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 Osimertinib (new therapeutic indication: non-small cell lung cancer, EGFR mutations, following platinum-based chemoradiation therapy)

of 3 July 2025

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 studies 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 osimertinib (Tagrisso) was listed for the first time on 15 March 2016 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 19 December 2024, osimertinib 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 8 January 2025, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with

Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient osimertinib with the new therapeutic indication

"Tagrisso as monotherapy is indicated for the treatment of adult patients with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and whose disease has not progressed during or following platinum-based chemoradiation therapy."

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 April 2025 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 osimertinib 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, as well of the addendum drawn up by the IQWiG on the benefit assessment. 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 osimertinib.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have 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 Osimertinib (Tagrisso) in accordance with the product information

Tagrisso as monotherapy is indicated for the treatment of adult patients with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and whose disease has not progressed during or following platinum-based chemoradiation therapy.

Therapeutic indication of the resolution (resolution of 03.07.2025):

See the approved therapeutic indication.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in ≥ 1% of tumour cells

Appropriate comparator therapy for osimertinib as monotherapy:

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

- Durvalumab

b) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in < 1% of tumour cells

Appropriate comparator therapy for osimertinib as monotherapy:

- 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 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. Medicinal products with the active ingredients cisplatin, docetaxel, etoposide, gemcitabine, ifosfamide, mitomycin, paclitaxel, nab-paclitaxel, pemetrexed, vindesine, vinorelbine, durvalumab, bevacizumab, ramucirumab, afatinib, dacomitinib, erlotinib and gefitinib are approved for the treatment of locally advanced NSCLC.

Medicinal products with exclusive marketing authorisation for a metastatic stage are not considered. Medicinal products with explicit marketing authorisation for the treatment of NSCLC with activating driver mutations other than EGFR mutations are also not considered.

On 2. Non-medicinal treatments are not considered.

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

- Dacomitinib: resolution of 17.10.2019
- Durvalumab: resolution of 04.04.2019
- Afatinib: resolution of 05.11.2015
- Ramucirumab: resolution of 20.08.2020

Annex VI to Section K of the Pharmaceuticals Directive – Prescribability of approved medicinal products in non-approved therapeutic indications (off-label use):

- carboplatin-containing medicinal products for advanced non-small cell lung cancer (NSCLC) – combination therapy.

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 indication according to Section 35a paragraph 7 SGB V. In this regard, a joint written statement from the German Society for Haematology and Medical Oncology (DGHO), the German Respiratory Society (DGP) and the Working Group for Pneumological Oncology of the German Cancer Society (POA) is available.

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

According to the guidelines, patients with locally advanced NSCLC whose disease has not progressed following platinum-based chemoradiation therapy should be offered consolidation with the active ingredient durvalumab for one year if PD-L1 expression is ≥ 1% on tumour cells. In their written statement, the scientific-medical societies state that there is no separate standard for the treatment of patients with locally advanced, unresectable stage III NSCLC with the EGFR del19 or L858R mutation and that the

standard is based on PD-L1 expression. For patients with PD-L1 expression ≥ 1%, the scientific-medical societies designate durvalumab as the treatment standard. In contrast, as part of the present written statement procedure, the scientific-medical societies state in their written statement that monitoring wait-and-see approach or placebo is a suitable comparison for patients with advanced NSCLC and EGFR del19 or L858R mutation following definitive chemoradiation therapy. When determining the appropriate comparator therapy, the actual medical treatment situation as it would be without the medicinal product to be assessed must however be taken into account. In this regard, it emerged from the oral hearing that only the PD-L1 expression of patients was determined in clinical practice prior to the marketing authorisation of osimertinib. Testing for EGFR mutations was not routinely performed in clinical practice prior to the marketing authorisation of osimertinib. Accordingly, the actual medical treatment situation without osimertinib is such that patients with EGFR mutations were also treated with durvalumab in clinical practice, provided that corresponding PD-L1 expression was present.

In the benefit assessment, the G-BA identified by resolution of 4 April 2019 a hint for a considerable additional benefit of durvalumab over best supportive care for the treatment of adults with locally advanced, unresectable NSCLC whose tumours express PD-L1 in ≥ 1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy. In accordance with the marketing authorisation and the results of the benefit assessment, and taking into account the actual medical treatment situation prior to the marketing authorisation of osimertinib, durvalumab is the appropriate comparator therapy for the patient population with PD-L1 expression ≥ 1%.

