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)
Selpercatinib (new therapeutic indication: solid tumours, RET fusion-positive)

of 7 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 active ingredient selpercatinib (Retsevmo) was listed for the first time on 15 March 2021 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 29 April 2024, selpercatinib received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 14 May 2024, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient selpercatinib with the new therapeutic indication

"Retsevmo as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive solid tumours, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 August 2024 on the G-BA website (www.g-ba.de), therefore initiating the written statement procedure. In addition, an oral hearing was held.

Based on 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, the G-BA decided on the question on whether an additional benefit of selpercatinib compared with the appropriate comparator therapy could be determined – Annex XII - Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V. In order to determine the extent of the additional benefit, the G-BA assessed the data justifying the finding of an additional benefit in accordance with the criteria laid down in Chapter Section 5, paragraph 7 VerfO on the basis of their therapeutic relevance (qualitative). The methodology proposed by the IQWiG in accordance with the General Methods[1] was not used in the benefit assessment of selpercatinib.

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 Selpercatinib (Retsevmo) in accordance with the product information

Retsevmo as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive solid tumours, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted.

Therapeutic indication of the resolution (resolution of 07.11.2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with advanced RET fusion-positive solid tumour, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted

Appropriate comparator therapy for selpercatinib as monotherapy:

- Best supportive care

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

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.
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.

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

On 1., 2. and 3.

To date, there are no specific medicinal products approved for the treatment of RET fusion-positive solid tumours in this therapeutic indication.

There are separate therapeutic indications for selpercatinib for the treatment of RET fusion-positive non-small cell lung cancer (NSCLC) and RET fusion-positive thyroid cancer. These therapeutic indications are not covered by this therapeutic indication.

According to this therapeutic indication, patients are treated, for whom treatment options not targeting RET provide limited clinical benefit, or have been exhausted, leaving patients with no satisfactory therapy options. This characteristic is interpreted in accordance with the corresponding statement in section 4.4 of the product information for selpercatinib as meaning that there are no treatment options for which a clinical benefit was shown, or if these treatment options have been exhausted.[2]

Against this background, research and information on all medicinal products approved for the treatment of solid tumours and other treatment options do not appear to be appropriate. However, an orientating literature research was carried out in relation to the biomarker.

On 4.

This therapeutic indication is a tumour diagnostic (histology-independent) therapeutic indication in which the histology or type of tumour disease is not specified in further detail.

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy").

The biomarker "RET fusion" is a new biomarker in cancer therapy. There is no evidence that patients with RET fusions are currently treated fundamentally differently from patients without RET fusions. Accordingly, the orientating literature research with regard to the biomarker in numerous S3 guidelines shows that no information on the research question is included and RET fusions are currently being evaluated as therapeutic targets in clinical studies, or a clinical assessment is not yet possible. The written statement of the scientific-medical societies indicates that there are no specific therapy recommendations for RET fusion-positive tumours. The current therapy recommendations are based on the standard of the respective tumour entity.

In view of the above interpretation of the characteristic "for whom treatment options not targeting RET provide limited clinical benefit, or have been exhausted", the comments made by the scientific-medical society and the fact that the planned

[2] Product information, Retsevmo, last revised; May 2024; Retsevmo® (fachinfo.de)

therapeutic indication in question comprises advanced malignant tumour diseases, best supportive care (BSC) is determined to be an appropriate comparator therapy.

"Best supportive care" is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life.

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 selpercatinib is assessed as follows:

Adults with advanced RET fusion-positive solid tumour, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted

An additional benefit is not proven.

Justification:

The pharmaceutical company did not identify any relevant studies to demonstrate an additional benefit of selpercatinib compared to the appropriate comparator therapy. Data that allow an indirect comparison of selpercatinib with the determined appropriate comparator therapy are also not available. In the dossier, the pharmaceutical company presented the results of a sub-population of the uncontrolled approval study LIBRETTO-001 as the best available evidence.

The LIBRETTO-001 study is a multicentre, single-arm, prospective basket study that has been ongoing since 2017. Adult patients with advanced or metastatic solid tumours, who showed disease progression under previous standard therapy or were intolerant thereto, or for whom no curative standard therapy existed, for whom standard therapy was unsuitable according to the principal investigator's assessment or who refused standard therapy were enrolled. The study consists of 2 phases. In the already completed 1st phase, dose escalation was performed to determine the maximum tolerated dose of selpercatinib. In the ongoing 2nd phase of the study, the maximum tolerated dose of selpercatinib was administered to patients with an alteration in the RET gene, including RET fusions, in several cohorts. Inclusion in the different cohorts was based on the primary tumour present, pretreatment, potential treatment and RET status.

Until the 5th data cut-off from 24.09.2021, 806 patients were enrolled in the study and received at least 1 dose of selpercatinib. For this therapeutic indication, adults with advanced RET fusion-positive solid tumours are relevant when treatment options not targeting RET provide limited clinical benefit, or have been exhausted. The results of the sub-population relevant to the benefit assessment presented by the pharmaceutical company as best

available evidence included 45 patients from phase 1 and phase 2 of the study, who were diagnosed with advanced RET fusion-positive solid tumours other than NSCLC and thyroid cancer, in whom the disease progressed during or after prior systemic therapy and for whom no satisfactory therapy options were available.

