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 Cemiplimab (new therapeutic indication: basal cell carcinoma, locally advanced or metastatic)

of 20 January 2022

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:

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 forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient cemiplimab (Libtayo) was listed for the first time on 1 August 2019 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 21 June 2021, cemiplimab 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 European 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, p. 7).

On 16 July 2021, 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 of the 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 cemiplimab with the new therapeutic indication (monotherapy for the treatment of adults with locally advanced or metastatic basal cell carcinoma (laBCC or mBCC), in whom disease progression has occurred in the presence of a Hedgehog pathway inhibitor (HHI) or who have an intolerance towards HHI).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de) on 1 November 2021, 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 cemiplimab 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 addendum to the benefit assessment prepared by 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 cemiplimab.

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 Cemiplimab (Libtayo) in accordance with the product information

LIBTAYO as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic basal cell carcinoma (laBCC or mBCC) who have progressed on or are intolerant to a hedgehog pathway inhibitor (HHI).

Therapeutic indication of the resolution (resolution of 20 January 2022):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with locally advanced or metastatic basal cell carcinoma (BCC) who have been previously treated with a Hedgehog pathway inhibitor and show disease progression or intolerance to it during this treatment.

Appropriate comparator therapy:

- Best supportive care

[1] General Methods, version 6.0 from 05.11.2020. 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:

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 Federal Joint Committee has already determined the patient-relevant advantage 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.

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

on 1. In addition to cemiplimab, the active ingredients vismodegib and sonidegib are approved for the present therapeutic indication.

on 2. It is assumed that the therapeutic indication only applies to patients for whom radiotherapy, surgery and local therapy are no longer an option.

on 3. For the present therapeutic indication, resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Vismodegib: resolution of 4 August 2016
- Sonidegib: resolution of 2 August 2018

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.

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.

Patients treated with a Hedgehog pathway inhibitor must not be eligible for surgery or radiotherapy according to the marketing authorisation of the Hedgehog pathway inhibitors vismodegib and sonidegib, which is why it is assumed that the present therapeutic indication only applies to patients for whom neither radiotherapy nor surgery and local therapy are possible.

The evidence for the treatment of patients with locally advanced or metastatic basal cell carcinoma who have previously been treated with a Hedgehog pathway inhibitor is extremely limited. There is no robust evidence on other treatment options with a primarily antineoplastic effect. In the written statement procedure on the present benefit assessment, clinical experts mentioned a therapy with one of the immune checkpoint inhibitors nivolumab or pembrolizumab in off-label use as another treatment option, but only based on the findings from case reports and case series.

For the present benefit assessment, the G-BA therefore considers it appropriate to determine best supportive care as the appropriate comparator therapy, which was also initially determined as the appropriate comparator therapy.

Best supportive care is the therapy that provides the best possible supportive treatment, optimised for each patient, 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.

2.1.3 Extent and probability of the additional benefit

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

a) Adults with locally advanced basal cell carcinoma (laBCC) who have been previously treated with a Hedgehog pathway inhibitor and show disease progression or intolerance to it during this treatment.

Hint for a minor additional benefit

b) Adults with metastatic basal cell carcinoma (mBCC) who have been previously treated with a Hedgehog pathway inhibitor and show disease progression or intolerance to it during this treatment.

An additional benefit is not proven.

Justification:

For the proof of additional benefit, the pharmaceutical company presented the results of the single-arm, open-label and multicentre phase II R2810-ONC-1620 study in the dossier.

Adults with locally advanced basal cell carcinoma (laBCC) or metastatic basal cell carcinoma (mBCC) who were pretreated with at least one Hedgehog pathway inhibitor (HHI) and had disease progression or intolerance to this therapy were enrolled in the study. In addition, patients had to have at least one measurable lesion with a diameter of at least 10 mm. For patients with laBCC, it was also defined that they had to have an unresctable tumour at the time of enrolment in the study and could not be eligible for radiotherapy. Only patients with good general condition (Eastern Cooperative Oncology Group Performance Status (ECOG-PS) of 0 or 1) were enrolled in the study.

A total of 132 patients, 84 with laBCC and 48 with mBCC, were enrolled in the study by the data cut-off from 17.02.2020.

The treatment with cemiplimab was carried out according to the specifications in the product information.

The primary endpoint of the study was objective response rate (ORR). Secondary endpoints were overall survival and endpoints of the endpoint categories of morbidity, health-related quality of life and side effects.

