Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Lenvatinib (Reassessment after the deadline: advanced renal cell carcinoma)

of 1 July 2021

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 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:

1st Approved therapeutic indications,

2nd Medical benefit,

3rd Additional medical benefit in relation to the appropriate comparator therapy,

4th Number of patients and patient groups for whom there is a therapeutically significant additional benefit,

5th Treatment costs for statutory health insurance funds,

6th 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 online and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The pharmaceutical company submitted a dossier for the early benefit assessment for the active ingredient lenvatinib) (Kisplyx) to be assessed for the first time on 29 September 2016. For the resolution of 16 March 2017 made by the G-BA in this resolution, a time limit of 31 December 2020 was pronounced.

In accordance with Section 4, paragraph 3 paragraph 5 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 5 VerfO, the procedure for the benefit assessment of the medicinal product Kisplyx recommences when the deadline has expired.

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 16 December 2020.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 April 2021 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was also held.

The G-BA came to a resolution on whether an additional benefit of lenvatinib 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, the statements submitted in the written statement and oral hearing procedure, and the addenda to the benefit assessment prepared by the IQWiG. 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 lenvatinibi.

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 lenvatinib (Kisplyx) in accordance with the product information

Kisplyx is indicated in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy.

Therapeutic indication of the resolution (resolution of 1 July 2021):

see approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy

Appropriate comparator therapy for lenvatinib in combination with everolimus:

- Nivolumab or cabozantinib

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

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.

1 General Methods, version 6.0 of 5.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. In the therapeutic indication, based on the authorisation status, are available cabozantinib, sunitinib, nivolumab, axitinib and everolimus as well as aldesleukin and interferon alfa-2a.

on 2. For the present therapeutic indication, a non-medicinal treatment is not considered as an appropriate comparator therapy.

on 3. The following resolutions of the G-BA are available for the therapeutic indication of lenvatinib that is the subject of the consultation:

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

- Cabozantinib (dated 15.10.2017) - advanced RCC after anti-VEGF therapy
- Nivolumab (dated 1.5.2016) - advanced RCC after previous therapy
- Axitinib (dated 4.1.2017) - advanced RCC after sunitinib or cytokine

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present therapeutic indication. 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.

For patients in the present therapeutic indication, it is assumed that surgery and/or radiotherapy with curative objectives are not (or no longer) an option at the time of the therapy decision and that the treatment is palliative. A non-medicinal treatment cannot be considered as an appropriate comparator therapy in this therapeutic indication. The use of resection and/or radiotherapy as a palliative patient-individual therapy option for symptom control depending on the localisation and symptomatology of the metastases remains unaffected.

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

For the treatment situation after a previous anti-angiogenic therapy, the active ingredients nivolumab and cabozantinib are consistently recommended as first-line therapy in the current German and international guidelines as well as in the statements of the scientific-medical societies.

The superiority of cabozantinib or nivolumab over everolimus in the therapeutic indication being evaluated was confirmed by the early benefit assessments of the G-BA.

For nivolumab, the benefit assessment identified a indication of a considerable additional benefit compared with everolimus for patients after previous anti-angiogenic therapy (resolution of 20 October 2016).

A indication for a minor additional benefit was identified for the active ingredient cabozantinib for the treatment of advanced renal cell carcinoma in adults after prior targeted therapy against VEGF compared with everolimus (resolution of 5 April 2018).

In contrast, monotherapy with everolimus in this therapy situation is described as an inferior option by comparison, to be used only when standard treatment is not an option.

The use of nivolumab in pretreated renal cell carcinoma has become much less important in the present trial, according to the statements of clinical experts. This would be due to new therapy options and recommendations in the first line, in particular the nowadays high value of immune checkpoint inhibitor combinations, after which treatment with nivolumab is inappropriate as a subsequent therapy option.

Taking into account the treatment situation described by the present therapeutic indication, the G-BA nevertheless considers it appropriate to designate monotherapy with nivolumab or with cabozantinib as the appropriate comparator therapy for adult patients with advanced renal cell carcinoma following one prior vascular endothelial growth factor (VEGF)-targeted therapy, both of which are equally appropriate therapeutic options.

