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: Blinatumomab (new therapeutic indication: acute lymphoblastic B-cell leukaemia, high-risk first relapse, Ph-, CD19+, ≥1 and <18 years)

of 20 January 2022

Contents

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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.

For medicinal products for the treatment of a rare disease (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 50 million in the last 12 calendar months. According to Section 35a paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, subsection 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a paragraph 1 sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the marketing authorisation studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the legal limit of € 50 million and is therefore subject to an unrestricted benefit assessment (cf. Section 35a paragraph 1, sentence 12 SGB V). According to Section 35a paragraph 2 SGB V, the assessment by the G-BA must be

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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 Blinatumomab (Blincyto) was listed for the first time on 15 December 2015 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 24 June 2021, blinatumomab 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).

Blinatumomab for the treatment of paediatric patients aged 1 year or older with high-risk first relapse of a Philadelphia chromosome negative (Ph-), CD19 positive (CD19+) B-precursor (acute lymphoblastic leukaemia (ALL)) is authorised as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the marketing authorisation studies by the G-BA.

On 19 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 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 blinatumomab with the new therapeutic indication (acute lymphoblastic B-cell leukaemia, high-risk first relapse, Ph-, CD19+, ≥1 and <18 years).

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 1 November 2021 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA has adopted its resolution on the basis of the dossier of the pharmaceutical company, the dossier assessment carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G21-23) prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure.

In order to determine the extent of the additional benefit, the G-BA has assessed the studies relevant for the marketing authorisation considering their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1,

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numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of blinatumomab.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Blinatumomab (Blincyto) in accordance with the product information

Blincyto is indicated as monotherapy for the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy

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

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

Paediatric patients aged 1 year or older with high-risk first relapse of a Philadelphia chromosome negative, CD19 positive B-precursor ALL as part of consolidation therapy

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

Indication of a considerable additional benefit

Justification:

For the benefit assessment, the pharmaceutical company submitted data from the pivotal 20120215 marketing authorisation study.

The 20120215 study is an ongoing, international, multicentre, randomised, controlled, open-label phase III study to investigate the efficacy, safety and tolerability of blinatumomab as consolidation therapy versus high-risk consolidation chemotherapy (HC) in paediatric patients with high-risk first relapse of Ph-, CD19+ B-precursor ALL. The study was conducted in 47 study sites across 13 countries.

Patients under 18 years of age in the first relapse after induction therapy and two cycles of HC were enrolled. The total of 108 patients enrolled were stratified according to age and bone marrow/ MRD status and randomised in a 1:1 ratio to the two study arms. They received either one cycle of blinatumomab (one treatment cycle over 4 weeks as a continuous infusion; N = 54) or HC3 (administration of the chemotherapy regimen[2] over one week as an infusion and three weeks treatment-free period; N = 54) as further consolidation therapy. Patients will be observed as part of a safety follow-up after the last dose with the study medication within seven days prior to allo-HSCT. In addition, they undergo a short-term efficacy follow-up of 12 months and a long-term follow-up of up to 36 months after allo-HSCT.

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.
[2] Dexamethasone: 10 mg/m²/day IV from day 1 until day 6; methotrexate: 1 g/m² IV over 36 hours, starting on day 1; vincristine: 1.5 mg/m²/day IV on day 1 and day 6; ifosfamide: 800 mg/m² IV every 12 hours on day 2 and day 4 (5 doses in total); daunorubicin: 30 mg/m² IV on day 5; PEG or Erwinia asparaginase: 1,000 U/m² IV or IM on day 6

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The primary endpoint of the study was progression-free survival (EFS). Among others, overall survival, MRD remission rate, cumulative relapse incidence and 100-day mortality after allo-HSCT were assessed as secondary endpoints.

Patient enrolment was stopped early in August 2019 following the recommendation of the Data Management Committee (DMC) after the results of the first interim analysis in July 2019 showed superiority of blinatumomab with respect to the primary endpoint of EFS. Long-term follow-up will continue until the last enrolled patient has been followed up for 36 months after allo-HSCT or has died, whichever comes first. For overall survival, in addition to the primary data cut-off from 17 July 2019, results are available from the second data cut-off from 14 September 2020. This second data cut-off for the endpoint of overall survival was requested by the EMA as part of the marketing authorisation process.