Two data cut-offs are available for the R2810-ONC-1620 study:

- 1. data cut-off from 17.02.2020 (primary efficacy analysis for the laBCC and interim analysis for efficacy (mBCC) and safety (laBCC and mBCC))
- 2. data cut-off from 30.06.2020 (additional efficacy and safety analysis submitted to the EMA for laBCC and mBCC)

For the present benefit assessment, the results of the pre-specified 1st data cut-off from 17.02.2020 are used.

Extent and probability of the additional benefit

a) Adults with locally advanced basal cell carcinoma (laBCC) who have been previously treated with a Hedgehog pathway inhibitor and show disease progression or intolerance to it during this treatment.

and

b) Adults with metastatic basal cell carcinoma (mBCC) who have been previously treated with a Hedgehog pathway inhibitor and show disease progression or intolerance to it during this treatment.

Mortality

The endpoint of overall survival was assessed as a secondary endpoint in the R2810-ONC-1620 study and was defined as the time between the start of treatment and the occurrence of death from any cause.

Overall, the results of the R2810-ONC-1620 study for the endpoint of overall survival do not allow a statement to be made on the extent of the additional benefit for the endpoint category of mortality, as no comparative data are available. The endpoint of overall survival is presented additionally.

Morbidity

Objective response rate/ clinical response

The endpoint of objective response rate (ORR) was assessed as the primary endpoint in the R2810-ONC-1620 study and operationalised as composite response, which includes clinical and radiological response. A distinction was made between complete or partial response, as well as stable disease and progression.

The clinical response was documented according to the World Health Organisation (WHO) criteria for the assessment of externally visible tumours using digital photography. The operationalisation for radiological response is based on the RECIST 1.1 criteria. The assessment of clinical and radiological response was done by an independent central review committee.

In the dossier, the pharmaceutical company submitted only evaluations of the ORR based on the composite response for patients with both laBCC and mBCC. Results on the individual components of the combined endpoint, especially clinical response, were completely missing.

Regarding the composite response, 28.6% of patients with laBCC and 21.4% of patients with mBCC showed a response.

With their statement, the pharmaceutical company submitted two different evaluations of the clinical response. The evaluations, based on the external assessment of the visible tumour lesions, were only carried out for patients with laBCC. For patients with mBCC, due to the presence of remote metastases, mere consideration of the clinical response is not expedient, as the assessment of the radiological response is also necessary for the evaluation of the overall tumour process here.

On the one hand, the pharmaceutical company submitted evaluations based on the operationalisation pre-specified in the R2810-ONC-1620 study. On the other, they presented evaluations based on the operationalisation used in the ERIVANCE study evaluated in the vismodegib procedure. For the present assessment, the evaluation based on the operationalisation from the vismodegib procedure was used.

This evaluation is divided into 3 phases: phase 1 includes complete elimination of lesions (decrease in visible lesion extent by 100%) and elimination of ulcerations, phase 2 includes marked but incomplete reduction of lesions (decrease in visible lesion extent from at least 30% to less than 100%) and elimination of ulcerations, and phase 3 includes marked, but incomplete reduction of lesions and persistence of ulcerations or no/minor reduction of lesion size (reduction of visible lesion extent less than 30%) but elimination of ulcerations.

To further characterise the individual clinical response, patients were assigned to two categories: category 1 includes patients in whom at least one target lesion was larger than 50 mm (measured by the longest extension) and category 2 includes patients in whom all target lesions were 50 mm or less.

Clinical response was observed in 30% of patients with laBCC. 23% of the patients with larger lesions (category 1) responded to treatment with cemiplimab, while 44% of the patients with smaller lesions (category 2) responded to the same.

In 9 of the patients who responded to treatment with cemiplimab, there was a complete remission of the lesions by 100% and elimination of ulcerations (11%). The other 15 patients showed a partial remission of stage 2 or 3. In patients with clinical response in category 1 (lesion size > 50 mm), the lesion size was reduced by about 39% on average, in patients with clinical response in category 2 (lesion size ≤ 50 mm) by about 65% on average.

In the indication of locally advanced basal cell carcinoma, there is the special case that the endpoint of objective response rate (ORR) is considered to be a patient-relevant endpoint due to the good external visibility of the tumour lesions and ulcerations, which sometimes manifest themselves in clearly visible disfigurements and can also be accompanied by an olfactory component, provided that it is shown by suitable operationalisation that tumour size and tumour ulcerations are correspondingly reduced. The evaluation made possible by submission of the individual components of the ORR showed results in the form of a relevant reduction in tumours and tumour ulcerations due to a clinical response in 24 of 81 patients with laBCC (30%) - including a complete remission in 9 patients (11%), which are to be considered patient-relevant.