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

2.1.3 Extent and probability of the additional benefit

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

Adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy

An additional benefit is not proven for lenvatinib in combination with everolimus.

Justification:

For the new benefit assessment after the expiry of the limited period of validity of the initial resolution of 16 March 2017, the pharmaceutical company submits an adjusted indirect comparison of lenvatinib in combination with everolimus versus cabozantinib. For this indirect comparison via the bridge comparator everolimus, the pharmaceutical company includes study 205 (lenvatinib + everolimus vs everolimus) and the METEOR study (cabozantinib vs everolimus).

About the 205 study

The 205 study is a randomised, open-label, actively controlled phase 1b/2 study. The phase 2 part of 205 study was used for the benefit assessment. In this study, a total of 153 patients were randomised to 3 study arms (lenvatinib + everolimus (51), lenvatinib (52), or everolimus (50)). Relevant for the present adjusted indirect comparison are the two study arms lenvatinib + everolimus and everolimus.

Adults with unresectable advanced or metastatic, predominantly clear cell, renal cell carcinoma were included, whereby there should be a disease progression within 9 months of previous treatment and disease progression following prior VEGF-targeted treatment of unresectable advanced or metastatic disease. The study participants had an ECOG-PS of 0 or 1, no brain metastases and were on average about 60 years old. In addition, they almost exclusively had clear cell renal cell carcinoma.

Treatment with lenvatinib + everolimus or everolimus was to be continued in the two study arms relevant for the benefit assessment at most until disease progression or until the occurrence of unacceptable toxicity, although subsequent therapies after discontinuation could be performed in both study arms. The treatment in both relevant study arms corresponded to the description in the product information.

The primary endpoint of Study 205 was progression-free survival (PFS); patient-relevant secondary endpoints were overall survival and adverse events (AEs). Health-related quality of life was not recorded in the 205 study.

For the present benefit assessment, the pharmaceutical company submitted the 3rd data cut-off from 31.7.2015, which was already relevant for the initial assessment.

About the METEOR study

For the adjusted indirect comparison, the pharmaceutical company submits the data of the pivotal METEOR study on which the benefit assessment on cabozantinib (resolution of 5 April 2018) is based. This is a randomised, open-label, active-controlled, phase 3 study comparing cabozantinib with everolimus.

The study included a total of 658 adult patients with advanced, metastatic clear cell renal cell carcinoma who had received at least one previous VEGF-directed therapy with a tyrosine kinase inhibitor and who had radiologically documented tumour progression during this therapy or within 6 months after the last dose. Study participants were randomised 1:1 to the two treatment arms, cabozantinib (330 patients) and everolimus (328 patients). They had a Karnofsky Status of ≥ 70% (equivalent to ECOG-PS of 0 or 1) and were aged 62 years on average.

Treatment with cabozantinib or everolimus was as described in the product information in both study arms and continued in both study arms as long as there was clinical benefit, and the therapy was tolerated. Even after disease progression, treatment could be continued.

After discontinuation of the study medication, the patients could be treated with subsequent therapies without restrictions; a switch from the comparator arm to the intervention arm was not planned.

The primary endpoint of the study was progression-free survival (PFS), secondary endpoints were overall survival, morbidity and side effects.

For the present benefit assessment, the results of the 3rd data cut-off from 2.10.2016 submitted by the pharmaceutical company are used.

On the similarities of the two studies 205 and METEOR in an indirect comparison

There are a number of ambiguities or uncertainties regarding the similarity of the studies presented for indirect comparison. These include differences in the proportion of patients included in Europe, differences in the duration of treatment, and differences in pre-treatment. In the overall picture, however, these do not lead to a fundamental questioning of the similarity of the studies.

For the present assessment, the adjusted indirect comparison according to Bucher based on studies 205 and METEOR can thus be used. The intervention side consists of the 205 study with lenvatinib in combination with everolimus, the comparison side consists of the METEOR study with cabozantinib. Everolimus acts as a bridge comparator.