According to the available guidelines, no standard antineoplastic therapy has been established for patients with PD-L1 expression < 1%. According to the statements of the scientific-medical societies, it can also be assumed that no further specific therapy is indicated for this patient population. Against the background of a disease stage that is potentially associated with symptoms, the G-BA specify best supportive care (BSC) as an appropriate comparator therapy for this patient population. Best supportive care (BSC) 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 osimertinib is assessed as follows:

a) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in ≥ 1% of tumour cells

An additional benefit is not proven.

b) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in < 1% of tumour cells

An additional benefit is not proven.

Justification:

In the dossier, the pharmaceutical company presented the results of the label-enabling LAURA study, but did not use them to derive an additional benefit.

LAURA study

The LAURA study is an ongoing, double-blind, randomised controlled trial comparing osimertinib to placebo.

Adult patients with locally advanced, unresectable NSCLC (stage III) with predominantly non-squamous histology whose disease has not progressed during or following definitive platinum-based chemoradiotherapy (simultaneous or sequential) were enrolled. Patients had to have a proven mutation of the EGFR gene as an exon 19 deletion or exon 21 substitution mutation (L858R), either alone or in combination with other EGFR mutations. The PD-L1 status of the patients was not collected.

A total of 216 patients were enrolled and randomised in a 2:1 ratio to treatment with osimertinib (N = 143) or placebo (N = 73). Stratification was performed according to the characteristics - strategy of previous chemoradiotherapy (simultaneous vs sequential), disease stage prior to chemoradiotherapy (IIIA vs IIIB / IIIC) and China cohort (patients enrolled at a Chinese site and self-identifying as being of Chinese descent vs patients enrolled at a non-Chinese site or self-identifying as being of non-Chinese descent).

The treatment with osimertinib in the intervention arm was largely carried out according to the product information.

Primary endpoint of the study is the progression-free survival (PFS); further endpoints were collected in the categories of mortality, morbidity, health-related quality of life and side effects.

Assessment

The determination of the appropriate comparator therapy results in patient groups that differ depending on the PD-L1 status of the patients. However, the PD-L1 status was not collected as part of the LAURA study. Consequently, it is not possible to assign the study population to the patient groups a) and b). According to the pharmaceutical company's statements at the oral hearing, there was no possibility of a retrospective follow-up survey of the PD-L1 status.

In the overall assessment, there are no suitable data for the assessment of the additional benefit of osimertinib for the patient groups a) and b). An additional benefit of osimertinib is therefore not proven for patient groups a) and b).

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the medicinal product Tagrisso with the active ingredient osimertinib.

The therapeutic indication assessed here is as follows: "Tagrisso as monotherapy is indicated for the treatment of adult patients with locally advanced, unresectable NSCLC whose tumours

have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and whose disease has not progressed during or following platinum-based chemoradiation therapy."

In the therapeutic indication to be considered, two patient populations were differentiated:

a) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in ≥ 1% of tumour cells

   and

b) adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in < 1% of tumour cells

On patient group a)

Durvalumab was determined to be the appropriate comparator therapy.

The determination of the appropriate comparator therapy results in patient groups that differ depending on the PD-L1 status of the patients. However, the PD-L1 status was not collected as part of the LAURA study. Consequently, it is not possible to assign the study population to the patient groups a) and b).

In the overall assessment, there are no suitable data for the assessment of the additional benefit of osimertinib for the patient group a). An additional benefit is therefore not proven.

On patient group b)

Best Supportive Care (BSC) was determined as the appropriate comparator therapy.

The determination of the appropriate comparator therapy results in patient groups that differ depending on the PD-L1 status of the patients. However, the PD-L1 status was not collected as part of the LAURA study. Consequently, it is not possible to assign the study population to the patient groups a) and b).