The study is being conducted in 84 study sites across Australia, Asia, Europe and North America.

Due to the single-arm study design, the LIBRETTO-001 study presented by the pharmaceutical company does not allow a comparison with the appropriate comparator therapy and is therefore unsuitable for the assessment of an additional benefit of selpercatinib compared with the appropriate comparator therapy.

An additional benefit of selpercatinib as monotherapy for the treatment of adult patients with an advanced RET fusion-positive solid tumour, in whom treatment options not targeting RET provide limited clinical benefit, or have been exhausted, is therefore not proven.

Conclusion

There are no suitable data available for an assessment of the additional benefit of selpercatinib. Consequently, an additional benefit of selpercatinib as monotherapy for the treatment of adults with an advanced RET fusion-positive solid tumour, in whom treatment options not targeting RET provide limited clinical benefit, or have been exhausted, compared with the appropriate comparator therapy is not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient selpercatinib.

The therapeutic indication assessed here is as follows:

"Retsevmo as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive solid tumours, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted."

The G-BA determined Best Supportive Care to be the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company submitted the results of the single-arm LIBRETTO-001 study. The data presented are unsuitable for comparison with the appropriate comparator therapy.

An additional benefit of selpercatinib as monotherapy for the treatment of adult patients with an advanced RET fusion-positive solid tumour, in whom treatment options not targeting RET provide limited clinical benefit, or have been exhausted, 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 dossier of the pharmaceutical company. The patient numbers are subject to uncertainties.

This is especially due to the operationalisation of treatment options not targeting RET, provide limited clinical benefit, or have been exhausted, the existence of at least one second-line therapy as well as several aspects of unclear transferability of the associated calculated percentage values to patients with an RET fusion-positive solid tumour.

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 Retsevmo (active ingredient: selpercatinib) at the following publicly accessible link (last access: 24 September 2024):

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

Treatment with selpercatinib should only be initiated and monitored by specialists experienced in the treatment of patients with solid tumours, specifically in the treatment of the respective tumour entity, and other doctors from specialist groups participating in the Oncology Agreement.

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.

RET testing

The selection of patients for treatment of advanced RET fusion-positive solid tumours should be based on a validated test method.

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).

The two weight-based dosages of selpercatinib recommended in the product information, either 160 mg twice daily for adults weighing ≥ 50 kg and 120 mg twice daily for adults weighing < 50 kg, are listed in the cost representation.

The costs for the first year of treatment are shown for the cost representation in the resolution.

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.

Adults with advanced RET fusion-positive solid tumour, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Selpercatinib	Continuously 2 x daily	365	1	365
Best supportive care	Different from patient to patient			
Appropriate comparator therapy				
Best supportive care	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 co-morbidities) are not taken into account when calculating the annual treatment costs.

The treatment costs for best supportive care are different from patient to patient. Because best supportive care has been determined as an appropriate comparator therapy, this is also reflected in the medicinal product to be assessed. The type and scope of best supportive care can vary depending on the medicinal product to be assessed and the comparator therapy.

Adults with advanced RET fusion-positive solid tumour, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted

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					
Selpercatinib	< 50 kg: 120 mg	240 mg	2 x 40 mg + 2 x 80 mg	365	730 x 40 mg + 730 x 80 mg
	≥ 50 kg: 160 mg	320 mg	4 x 80 mg	365	1,460 x 80 mg
Best supportive care[3]	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care[1]	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.

[3] When comparing selpercatinib with best supportive care, the costs of best supportive care must also be additionally considered for the medicinal product to be assessed.

Costs of the medicinal products:

Adults with advanced RET fusion-positive solid tumour, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted

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					
Selpercatinib 40 mg	168 HC	€ 2,863.93	€ 2.00	€ 160.27	€ 2,701.66
Selpercatinib 80 mg	112 HC	€ 3,799.36	€ 2.00	€ 213.69	€ 3,583.67
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				
Abbreviations: HC = hard capsules					

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.

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 1.10.2009 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-use 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.

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 advanced RET fusion-positive solid tumour, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted

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.

References:
Product information for selpercatinib (Retsevmo); product information for Lilly Retsevmo; last revised: July 2024

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 6 September 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at its session on 28 May 2024.

On 14 May 2024, the pharmaceutical company submitted a dossier for the benefit assessment of selpercatinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 2 VerfO.

By letter dated 14 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 selpercatinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 August 2024, and the written statement procedure was initiated with publication on the G-BA website on 15 August 2024. The deadline for submitting written statements was 5 September 2024.

The oral hearing was held on 23 September 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 29 October 2024, and the proposed draft resolution was approved.

At its session on 7 November 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	6 September 2022	Determination of the appropriate comparator therapy
Subcommittee Medicinal products	28 May 2024	New determination of the appropriate comparator therapy
Working group Section 35a	17 September 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	23 September 2024	Conduct of the oral hearing
Working group Section 35a	30 September 2024 15 October 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	29 October 2024	Concluding discussion of the draft resolution
Plenum	7 November 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 7 November 2024

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

Prof. Hecken