On the implementation of conditions for a time limit

According to the justification of the initial resolution of 16 March 2017, the reason for the time limit was that the evidence submitted by the pharmaceutical company was assessed as insufficient in terms of both scope and reliability of data to assess the additional benefit of lenvatinib compared with the appropriate comparator therapy. For the new benefit assessment after expiry of the deadline, data on all patient-relevant endpoints - mortality, morbidity, health-related quality of life and side effects - should be collected on the basis of comparative clinical studies compared with the appropriate comparator therapy. The data should guarantee a sufficiently high statistical power of the study with adequate case number coverage and allow statements on disease-specific morbidity, health-related quality of life as well as more reliable statements on side effects. In addition, it was desired that the study population also included patients with brain metastases and that it adequately reflected the German health care reality by also including patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 2 or higher.

For the reassessment after the deadline, the pharmaceutical company only submits an adjusted indirect comparison of the data of 205 study, which were the basis of the initial evaluation of lenvatinib in combination with everolimus, with data from the METEOR study.

It thus complies with the modified appropriate comparator therapy in contrast to the initial assessment. However, comparative statements on disease-specific morbidity, health-related quality of life and more reliable statements on side effects can still not be derived on the basis of this comparison. For patient-relevant endpoints of morbidity and health-related quality of life, no data from the 205 study are available, so an indirect comparison for these categories is not feasible. For the endpoints on side effects, the risk of bias in the respective study from the indirect comparison is high, so that the results from the indirect comparisons are subject to uncertainty. Furthermore, no statement is possible on the additional benefit for patients with brain metastases or an ECOG performance status of 2 or higher, who were not eligible in the 205 study.

Overall, the conditions for a time limit were not implemented. However, in the present assessment, the G-BA comes to the conclusion that, despite the fact that the conditions for a time limit were not met and an adjusted indirect comparison was submitted, it is appropriate to use the comparison submitted by the pharmaceutical company to derive an additional benefit of lenvatinib in combination with everolimus compared to the appropriate comparator therapy cabozantinib.

Extent and probability of the additional benefit

Mortality

The adjusted indirect comparison showed no statistically significant difference between lenvatinib + everolimus and cabozantinib. An additional benefit of lenvatinib + everolimus in the category Mortality is therefore not proven.

Morbidity

Progression-free survival

The endpoint progression-free survival (PFS) was the primary endpoint in both the 205 Study and METEOR Study. In both studies, PFS was operationalised as the time between randomisation and radiologically confirmed disease progression or death from any cause.

In the adjusted indirect comparison, there is no statistically significant difference between lenvatinib in combination with everolimus versus cabozantinib.

The PFS is a combined endpoint composed of endpoints of the Mortality and Morbidity categories. The endpoint component Mortality was collected in both studies via the endpoint Overall survival as an independent endpoint. In both studies, the component morbidity was not assessed on the basis of symptoms, but exclusively on the basis of imaging procedures.

Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient relevance of the endpoint PFS. The overall statement on the extent of the additional benefit remains unaffected.

Symptomatology (FKSI-DRS), health status (EQ-5D VAS), skeletal-associated events

The endpoints mentioned above were only recorded in the METEOR study, so that no adjusted, indirect comparison can be made on the basis of these endpoints.

As a result, there are no data for morbidity that can be used for an adjusted indirect comparison.

Quality of life

No data on health-related quality of life were collected in either the 205 study or the METEOR study.

Side effects

Adverse events

The results for the endpoint Total adverse events are only presented supplementary.

In both studies, all patients experienced at least one adverse event.

Serious AEs and severe AEs [CTCAE grade ≥ 3)

In the 205 study, as already stated in the initial assessment, both positive and negative effects may generally remain undetected due to the small number of patients and the associated low power to identify statistically significant effects. The resulting uncertainty tends to be additionally increased by performing an indirect comparison.

Regardless, for the endpoints Severe AEs (CTCAE grade ≥ 3) and SAEs, the adjusted indirect comparison showed no statistically significant differences between lenvatinib in combination with everolimus versus cabozantinib.

Discontinuation due to AE

For the endpoint Discontinuation due to AE, no adjusted indirect comparison is performed due to the open-label study design.

In the overall view of the results on side effects, results from the adjusted indirect comparison are only available for the endpoint Severe AEs and SAEs. Based on these, there are no statistically significant differences between lenvatinib in combination with everolimus and cabozantinib.