Mortality

Overall survival is the secondary endpoint of the 20120215 study and is defined as the time from randomisation to death from any cause.

For overall survival, data are available for two data cut-offs (17 July 2019 and 14 September 2020). The second data cut-off was requested by the EMA as part of the marketing authorisation process.

For the endpoint of overall survival, the corresponding results of both data cut-offs show a statistically significant difference between the treatment arms in favour of blinatumomab. The results of the second data cut-off confirm the improvement in overall survival already present in the first data cut-off and also allow a more precise estimation of the results compared to the first data cut-off. The medians of the survival time was not reached in either study arm.

The benefit assessment criticised the fact that a survey of survival status beyond the consolidation phase was only planned for patients who received allo-HSCT. In the written statement procedure, the pharmaceutical company specified that the traceability of all patients in the ITT population, including patients without allo-HSCT, was guaranteed for the entire study period, which means that the operationalisation of the endpoint of overall survival with regard to the follow-up is considered valid.

The result shows a statistically significant difference in overall survival in favour of blinatumomab compared to HC3 to an extent that is assessed as a very significant improvement.

Morbidity

Event-free survival

Patients in the present therapeutic application are treated with a curative therapeutic approach. The failure of a curative therapeutic approach is fundamentally patient-relevant. The significance of the endpoint depends on the extent to which the selected individual components are suitable for adequately reflecting the failure of potential cure by the present curative therapy approach.

Event-free survival (EFS) is the primary endpoint of the 20120215 study and is defined as the time from randomisation to any cause of therapy failure, defined as:

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- a relapse or presence of an M2 type bone marrow status (≥ 5% to < 25% blasts in the bone marrow) after achieving a CR or
- absence of CR at the end of treatment or
- secondary tumour or
- death from any cause

depending on which occurred first.

For the EFS endpoint, the results are available for the data cut-off from 17 July 2019.

Among the events that occurred first in each case, relapse events occurred most frequently (24% with blinatumomab and 54% with HC3), followed by a few death events in each of the two treatment arms.

With regard to the individual components "no CR after treatment with test substance" and "secondary malignancy", no events occurred in both study arms or no events that occurred first in relation to the other events.

The pharmaceutical company states in the written statement procedure that the traceability of all patients in the ITT population, including patients without allo-HSCT, was ensured for the entire study period for the EFS endpoint analogous to overall survival.

With regard to the individual components "no CR after treatment with test substance" and "relapses", it was clarified by the pharmaceutical company in the written statement procedure that standardised criteria were used in each case to assess a relapse and a CR with regard to the criticism in the benefit assessment, with regard to the uncertainty as to whether standardised criteria were taken into account in the assessment in each case and with regard to the lack of clarity as to who carried out the assessment of a relapse and a CR. Since this assessment was carried out in the present case within the framework of an open-label study by a local principal investigator in an unblinded manner, uncertainty remains in the view of the G-BA as to the extent to which knowledge about the therapy in the study may have influenced the assessment.

Overall, on the basis of the available operationalisation and results of the EFS endpoint, sufficiently plausible conclusions on patient-relevant therapeutic effects can be derived, even taking into account the uncertainty described.

The result for the EFS endpoint shows a statistically significant benefit of blinatumomab compared to HC3.

MRD remission

MRD remission rate within a treatment cycle was determined by PCR analysis or by flow cytometry by the reduction of leukaemia cells to below < 10^{-4} (less than one leukaemia cell in 10,000 normal cells) at the end of treatment.

Achieving MRD negativity is considered an important prognostic factor in the treatment of ALL. However, studies in this regard specifically for the patient population with relapsed or refractory B-precursor ALL are not available. A validation of MRD negativity as a surrogate parameter for overall survival is not available. Therefore, the endpoint of MRD negativity is classified as endpoint of unclear relevance in the assessment and presented additionally.

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Quality of life

No health-related quality of life data was collected in the 20120215 study.

