Gemeinsamer Bundesausschuss

Justification

to 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 relapsed, Ph-, CD19+, ≥1 month and <1 year)

of 21 August 2025

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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) assess the benefit of all reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of rare diseases (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 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 € 30 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, paragraphs 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 their 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 approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at their 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 turnover threshold according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit

assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the G-BA must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient 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 23 January 2025, 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 Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

Blinatumomab for the treatment of paediatric patients aged ≥ 1 month to < 1 year with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-cell precursor ALL as part of the consolidation therapy is approved 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 approval studies by the G-BA.

On 18 February 2025, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company have 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

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

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The G-BA carried out the benefit assessment and commissioned the IQWiG to assess 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 02 June 2025 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 have adopted their 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 G25-08) 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 have evaluated the studies relevant for the marketing authorisation with regard to their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7, sentence 1, 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 month or older with high-risk first relapsed Philadelphia chromosome-negative CD19 positive B-cell precursor ALL as part of the consolidation therapy.

Therapeutic indication of the resolution (resolution of 21 August 2025):

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

2.1.2 Extent of the additional benefit and significance of the evidence

Paediatric patients aged ≥ 1 month to < 1 year with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy

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

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Justification:

Data basis

No clinical data are available for the benefit assessment of blinatumomab in paediatric patients aged ≥ 1 month to < 1 year (infants) with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-cell precursor ALL as part of the consolidation therapy.

Based on the marketing authorisation, the pharmaceutical company refers in the dossier to the patient population ≥ 1 year to < 18 years in the same therapeutic indication, which was assessed in the benefit assessment procedure for blinatumomab by resolution of 20 January 2022. The subject of this benefit assessment procedure was the 20120215 study, which investigated the efficacy and safety of blinatumomab as consolidation therapy versus high-risk consolidation therapy in paediatric patients with high-risk first relapsed Ph- CD19+ B-ALL. Participation in the study was possible from the age of 28 days; however, no infants were enrolled. Using the data from the interim data cut-off from 17 July 2019 and 14 September 2020 in the benefit assessment procedure, a major additional benefit of blinatumomab was identified for patients aged ≥ 1 year to < 18 years in the present therapeutic indication, based on the data for overall survival, event-free survival and side effects[2].

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

[2] Blinatumomab for paediatric patients aged ≥ 1 year to < 18 years with high-risk first relapsed B-cell ALL – Resolution of 20 January 2022

The marketing authorisation of blinatumomab in infants with high-risk first relapsed Ph-, CD19+ B-cell precursor ALL as part of the consolidation therapy is based on population pharmacokinetic (pop PK) and mechanistic physiology-based pharmacokinetic (M-PBPK) modelling conducted by the EMA with data from adult and paediatric patients older than 1 year with (B)-ALL and non-Hodgkin lymphoma (NHL). Patients at different stages of the disease (high-risk first relapsed, 1st relapse; ≥ 2 relapses or refractory) of B-ALL are taken into account[3]. The extrapolation carried out by the EMA is therefore primarily based on exposure modelling and not on clinical data in the present therapeutic indication.

Assessment

The EMA's findings on the medical rationale for transferring data from older patient groups or patients with other disease stages and other diseases to patients aged < 1 year are a prerequisite for the transfer of evidence.

Based on the statements made by clinical experts at the oral hearing, it can be assumed that there is sufficient comparability between the high-risk group of infants and the high-risk group of paediatric patients aged ≥1 year to <18 years. In this regard, the experts explained that a high-risk relapse is defined as a relapse within the first 18 months of diagnosis, and therefore all relapses in infancy (up to a maximum of 12 months) are by definition high-risk relapses. As a result, a comparable treatment setting between infants and older paediatric patients can be assumed in the present therapeutic indication.

ALL is the most common cancer in childhood, with children between the ages of 2 and 5 years being the most frequently affected[4]. In the case of high-risk relapses in infancy, there is a very small patient population in terms of an orphan marketing authorisation. Relevant clinical data on this patient group is not expected even in the future due to the small number of patients who can be recruited.

The standards to be applied for the acceptance of evidence from other patient populations will take into account the specificities and limitations in the conduct of paediatric clinical studies.

A patient population that is directly related to the present patient population in terms of age was enrolled in the comparator study 20120215, on which the transfer of the additional benefit was based. Participation in the study was possible from the age of 28 days, but only subjects aged ≥ 1 year to < 18 years could be enrolled.

The corresponding benefit assessment (resolution of 20 January 2022) showed very significant advantages of blinatumomab in paediatric patients aged ≥ 1 year or older with high-risk first relapsed Ph-, CD19+ B-cell precursor ALL. An indication of a major additional benefit was found due to the extent of the prolongation of survival and in view of the results on event-free survival and side effects, which support the additional benefit overall.

In view of the fact that a sufficiently comparable treatment setting exists, and taking into account the EMA's findings on the medical rationale for transferring the data, transferability of the positive effects of blinatumomab from the population of older paediatric patients (≥ 1 year to < 18 years) to the population of infants (≥ 1 month to < 1 year) is assumed. Due to the

[3] European Medicines Agency (EMA). Blincyto (blinatumomab): European public assessment report EMEA/H/C/003731/0000 [online]. 07.12.2015. Amsterdam (NED): EMA. [Accessed: 06.03.2025]. URL: https://www.ema.europa.eu/en/documents/assessment-report/blincyto-epar-public-assessment-report_en.pdf.
[4] S1 guideline Acute lymphoblastic leukaemia – ALL in childhood, last revised: 31.05.2021; https://register.awmf.org/assets/guidelines/025-014l_S1_Akute-lymphoblastische-Leukaemie-ALL-im-Kindesalter_2021-07.pdf

associated uncertainties and limitations of the available evidence, the extent of the additional benefit is non-quantifiable.

