Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) 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 Bosutinib (reassessment after the deadline: chronic myelogenous leukaemia, Ph+, first-line)

of 19 November 2021

Contents

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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 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 benefits,
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 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.

Key points of the resolution

The pharmaceutical company submitted a dossier for the early benefit assessment of the active ingredient bosutinib (Bosulif) for the first time on 28 March 2018. For the resolution of 22 November 2018 made by the G-BA in this procedure, a time limit of 1 June 2021 was declared.

In accordance with Section 4, paragraph 3, No. 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 Bosulif 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 28 May 2021.

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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 September 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 bosutinib 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, and the addendum to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA has assessed 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 bosutinib.

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 bosutinib (Bosulif) in accordance with the product information

Bosulif is indicated for the treatment of adult patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML).

Therapeutic indication of the resolution (resolution from 19.11.2021):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adult patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML).

Appropriate comparator therapy for bosutinib:

- imatinib

or

- nilotinib

or

- dasatinib

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

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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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 benefit 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.

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

on 1. Hydroxycarbamide has a marketing authorisation for the treatment of patients with chronic myelogenous leukaemia (CML) in the chronic or accelerated phase of the disease. The tyrosine kinase inhibitors dasatinib, imatinib, nilotinib and bosutinib are approved for the treatment of newly diagnosed Ph+ CML in the chronic phase. Interferon alfa-2a and interferon alfa-2b are also approved for this therapeutic indication.

on 2. A non-medicinal treatment cannot be considered as an appropriate comparator therapy in this therapeutic indication.

on 3. No corresponding resolutions or assessments of the G-BA are available.

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 therapeutic indication according to Section 35a paragraph 7 SGB V.

According to the approved therapeutic indication, adult patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML).are covered by the 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.

Relevant guidelines recommend the tyrosine kinase inhibitors (TKIs) imatinib, dasatinib, nilotinib and bosutinib for the first-line treatment of Ph+ CML in the chronic phase. While imatinib as the first representative of TKIs for the treatment of Ph+ CML in the chronic phase is referred to as a TKI of the first generation, while nilotinib, dasatinib and bosutinib are classified as TKIs of the 2nd generation. The TKI for first-line treatment should be selected on the basis of the range of side effects, taking risk factors

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into account. Interferon alfa (in combination with cytarabine) is no longer recommended for first-line treatment of CML. Hydroxycarbamide is used exclusively in initial or palliative cytoreductive therapy. Thus, hydroxycarbamide and interferon alfa (in combination with cytarabine) are not considered to be appropriate comparator therapy.

With regard to the importance of the TKIs among each other, the corresponding systematic reviews show that the TKIs of the 2nd generation show statistically significant advantages over imatinib in terms of molecular response. However, there is no consistent benefit in terms of overall survival in these studies. In the systematic review by Pan P et al, 2020, a statistically significant difference in overall survival of TKIs of the 2nd generation versus imatinib could be shown after 12 months; however, it was no longer detectable after 2, 3, and 5 years. Overall, there is no evidence that adequately demonstrates the significance of one of these TKIs. Also, current guidelines highlight that in large randomised phase III studies comparing imatinib with TKIs of the 2nd generation, similar results were shown for the mentioned active ingredients.

The scientific-medical societies state that the administration of one of the oral BCR-ABL1 tyrosine kinase inhibitors approved in this indication represents the therapy standard in the mentioned therapeutic indication.

Thus, imatinib, dasatinib and nilotinib are equally eligible appropriate comparator therapies.

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 bosutinib is assessed as follows:

An additional benefit is not proven for bosutinib in the treatment of adult patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML).

Justification:

For the benefit assessment, the pharmaceutical company uses the BFORE study. This is an open-label, randomised controlled trial comparing bosutinib to the comparator therapy imatinib in the treatment of adults with newly diagnosed chronic myelogenous leukaemia in the chronic phase. 268 patients were randomised to each of the two treatment arms; of these, the presence of the Philadelphia chromosome was detected in 246 patients in the bosutinib arm and in 241 patients in the imatinib arm. For the present benefit assessment, only patients with a confirmed Philadelphia chromosome were considered (modified intention-to-treat (mITT) population). The mean age of this population was 51 years. At start of study, approximately 20% of patients had a Sokal score for high risk and approximately 40% each for low and moderate risk. The study was conducted in 146 centres across 26 countries.
The primary endpoint was major molecular response (MMR) after 12 months. Patient-relevant secondary endpoints were overall survival, morbidity, health-related quality of life and adverse events (AEs).