In the overall assessment, there are no suitable data for the assessment of the additional benefit of osimertinib for the patient group b). An additional benefit 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 G-BA base their resolution on the patient numbers from the statements submitted by the pharmaceutical company. The procedure of the pharmaceutical company is mathematically comprehensible. Overall, it is assumed that the adjustments - made by the pharmaceutical company in their statement - to the derivation compared to the original procedure lead to a better estimate of the patient numbers in the lower limit. In contrast, the upper limit derived in the statement is considered to be potentially underestimated, as the pharmaceutical company refrains from using a percentage range with regard to the percentage values of patients whose disease has not progressed during or following chemoradiation therapy compared to the procedure in the dossier.

In addition, further uncertainties in some derivation steps arise from the questionable transferability of the used percentage values, which refer generally to lung cancer and not specifically to NSCLC, and the potential exclusion of patients who were already in locally advanced stage III in the previous year and who are eligible for treatment with osimertinib in the current year under review.

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 Tagrisso (active ingredient: osimertinib) at the following publicly accessible link (last access: 28 May 2025):

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

Treatment with osimertinib may only be initiated and monitored by specialists in internal medicine, haematology and oncology who are experienced in the treatment of patients with non-small cell lung cancer, as well as specialists in internal medicine and pulmonology or specialists in pulmonary medicine and doctors from other specialist groups participating in the Oncology Agreement.

If the use of osimertinib is considered, EGFR mutational status must be determined using a validated assay.

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 2025).

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 for the maximum treatment duration, if specified in the product information.

a) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in ≥ 1% of tumour cells

Treatment with durvalumab is limited to a maximum duration of one year according to the product information.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Osimertinib	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Durvalumab	1 x per 14-day cycle	26	1	26
	or			
	1 x per 28-day cycle	13	1	13

b) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in < 1% of tumour cells

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 extent of best supportive care can vary between the medicinal product to be assessed and the comparator 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				
Osimertinib	Continuously, 1 x daily	365.0	1	365.0
BSC	Different from patient to patient			
Appropriate comparator therapy				
BSC	Different from patient to patient			

Consumption:

a) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in ≥ 1% of tumour cells

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements of the official representative statistics "Microcensus 2021 – body

measurements of the population" were applied (average body height: 1.72 m; average body weight: 77.7 kg).[2]

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					
Osimertinib	80 mg	80 mg	1 x 80 mg	365.0	365 x 80 mg
Appropriate comparator therapy					
Durvalumab	10 mg/kg BW	777.0 mg	1 x 500 mg + 3 x 120 mg	26.0	26 x 500 mg + 78 x 120 mg
	or				
	1500 mg	1500 mg	3 x 500 mg	13.0	39 x 500 mg

b) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in < 1% of tumour cells

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption according to potency / treatment days	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Osimertinib	80 mg	80 mg	1 x 80 mg	365.0	365 x 80 mg
BSC	Different from patient to patient				
Appropriate comparator therapy					
BSC	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

[2] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

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:

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					
Osimertinib 80 mg	30 FCT	€ 5,760.15	€ 1.77	€ 325.67	€ 5,432.71
Appropriate comparator therapy					
Durvalumab 500 mg	1 CIS	€ 2,105.19	€ 1.77	€ 116.94	€ 1,986.48
Durvalumab 120 mg	1 CIS	€ 518.21	€ 1.77	€ 28.06	€ 488.38
Abbreviations: FCT = film-coated tablets; CIS = concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 15 June 2025

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 had 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 October 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 designate 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 have 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 have 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 have 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:

a) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in ≥ 1% of tumour cells

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.

b) Adults with locally advanced, unresectable NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations, whose disease has not progressed during or following platinum-based chemoradiation therapy and whose tumours express PD-L1 in < 1% of tumour cells

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 their session on 27 June 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 8 January 2025, the pharmaceutical company submitted a dossier for the benefit assessment of osimertinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO number 2.

By letter dated 13 January 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits 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 osimertinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 10 April 2025, and the written statement procedure was initiated with publication on the G-BA website on 15 April 2025. The deadline for submitting statements was 6 May 2025.

The oral hearing was held on 26 May 2025.

By letter dated 27 May 2025, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 13 June 2025.

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 24 June 2025, and the proposed draft resolution was approved.

At their session on 3 July 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	27 June 2023	Determination of the appropriate comparator therapy
Working group Section 35a	13 May 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	26 May 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	3 June 2025 17 June 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	24 June 2025	Concluding discussion of the draft resolution
Plenum	3 July 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 3 July 2025

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

Prof. Hecken