Overall assessment

For the evaluation of the additional benefit of lenvatinib in combination with everolimus for the treatment of adults with advanced renal cell carcinoma after prior treatment directed against vascular endothelial growth factor (VEGF), patient-relevant results on mortality and side effects compared to the appropriate comparator therapy cabozantinib are available from an adjusted indirect comparison. The present evaluation takes place after the expiry of the

time limit of the resolution of 16 March 2021. However, the conditions for a time limit were not met overall. These had envisaged, in particular, the presentation of data that, in addition to statements on overall survival, would also allow statements on disease-specific morbidity, health-related quality of life and more reliable statements on side effects with adequate case number coverage.

An adjusted indirect comparison of the 205 study (lenvatinib + everolimus vs everolimus) and METEOR study (cabozantinib vs everolimus) according to Bucher was submitted by the pharmaceutical company on the bridge comparator everolimus. Although the conditions for a time limit were not fulfilled overall, the G-BA concludes that it is appropriate to use the adjusted indirect comparison used in the present benefit assessment.

For the endpoint Overall survival, the adjusted indirect comparison showed no statistically significant difference between lenvatinib in combination with everolimus and cabozantinib. An additional benefit of lenvatinib in combination with everolimus in the mortality category is therefore not proven.

In the endpoint category Morbidity, data on patient-relevant endpoints are only available for the METEOR study, so that no results relevant for the benefit assessment emerge from the adjusted indirect comparison.

Similarly, with regard to health-related quality of life, there are no usable data for an indirect comparison, as no data on health-related quality of life were collected in the 205 and METEOR studies.

With regard to side effects, the adjusted indirect comparison only allows conclusions to be drawn for the endpoints Severe AEs and Serious AEs. There were no statistically significant differences between lenvatinib in combination with everolimus versus cabozantinib.

Overall, based on the data presented, there is no evidence of additional benefit for lenvatinib in combination with everolimus compared to cabozantinib for the treatment of adults with advanced renal cell carcinoma after prior treatment directed against vascular endothelial growth factor (VEGF).

2.1.4 Summary of the assessment

The present assessment is a new benefit assessment of the active ingredient lenvatinib in combination with everolimus due to the expiry of the limitation of the resolution of 16 March 2017. Lenvatinib is indicated in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy.

Nivolumab or cabozantinib is determined as the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company submits an adjusted indirect comparison of the 205 and METEOR studies according to Bucher. However, the conditions for a time limit were not met overall. These had envisaged, in particular, the presentation of data that, in addition to statements on overall survival, would also allow statements on disease-specific morbidity, health-related quality of life and more reliable statements on side effects with adequate case number coverage. Nevertheless, the adjusted indirect comparison is generally used in the present benefit assessment.

There is no statistically significant difference for the endpoint Overall survival. An additional benefit of lenvatinib in combination with everolimus in the mortality category is therefore not proven.

For morbidity, the adjusted indirect comparison did not yield any results relevant for the benefit assessment.

Similarly, no usable data are available for health-related quality of life, as this was not collected in either study.

With regard to side effects, conclusions can only be drawn for the endpoints Severe AEs and Serious AEs, with no statistically significant differences.

Overall, based on the data presented, there is no evidence of additional benefit for lenvatinib in combination with everolimus compared to cabozantinib.

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 bases its resolution on the patient numbers from the dossier submitted by the pharmaceutical company. This is a better estimate overall than the patient numbers previously used as a basis in the area therapeutic indication due to more recent proportions. Regardless of this, there is an overestimation of the upper limit as the application of a progression rate to the upper limit results in double counting.

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 Kisplyx (active ingredient: lenvatinib) at the following publicly accessible link (last access: 3 March 2021):

https://www.ema.europa.eu/en/documents/product-information/kisplyx-epar-product-information_de.pdf

Treatment with lenvatinib should only be initiated in patients with advanced renal cell carcinoma and monitored by specialists in internal medicine, haematology, and oncology, specialists in internal medicine and nephrology, and specialists participating in the Oncology Agreement.