Side effects

Adverse events (AEs) were presented from the start of treatment until the end of treatment plus 30 days or until the last observation in the study, whichever occurred first. Since chemotherapy was administered over six days and blinatumomab over 28 days, the median observation was 1.93 months in the blinatumomab arm and 1.18 months in the HC3 arm.

Adverse events (AEs)

Overall, adverse events occurred in all patients in the blinatumomab arm and in 96.1% of patients in the HC3 arm. The results for the endpoint "Adverse events" (AEs) are presented additionally.

Serious adverse events (SAE)

For the serious adverse events, a statistically significant difference was detected in favour of blinatumomab.

In detail, for SAE there is an increased risk for SOC blood and lymphatic system disorders and PT febrile neutropenia with HC3 compared to blinatumomab.

Severe AE (CTCAE grade ≥ 3)

There was a statistically significant advantage of blinatumomab over HC3 with regard to severe adverse events with CTCAE grade ≥ 3.

In detail, the severe AE "blood and lymphatic system disorders" and "gastrointestinal disorders" occurred statistically significantly less frequently during treatment with blinatumomab compared to HC3; the severe AE "general disorders and administration site conditions" occurred statistically significantly more frequently during treatment with blinatumomab.

Discontinuation due to AEs

For the endpoint "discontinuation due to AEs", only descriptive evaluations are available. In two patients, the therapy with blinatumomab was discontinued due to AEs. This was triggered by a nervous system disorder in one patient and the occurrence of seizures in another.

AEs of special interest

Capillary leak syndrome, cytokine release syndrome, decreased immunoglobulin levels, elevated liver levels, embolic and thrombotic events, infections, infusion reactions without consideration of infusion duration, medication errors, neurologic events, neutropenia and febrile neutropenia, immunogenicity, tumour lysis syndrome, leukoencephalopathy, pancreatitis, bone marrow toxicity (cytopenia), hepatotoxicity, nephrotoxicity and QT prolongation were evaluated as AEs of special interest in the 20210215 study.

In summary, AEs of special interest showed an increased risk of infusion reactions and neurologic events during treatment with blinatumomab, while the HC3 group had an increased risk of neutropenia as well as elevated liver levels.

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In the overall assessment of the endpoints of side effects, there is a statistically significant advantage of blinatumomab with regard to the severe AEs (CTCAE grade ≥ 3) and with regard to the SAEs". In the category of side effects, a significant advantage of blinatumomab over HC3 was found in the overall assessment.

Overall assessment / conclusion

For the present benefit assessment of blinatumomab for the treatment of paediatric patients aged 1 year or older with high-risk first relapse of Philadelphia chromosome negative, CD19 positive B-precursor ALL as part of consolidation therapy, results are available from the randomised, controlled, open-label 20120215 study on the endpoint categories of mortality, morbidity and side effects compared with high-risk consolidation chemotherapy (HC3).

For the endpoint of overall survival, there is a statistically significant difference in favour of blinatumomab compared to HC3 to an extent that is assessed as a very significant improvement.

The result for the EFS endpoint shows a statistically significant benefit of blinatumomab compared to HC3.

No data were collected on the health-related quality of life.

In the overall assessment of the endpoints of side effects, there is a statistically significant advantage of blinatumomab with regard to the severe AEs (CTCAE grade ≥ 3) and with regard to the SAEs". In the category of side effects, a significant advantage of blinatumomab over HC3 was found in the overall assessment.

In the overall assessment, the G-BA comes to the conclusion that a considerable additional benefit of blinatumomab over HC3 is established for paediatric patients aged 1 year or older with high-risk first relapse of Philadelphia chromosome negative, CD19 positive B-precursor ALL as part of consolidation therapy especially due to the extent of the prolongation of survival and in view of the available results on event-free survival and side effects, which support the overall additional benefit.

Significance of the evidence

The results of an RCT are available for the present assessment.

At the endpoint level, the reliability of data for the overall survival endpoint, in particular, must be taken into account for the overall assessment. The risk of bias for overall survival is assessed as low.

With regard to the EFS endpoint, a high risk of bias is assumed due to the unblinded assessment of CR and relapse in the context of the present open-label study by the local principal investigator.

In the case of adverse events, uncertainties arise from the relatively short duration of observation.