To assess the magnitude of the effect of therapy with cemiplimab, the single-arm R2810-ONC-1620 study was submitted by the pharmaceutical company. Thus, there is no comparison with the appropriate comparator therapy of best supportive care. However, it can be assumed with sufficient certainty that no spontaneous remissions occur under best supportive care or that no relevant effects with regard to a clinical response can be achieved through best supportive care. This view was expressed in the statements of clinical experts specifically for the present treatment setting; moreover, there are no reports of spontaneous remissions from the literature. Thus, the present results suggest an increase in clinical response with cemiplimab treatment compared to best supportive care in patients with laBCC.

Progression-free survival

Progression-free survival (PFS) was defined as the time between the start of treatment and the onset of relapse or disease progression (photographic or radiological) or the time of death from any cause. PFS was assessed by a blinded, independent central review committee.

The endpoint component of mortality was assessed in the present study via the endpoint of overall survival as an independent endpoint. The morbidity component of disease progression was assessed by means of imaging procedures (photographically or radiologically determined disease progression according to the RECIST criteria).

The endpoint of progression-free survival cannot be clearly assessed in terms of its patient relevance due to its composition from different endpoint categories with varying relevance and severity, which is why no overall statement on the additional benefit can be made.

Notwithstanding that, the results of the R2810-ONC-1620 study for the endpoint of progression-free survival do not allow a statement to be made on the extent of the additional benefit for the endpoint category of mortality as no comparative data are available. The endpoint of progression-free survival is presented additionally.

Symptomatology

Symptomatology was assessed in the R2810-ONC-1620 study using the symptom scales of the disease-specific EORTC QLQ-C30 questionnaire.

The results on symptomatology cannot be assessed as no comparative data are available.

Quality of life

Health-related quality of life was assessed in the R2810-ONC-1620 study using the global health status and functional scales of the EORTC QLQ-C30 questionnaire as well as the SKINDEX-16 questionnaire.

The results on health-related quality of life cannot be assessed as no comparative data are available.

Side effects

Adverse events (AEs) in total

Adverse events (AEs) occurred in almost all study participants. However, there are no comparative data for the adverse events.

Serious adverse events (SAEs), severe AEs (CTCAE grade ≥ 3), therapy discontinuations *due to AEs and AEs of special interest*

There are no comparative data for serious adverse events (SAEs), severe AEs (CTCAE grade ≥ 3), therapy discontinuations due to AEs and AEs of special interest.

Overall, the results of the R2810-ONC-1620 study on adverse events do not allow a statement to be made on the extent of additional benefit for the endpoint category of side effects as no comparative data are available. The results of the endpoint category of side effects are only presented additionally.

Overall assessment

For the benefit assessment of cemiplimab for the treatment of adult patients with locally advanced or metastatic basal cell carcinoma (BCC) who have been pretreated with a Hedgehog pathway inhibitor and show disease progression or intolerance to it during this treatment, results of the single-arm R2810-ONC-1620 study are available for the endpoint categories of mortality, morbidity, quality of life and side effects.

The results for the endpoints of overall survival, symptomatology, quality of life and side effects cannot be assessed because no comparative data are available.

In the morbidity endpoint category, a good clinical response was shown by patients with locally advanced basal cell carcinoma (laBCC) for the clinical response endpoint component of the composite endpoint of objective response rate (ORR). Since it can be assumed with sufficient certainty that no relevant effects can be achieved with regard to a clinical response under the comparator therapy of best supportive care, a clinical response to this relevant extent is considered patient-relevant in the present therapeutic indication and can be used with sufficient certainty for the benefit assessment.

The positive effect on clinical response is offset by adverse events during treatment with cemiplimab.

Thus, in the overall assessment, there is a relevant difference or assessable data for the benefit assessment only for the clinical response. The results on clinical response only allow statements for patients with laBCC; overall, there are no assessable data for patients with metastatic basal cell carcinoma (mBCC). For the assessment, the patient population was therefore divided into patients with laBCC and mBCC.

In conclusion, the G-BA determines a patient-relevant advantage for cemiplimab in terms of tumour response, taking into account the statements of medical experts as well as the present treatment setting for patients with laBCC. The overall extent of the additional benefit of cemiplimab compared to the appropriate comparator therapy of best supportive care is rated as low for patients with laBCC.