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There are a total of 7 data cut-offs for the BFRORE study. The benefit assessment is based on the final data cut-off of 12.06.2020, on the basis of which the final analysis was performed at the end of study after an observation period of ≥ 60 months.

Extent and probability of the additional benefit

Mortality

For the endpoint on overall survival, no statistically significant difference was detected between the treatment arms. For overall survival, an additional benefit of bosutinib compared to imatinib is therefore not proven.

Similar to the first assessment, which was based on a data cut-off with an observation period of at least 24 months, only a small number of events occurred in both arms, even against the background of an overall survival under TKI therapy approximately corresponding to the normal population, also in the present final data cut-off, which allowed observation of all patients for at least 5 years.

Morbidity

Molecular response

Major molecular response (MMR) after 12 months was the primary endpoint of the BFORE study. This endpoint showed a statistically significant advantage of therapy with bosutinib compared to imatinib.

The endpoint is based on the molecular genetic determination of BCR-ABL transcripts in peripheral blood and, thus, on haematological findings that are not directly relevant to the patient.

In clinical practice, the MMR represents a relevant prognostic factor and parameter for therapy planning.

A validation of MMR as a surrogate parameter for overall survival is also not available for the present assessment after the deadline. The endpoint MMR is neither assessed as a directly patient-relevant endpoint nor as a validated surrogate endpoint and is therefore not used for the present assessment.

Transition to the blast phase

The endpoint is classified as patient-relevant because a transition to blast phase is associated with a deterioration in health status that is directly perceptible to the patient. In comparison to the first assessment, the pharmaceutical company submits evaluations for this assessment which only cover events for the transition to the blast phase and no events for the transition to the accelerated phase. In contrast to the transition to blast phase, the transition to the accelerated phase is rarely accompanied by symptoms.

However, there was no statistically significant difference between the two treatment arms for this endpoint. Only a small number of events occurred in both arms. An additional benefit of bosutinib compared to imatinib is therefore not proven.

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Health status (EQ-5D, visual analogue scale)

The health status was assessed using the visual analogue scale of EQ-5D. For the benefit assessment, the pharmaceutical company submitted responder analyses for the time to deterioration by ≥ 7 or ≥ 10 points from the baseline and by 15% of the scale range. For the present benefit assessment, these responder analyses are used for the three threshold values.

Analyses show no statistically significant difference between the treatment arms for the time to deterioration.

Overall, an additional benefit of bosutinib compared to imatinib for the endpoint category of morbidity is therefore not proven.

Quality of life

Health-related quality of life was assessed in the study using the Functional Assessment of Cancer Therapy - Leukaemia (FACT-Leu). This is composed of four generic subscales for physical well-being (PWB), functional well-being (FWB), social well-being (SWB), and emotional well-being (EWB), as well as a leukaemia-specific subscale (FACT-Leu).

In this assessment, the FACT-Leu total score is primarily considered. The pharmaceutical company submits time-to-event analyses based on scale-specific MIDs for both the subscales and the FACT-Leu total score. In addition, the pharmaceutical company submits corresponding further responder analyses against the background of the ranges given in the literature for the MID and the MID corresponding to 15% of the respective scale range proposed according to IQWiG methods paper 6.0.

The 15% scale range is used for the present benefit assessment as the sources provided by the pharmaceutical company are not considered sufficient to justify the validity of the scale-specific MIDs.

For the endpoint on health-related quality of life according to the FACT-Leu total score, there was no significant difference between the treatment arms.

For health-related quality of life, an additional benefit of bosutinib compared to imatinib is therefore not proven.

Side effects

Adverse events (AEs)

Overall, adverse events occurred in 98.8% of patients in the bosutinib arm and in 98.7% of patients in the imatinib arm. The results for the endpoint "Adverse events" (AE) are presented additionally.

Serious adverse events (SAE)

For the serious adverse events, there was no statistically significant difference between the treatment arms.

Severe AEs (CTCAE grade 3 or 4)

There was a statistically significant disadvantage of bosutinib over imatinib with regard to serious adverse events with CTCAE grade ≥ 3.