Conclusion

In the overall assessment, the G-BA considers a transfer of the results on the additional benefit of blinatumomab from the benefit assessment on paediatric patients aged ≥ 1 year to < 18 years to paediatric patients aged ≥ 1 month to < 1 year (infants) with high-risk first relapsed Ph- CD19+ B-ALL as appropriate in this case. Due to the associated uncertainties and limitations of the available evidence, the extent of the additional benefit is non-quantifiable. There is an additional benefit in accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SBG V, but it is non-quantifiable since the scientific data does not allow a quantification.

Significance of the evidence

A hint is derived overall due to the uncertainties associated with the transfer of the results on the additional benefit to the present patient population.

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: Blincyto is indicated as monotherapy for the treatment of paediatric patients aged ≥ 1 month to < 1 year with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy.

No data are available from clinical studies for assessment of the additional benefit for infants with high-risk first relapsed Philadelphia chromosome negative CD19-positive B-cell precursor ALL as part of the consolidation therapy. The EMA's findings on the medical rationale for transferring data from older patient groups or patients with other disease stages and other diseases to patients aged < 1 year based on pharmacokinetic modelling are a prerequisite for the transfer of evidence. The pharmaceutical company based the proof of additional benefit on an evidence transfer of the results of the 20120215 clinical study from older paediatric patients aged ≥ 1 year to < 18 years to infants aged ≥ 1 month to < 1 year.

In view of the fact that relevant clinical data on this patient group is not expected even in the future and a sufficiently comparable treatment setting exists, and taking into account the EMA's findings on the medical rationale for transferring the data, transferability of the positive effects of blinatumomab from the population of older paediatric patients (≥ 1 year to < 18 years) to the population of infants (≥ 1 month to < 1 year) is assumed.

In the overall assessment, the G-BA considers a transfer of the results on the additional benefit of blinatumomab from the benefit assessment on paediatric patients aged ≥ 1 year to < 18 years to paediatric patients aged ≥ 1 month to < 1 year (infants) with high-risk first relapsed Ph- CD19+ B-ALL as appropriate in this case. Due to the associated uncertainties and limitations of the available evidence, the extent of the additional benefit is non-quantifiable. There is an additional benefit in accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SBG V, but it is non-quantifiable since the scientific data does not allow a quantification.

Due to the limitations of the available evidence, the reliability of data is rated as a hint.

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

The pharmaceutical company estimates the number of patients in the SHI target population using two approaches, firstly on the basis of a registry analysis and secondly on the basis of literature data.

The pharmaceutical company's procedure for estimating the number of patients in the SHI target population is mathematically and methodically plausible for both approaches. Despite some aspects addressed in the benefit assessment possibly leading to certain uncertainties in the estimate, the number of patients in the SHI target population stated by the pharmaceutical company is in a plausible range overall.

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: 23 May 2025):

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 paediatrics and adolescent medicine with a focus on paediatric haematology and oncology who are experienced in the treatment of patients with acute lymphoblastic leukaemia.

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 August 2025).

According to the product information, the approved dosage (body surface area (BSA)-based dose) for subjects with a body weight < 45 kg is 15 µg/m^2/day and must not exceed 28 µg/day. Patients with high-risk first relapsed B-cell precursor ALL can receive 1 cycle of blinatumomab after induction therapy and 2 blocks of consolidation chemotherapy. A single treatment cycle comprises a 28-day (4-week) continuous infusion.

For paediatric patients < 45 kg, the consumption is based on body surface area. The calculations are based on the DuBois formula and the average body measurements for infants less than 1 year old according to the 2017 Microcensus data[5]. This results in a body surface area of 0.36 m^2.

[5] Statistisches Bundesamt (Federal Statistical Office). Body measurements by age group and sex 2021 [online]. 2023 [accessed: 02.09.2024]. URL: https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt /Gesundheit/ Gesundheits-zustand-Relevantes-Verhalten/Tabellen/liste-koerpermasse.html.

The 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	15 µg/m^2/day from day 1 to 28	5.4 µg/day from day 1 – 28	7 * 38.5 µg	28	7 * 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 consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Costs of the medicinal products:

Paediatric patients aged ≥ 1 month to < 1 year with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy

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	€ 2,615.04	€ 1.77	€ 148.75	€ 2,464.52
Abbreviations: PCI = powder for a concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 1 August 2025

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

No additionally required SHI services are taken into account for the cost representation.

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered

due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed

therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA have decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

Paediatric patients aged ≥ 1 month to < 1 year with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

3. Bureaucratic costs calculation

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

4. Process sequence

On 18 February 2025 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 2 June 2025 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 statements was 23 June 2025.

The oral hearing was held on 7 July 2025.

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

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 12 August 2025, and the draft resolution was approved.

At their session on 21 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	**Date**	**Subject of consultation**
Subcommittee on Medicinal Products	27 May 2025	Information of the benefit assessment of the G-BA
Working group Section 35a	2 July 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	7 July 2025	Conduct of the oral hearing
Working group Section 35a	16 July 2025 6 August 2025	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
Subcommittee on Medicinal Products	12 August 2025	Concluding discussion of the draft resolution
Plenum	21 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 21 August 2025

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

Prof. Hecken