 May 2024, the pharmaceutical company submitted a dossier for the benefit assessment of futibatinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 30 May 2024 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 futibatinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 26 August 2024, and the written statement procedure was initiated with publication on the G-BA website on 2 September 2024. The deadline for submitting statements was 23 September 2024.

The oral hearing was held on 7 October 2024.

By letter dated 10 October 2024, IQWiG was commissioned with a supplementary determination of the patient number in the SHI target population. The addendum prepared by IQWiG was submitted to the G-BA on 28 October 2024.

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 was discussed at the session of the subcommittee on 12 November 2024, and the proposed draft resolution was approved.

At its session on 22 November 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	21 November 2021	Determination of the appropriate comparator therapy
Subcommittee Medicinal products	12 September 2023	New determination of the appropriate comparator therapy
Working group Section 35a	30 September 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	7 October 2024	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary determination of patient numbers
Working group Section 35a	15 October 2024 5 November 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	12 November 2024	Concluding discussion of the draft resolution
Plenum	22 November 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 22 November 2024

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

Prof. Hecken