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In addition, an effect modification for the age characteristic is available for this endpoint. For patients < 65 and ≥ 65 years, there is a statistically significant difference to the disadvantage of bosutinib with varying degrees in each case, with patients ≥ 65 years more frequently affected by severe AE.

Discontinuation due to AE

For the endpoint on therapy discontinuation due to AE, there was a statistically significant effect to the disadvantage of bosutinib.

The reliability of data of this endpoint is potentially limited due to possible competing events (reasons for discontinuation other than AEs, especially progress).

Specific AEs

The selection of specific AEs was done according to the methodology of the IQWiG using events based on frequency and differences between treatment arms and taking into account patient relevance.

When considering the specific AEs in detail, a statistically significant advantage can be observed for bosutinib compared to imatinib with regard to the specific AEs eye disorders (SOC, UE), oedema, peripheral (PT, AEs), musculoskeletal and connective tissue disorders (SOC, AEs) and neutropenia (PT, severe AEs).

In contrast, bosutinib showed a statistically significant disadvantage with respect to the specific AE gastrointestinal disorders (SOC, AEs), pruritus (PT, AEs), thrombocytopenia (PT, severe AEs), cardiac disorders (SOC, severe AEs) and lipase elevation (PT, severe AEs), diarrhoea (PT, severe AEs) and impaired liver function (CMQ, severe AEs).

In the overall assessment of the endpoints on side effects, there is a statistically significant disadvantage of bosutinib with regard to the severe AEs (CTCAE grade ≥ 3) and with regard to the endpoint "discontinuation due to AEs". In detail, both advantages and disadvantages of bosutinib compared to imatinib can be identified in the specific AEs. For the serious adverse events, there is no statistically significant difference between the treatment arms. In the category of side effects, a disadvantage of bosutinib over imatinib is thus established in the overall assessment.

<u>Overall assessment / conclusion</u>

For the present benefit assessment of bosutinib for the treatment of adult patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML), results from the randomised controlled phase III BFORE study are available for the endpoint categories of mortality, morbidity, quality of life and side effects compared to the appropriate comparator therapy with imatinib.

For the endpoint on overall survival, there was no statistically significant difference between the treatments with bosutinib and imatinib, respectively. When interpreting the overall survival results, it should be noted that the number of events in both treatment arms of the BFORE study is low, even with longer follow-up in the present assessment, compared to the previous one.

In the endpoint categories of morbidity and health-related quality of life, no additional benefit can be identified for bosutinib on the basis of the available data.

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In the overall assessment of the endpoints on side effects, there is a statistically significant disadvantage of bosutinib with regard to the severe AEs (CTCAE grade ≥ 3) and with regard to the endpoint "discontinuation due to AEs". In detail, both advantages and disadvantages of bosutinib compared to imatinib can be identified when analysing the specific AEs. For the serious adverse events, there is no statistically significant difference between the treatment arms. In the overall assessment, a disadvantage of bosutinib over imatinib in terms of side effects is found. However, taking into account the clinical relevance, this is not of a magnitude that would justify a lower benefit in the overall assessment of all endpoints.

This assessment by the G-BA is also in line with the benefit-risk assessment of bosutinib conducted by the EMA marketing authorisation authority. This assessment by the EMA has not changed in the context of the annual review following the marketing authorisation under "special conditions".

In the overall assessment, the G-BA came to the conclusion that an additional benefit of bosutinib over imatinib is not proven in the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive, chronic myelogenous leukaemia in the chronic phase.

2.1.4 Summary of the assessment

The present assessment is a new benefit assessment the active ingredient bosutinib due to the expiry of the time limit of the resolution of 22 November 2018.
The present assessment relates to the use of bosutinib for the treatment of chronic myelogenous leukaemia (CML) in the following patient population:

Adult patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML)

The appropriate comparator therapy was determined as follows by the G-BA:

- imatinib

or

- nilotinib

or

- dasatinib.

For the benefit assessment, the pharmaceutical company submits the final results of the open-label, randomised and controlled BFORE study, in which bosutinib was compared to the appropriate comparator therapy with imatinib in the treatment of adult patients with newly diagnosed chronic myelogenous leukaemia in the chronic phase.