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Overall, the reliability of data for the additional benefit determined is classified in the category “indication” despite the mentioned uncertainties.

2.1.3 Summary of the assessment

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

Blinatumomab was approved as an orphan drug.

The present therapeutic indication assessed is as follows: Treatment of f paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy

The pharmaceutical company presents the results of the ongoing randomised, controlled, open-label phase III 20120215 study for the endpoint categories of mortality, morbidity and side effects, in which blinatumomab was compared to high-risk consolidation chemotherapy (HC3) in the therapeutic indication.

For the endpoint of overall survival, there is a statistically significant difference in favour of blinatumomab compared to HC3 to an extent that is assessed as a very significant improvement.

The result for the EFS endpoint shows a statistically significant benefit of blinatumomab compared to HC3.

No data were collected on the health-related quality of life.

In the overall assessment of the endpoints of side effects, there is a statistically significant advantage of blinatumomab with regard to the severe AEs (CTCAE grade ≥ 3) and with regard to the SAEs". In the category of side effects, a significant advantage of blinatumomab over HC3 was found in the overall assessment.

In the overall assessment, the G-BA comes to the conclusion that a considerable additional benefit of blinatumomab over HC3 is established for paediatric patients aged 1 year or older with high-risk first relapse of Philadelphia chromosome negative, CD19 positive B-precursor ALL as part of consolidation therapy especially due to the extent of the prolongation of survival and in view of the available results on event-free survival and side effects, which support the overall additional benefit.

The reliability of data of the additional benefit identified is classified in the "indication" category.

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 regarding the number of patients. The information there is mathematically and methodologically comprehensible. The number of patients in the SHI target population stated

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by the pharmaceutical company is therefore plausible in the order of magnitude on the basis of the sources cited by it and used in the assessment.

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 Blincyto (active ingredient: blinatumomab) at the following publicly accessible link (last access: 29 November 2021):

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

Treatment with blinatumomab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with acute lymphoblastic leukaemia, or specialists in paediatrics and adolescent medicine specialising in paediatric haematology and oncology.

In accordance with the requirements of the EMA regarding additional risk minimisation measures, the pharmaceutical company must provide training material for physicians, pharmacists, healthcare professionals and patients/ healthcare professionals, as well as a patient card.

In particular, the training material contains instructions on the administration of BLINCYTO and on neurological events.

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).

Paediatric patients with high-risk first relapse of B-precursor ALL may receive 1 cycle of BLINCYTO therapy after induction and 2 blocks of consolidation chemotherapy. A single treatment cycle comprises one continuous infusion over 28 days. Patients with a body weight of 45 kg or more receive 28 µg/day, patients with a lower body weight receive 15 µg/m^2/day (maximum 28 µg/day).

For dosages depending on body weight (bw) or body surface area (BSA), the average body measurements were applied. The average body weight of 17-year-olds is 67 kg. The average height of one-year-old children is 0.83 m and the average body weight is 11.6 kg. [3] This results in a body surface area of 0.50 m² (calculated according to Du Bois 1916).

[3] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

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A single blinatumomab preparation can be infused for up to 96 hours. For the calculation of treatment costs, the infusion duration associated with the lowest blinatumomab consumption was used in each case.

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				
Blinatumomab	on day 1 - 28 of a 28 day cycle	1	28	28

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					
Blinatumomab	7.5 µg - 28 µg	15 µg/m² = 7.5 µg - 28 µg	1 x 38.5 µg every 72 hours - 1 x 38.5 µg every 24 hours	28	10 x 38.5 µg - 28 x 38.5 µg

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.

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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					
Blinatumomab	1 PCI	€ 637.48	€ 1.77	€ 147.34	€ 488.37
Abbreviations: PCI = Powder for concentrate for solution for infusion					

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.

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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

On 19 July 2021 the pharmaceutical company submitted a dossier for the benefit assessment of blinatumomab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

The benefit assessment of the G-BA was published on 1 November 2021 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 22 November 2021.

The oral hearing was held on 6 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 subcommittee session on 11 January 2022, and the draft 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	26 October 2021	Information of the benefit assessment of the G-BA
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
Working group Section 35a	15 December 2021 5 January 2022	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure

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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

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