For patients with mBCC, no data suitable for deriving an additional benefit are available, so that an additional benefit is not conclusively proven for these patients.

Reliability of data (probability of additional benefit)

The present benefit assessment is based on the results of the single-arm, open-label and multicentre phase II R2810-ONC-1620 study.

Due to the small number of patients in the target population and the limited data basis on the patient-relevant endpoints and the lack of a control group, only a hint for the reliability of data can be derived.

2.1.4 Summary of the assessment

The present benefit assessment is based on the results of the single-arm, open-label and multicentre phase II R2810-ONC-1620 study. Results on mortality, morbidity, quality of life and side effects are available.

No data are available for comparative assessment due to the single-arm design of the study.

No assessable data are available for overall survival, symptomatology, quality of life and side effects.

In the endpoint category of morbidity, a good clinical response was shown by patients with locally advanced basal cell carcinoma for the endpoint of objective response rate, which is considered relevant to patients to this extent in the present indication and can be used with sufficient certainty for the benefit assessment.

The positive effect on clinical response is offset by adverse events during treatment with cemiplimab.

Overall, assessable data were only available for patients with locally advanced basal cell carcinoma. For the assessment, the patient population was therefore divided into patients with locally advanced basal cell carcinoma and patients with metastatic basal cell carcinoma.

For patients with locally advanced basal cell carcinoma, a hint for a minor additional benefit is identified due to the advantage in clinical response.

For patients with metastatic basal cell carcinoma, no data suitable for deriving an additional benefit are available, so that an additional benefit is not conclusively proven for patients with metastatic basal cell carcinoma.

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 based its resolution on the data from the pharmaceutical company's dossier, but additionally divided the SHI target population into patients with laBCC and mBCC. The pharmaceutical company's calculation approach is basically comprehensible, but there are significant uncertainties in individual calculation steps, which means that the number of patients in the target population estimated by the pharmaceutical company is uncertain. The division of the target population into patients with laBCC and mBCC was approximated on the basis of the percentage of incident and prevalent patients with mBCC in those with advanced basal cell carcinoma.

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 Libtayo (active ingredient: cemiplimab) at the following publicly accessible link (last access: 28 September 2021):

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

Treatment with cemiplimab should only be initiated and monitored by specialists in internal medicine, haematology and oncology who are experienced in the treatment of adults with basal cell carcinoma, specialists in skin and sexually transmitted diseases as well as other doctors from specialist groups participating in the Oncology Agreement.

According to the requirements for risk minimisation activities in the EPAR (European Public Assessment Report), the pharmaceutical company must provide the following information material on cemiplimab:

- information brochure for patients
- patient pass

The training material contains, in particular, instructions on the management of immune-mediated side effects potentially occurring with cemiplimab as well as on infusion-related reactions.

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 January 2022).

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

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 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.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Cemiplimab	1 x every 21 days	17.4	1	17.4
Best supportive care	Different from patient to patient			
Appropriate comparator therapy for a) and b)				
Best supportive care	Different from patient to patient			

Consumption:

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					
Cemiplimab	350 mg	350 mg	1 x 350 mg	17.4	17.4 x 350 mg
Best supportive care	Different from patient to patient				
Appropriate comparator therapy for a) and b)					
Best supportive care	Different from patient to patient				

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of usage. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
cemiplimab 350 mg	1 CIS	€ 4,549.10	€ 1.77	€ 256.51	€ 4,290.82
Best supportive care	Different from patient to patient				
Appropriate comparator therapy for a) and b)					
Best supportive care	Different from patient to patient				
Abbreviations: CIS = concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 01 January 2022

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 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic drugs a maximum amount 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 purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

3. Bureaucratic costs calculation

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

4. Process sequence

At its session on 28 July 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 16 July 2021 the pharmaceutical company submitted a dossier for the benefit assessment of cemiplimab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

By letter dated 21 July 2021 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 cemiplimab.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 October 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 1 November 2021. The deadline for submitting written statements was 22 November 2021.

The oral hearing was held on 6 December 2021.

By letter dated 7 December 2021, 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 21 December 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 was discussed at the session of the subcommittee on 11 January 2022, and the proposed resolution was approved.

At its session on 20 January 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	28 July 2020	Implementation of the appropriate comparator therapy
Working group Section 35a	1 December 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	6 December 2021	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	15 December 2021 5 January 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	11 January 2022	Concluding discussion of the draft resolution
Plenum	20 January 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 20 January 2022

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

Prof. Hecken