Patients with brain metastases were not studied in the 205 study. Especially in these patients, a careful risk-benefit assessment must be made before starting therapy.

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 2021).

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual 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.

Treatment duration:

Designation of the therapy	Treatment mode	Number of treatments/patient/year	Treatment duration/treatment (days)	Days of treatment/patient/ year
Medicinal product to be assessed				
Lenvatinib	1 x daily	365	1	365
Everolimus	1 x daily	365	1	365
Appropriate comparator therapy				
Nivolumab	once every 14 days	26.1	1	26.1
	or			
	once every 28 days	13	1	13.0
Cabozantinib	1 x daily	365	1	365

Consumption:

Designation of the therapy	Dosage/ application	Dosage/patient/days of treatment	Usage by potency/day of treatment	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Lenvatinib	18 mg	18 mg	1 x 10 mg + 2 x 4 mg	365	365 x 10 mg + 730 x 4 mg
Everolimus	5 mg	5 mg	1 x 5 mg	365	365 x 5 mg
Appropriate comparator therapy					
Nivolumab	240 mg	240 mg	2 x 100 mg + 1 x 40 mg	26.1	52.2 x 100 mg + 26.1 x 40 mg
	or				
	480 mg	480 mg	4 x 100 mg + 2 x 40 mg	13.0	52 x 100 mg + 26 x 40 mg
Cabozantinib	60 mg	60 mg	1 x 60 mg	365	365 x 60 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 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.

Cost of medicinal product:

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					
Lenvatinib 10 mg	30 HC	€ 1,496.60	€ 1.77	€ 82.25	€ 1,412.58
Lenvatinib 4 mg	30 HC	€ 1,496.60	€ 1.77	€ 82.25	€ 1,412.58
Everolimus 5 mg[2]	30 TAB	€ 871.77	€ 1.77	€ 40.85	€ 829.15
Appropriate comparator therapy					
Nivolumab 100 mg	1 IFC	€ 1,344.24	€ 1.77	€ 73.81	€ 1,268.66
Nivolumab 40 mg	1 IFC	€ 544.32	€ 1.77	€ 29.53	€ 513.02
Cabozantinib 60 mg	30 FCT	€ 5,709.38	€ 1.77	€ 322.79	€ 5,384.82
Abbreviations: HC = hard capsules; CIS =concentrate for infusion solution; FCT = film-coated tablets; TAB = tablets					

Last revised LAUER-TAXE®: 15 June 2021

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 standard expenditure in the course of the treatment are not shown.

[2] The costs are presented on the basis of the low-priced medicinal products, also taking into account the requirements of Section 129 SGB V and the possibility of prescribing medicinal products under their active ingredient name. Irrespective of this, the prescription of corresponding medicinal products must take into account the respective approved therapeutic indications.

Designation of the therapy	Type of service	Costs/ unit	Number/ patient/ year	Costs/ patient/ year
Lenvatinib	Quantitative determination by immunoassay, Thyrotropin (TSH); GOP 32101	€ 3	before initiation and at regular intervals during treatment	Patient-individual

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 special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), all surcharges for the production of parenteral preparations containing cytostatic drugs a maximum of € 81 per ready-to-use preparation and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 71 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 sales price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

3. Bureaucratic costs calculation

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

4. Process sequence

At its session on 9 June 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 16 December 2020 the pharmaceutical company submitted a dossier for the benefit assessment of lenvatinib to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 5 VerfO.

By letter dated 16 December 2020 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 lenvatinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 30 March 2021, and the written statement procedure was initiated with publication on the G-BA website on 1 April 2021. The deadline for submitting written statements was 22 April 2021.

The oral hearing was held on 10 May 2021.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing were discussed at the session of the subcommittee on 22 June 2021, and the draft resolution was approved.

At its session on 1 July 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	9 June 2020	Implementation of the appropriate comparator therapy
Working group Section 35a	4 May 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	10 May 2021	Conduct of the oral hearing
Working group Section 35a	18 May 2021 1 June 2021 15 June 2021	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	22 June 2021	Concluding discussion of the draft resolution
Plenum	1 July 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 1 July 2021

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

Prof. Hecken