For the endpoint on overall survival, there was no statistically significant difference between the treatments with bosutinib and imatinib, respectively. When interpreting the overall survival results, it should be noted that the number of events in both treatment arms of the BFORE study is low, even with longer follow-up in the present assessment, compared to the previous one.

In the endpoint categories of morbidity and health-related quality of life, no additional benefit can be identified for bosutinib on the basis of the available data.

In the overall assessment of the endpoints on side effects, there is a statistically significant disadvantage of bosutinib with regard to the severe AEs (CTCAE grade ≥ 3) and with regard to the endpoint "discontinuation due to AEs". In detail, both advantages and disadvantages of bosutinib compared to imatinib can be identified when analysing the specific AEs. For the

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serious adverse events, there is no statistically significant difference between the treatment arms. In the overall assessment, a disadvantage of bosutinib over imatinib in terms of side effects is found. However, taking into account the clinical relevance, this is not of a magnitude that would justify a lower benefit in the overall assessment of all endpoints.

This assessment by the G-BA is also in line with the benefit-risk assessment of bosutinib conducted by the EMA marketing authorisation authority. This assessment by the EMA has not changed in the context of the annual review following the marketing authorisation under "special conditions".

In the overall assessment, the G-BA came to the conclusion that an additional benefit of bosutinib over imatinib is not proven in the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive, chronic myelogenous leukaemia in the chronic phase.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The resolution is based on the information from the dossier of the pharmaceutical company.

The methodological approach is the same as that in the 2018 dossier for bosutinib. The slightly higher figures in comparison especially result from the current baseline (number of new cases of leukaemia for 2017). Overall, the number of patients indicated in the SHI target population is within a plausible range.

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 Bosulif (active ingredient: bosutinib) at the following publicly accessible link (last access: 2 September 2021):

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

Initiation and monitoring of treatment with bosutinib should be performed only by specialists in internal medicine, haematology and oncology, experienced in the therapy of patients with chronic myelogenous leukaemia.

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 November 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

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of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

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

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Bosutinib	continuously, 1 x daily	365	1	365
Appropriate comparator therapy				
dasatinib	continuously, 1 x daily	365	1	365
imatinib	continuously, 1 x daily	365	1	365
nilotinib	continuously, 2 x daily	365	1	365

Consumption:

Designation of the therapy	Dosage/ application	Dosage/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Bosutinib	400 mg	400 mg	1 x 400 mg	365	365 x 400 mg
Appropriate comparator therapy					
dasatinib	100 mg	100 mg	1 x 100 mg	365	365 x 100 mg
imatinib	400 mg	400 mg	1 x 400 mg	365	365 x 400 mg
nilotinib	300 mg	600 mg	4 x 150 mg	365	1,460 x 150 mg

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Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated based on 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					
Bosutinib	28 FCT	€ 2,514.66	€ 1.77	€ 0.00	€ 2,512.89
Appropriate comparator therapy					
dasatinib	30 FCT	€ 1,074.33[2]	€ 1.77	€ 50.46	€ 1,022.10
Imatinib[3]	90 HC	€ 538.06	€ 1.77	€ 41.68	€ 494.61
nilotinib	392 HC	€ 13,640.71	€ 1.77	€ 775.75	€ 12,863.19
Abbreviations: FCT = film-coated tablets; HC = hard capsules					

LAUER-TAXE® last revised: 1 November 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.

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.

[2] The costs are represented 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.

[3] Fixed reimbursement rate

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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.

Process sequence

At its session on 26 January 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 28 May 2021, the pharmaceutical company submitted a dossier for the benefit assessment of bosutinib to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 5 VerfO.

By letter dated 1 June 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 bosutinib.

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

The oral hearing was held on 11 October 2021.

By letter dated 11 October 2021, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addenda prepared by IQWiG was submitted to the G-BA on 29 October 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 9 November 2021, and the proposed resolution was approved.

At its session on 19 November 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

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Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	26 January 2021	Determination of the appropriate comparator therapy
Working group Section 35a	6 October 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	11 October 2021	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	20 October 2021 3 November 2021	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	9 November 2021	Concluding discussion of the draft resolution
Plenum	19 November 2021	Adoption of the resolution on the amendment of Annex XII AM-RL (Pharmaceuticals Directive)

Berlin, 19 November 2021

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

Prof. Hecken

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