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
Nirsevimab (first dossier requirement: prevention of RSV diseases, children during their 1st RSV season who are not addressed in the therapeutic information on RSV antibodies)

of 21 August 2025

Contents

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. 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 have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.
7. Number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

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 is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The medicinal product Beyfortus with the active ingredient nirsevimab was approved for the indication Prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants during their first RSV season on 31 October 2022. Beyfortus was listed for the first time on 1 September 2023 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices.

The active ingredient nirsevimab is a new active ingredient within the meaning of Chapter 5 Section 2, paragraph 1, sentences 1 and 2 of the VerfO, which is subject to the scope of application of Section 35a paragraph 1 SGB V.

On 15 August 2024, the G-BA adopted a benefit assessment resolution on nirsevimab in the indication "Prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants with indication of secondary prevention during their first RSV season" according to Section 35a SGB V.

On 14 September 2024, the "Ordinance on the entitlement to measures for specific prevention against respiratory syncytial viruses" took effect. Insured persons who have not yet reached the age of one are thus entitled to a one-off supply of healthcare containing the monoclonal antibody nirsevimab for prevention against Respiratory Syncytial Virus (RSV).

In light of the entry into force of the regulations in the "Ordinance on the entitlement to measures for specific prevention against respiratory syncytial viruses", nirsevimab is now reimbursable without limitations for neonates and infants during their first RSV season. The reimbursable patient population of nirsevimab is therefore now broader than at the time of adoption of the resolution on 15 August 2024.

The pharmaceutical company was therefore requested by the G-BA to submit a dossier on the benefit assessment of nirsevimab for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in newborns and infants during their first RSV season, who are not addressed in the therapeutic information on RSV antibodies, by 18 February 2025 at the latest.

On 17 February 2025, the pharmaceutical company submitted a dossier on the active ingredient nirsevimab in the therapeutic indication "Prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants during their first RSV season, who are not addressed in the therapeutic information on RSV antibodies" in due time.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 June 2025 on the G-BA website (www.g-ba.de), 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 nirsevimab 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. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of nirsevimab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have 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 Nirsevimab (Beyfortus) in accordance with the product information

Beyfortus is indicated for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in:

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

- Neonates and infants during their first RSV season.
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Beyfortus should be used in accordance with official recommendations.

Therapeutic indication of the resolution (resolution of 21.08.2025):

Beyfortus is indicated for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in:

- Neonates and infants during their first RSV season who are not addressed in the therapeutic information on RSV antibodies.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies

Appropriate comparator therapy for nirsevimab:

- Monitoring wait-and-see approach

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine

the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1. In addition to nirsevimab, the active ingredient palivizumab is approved in the therapeutic indication for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants during their first RSV season. However, only the active ingredient nirsevimab is approved for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in children during their first RSV season, who are not addressed in the therapeutic information on RSV antibodies.

On 2. Non-medicinal treatment alone is not an option for the prevention of RSV-related lower respiratory tract infections.

On 3. For the prevention of RSV-related lower respiratory tract infections, the following resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Nirsevimab (secondary prevention of RSV infections, children during their first RSV season) from 15 August 2024
- Nirsevimab (secondary prevention of RSV infections, children during their second RSV season, ≤ 24 months of age) from 20 February 2025

Furthermore, the therapeutic information on respiratory syncytial virus antibodies (Pharmaceuticals Directive Annex IV - Therapeutic information in accordance with Section 92, paragraph 2, sentence 7 SGB V) dated 2 November 2023 must be taken into account.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the

comparator therapy in the present indication according to Section 35a, paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy"). However, no corresponding feedback was received.

The subject of the present assessment is exclusively the sub-population "Children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies". The following patient groups are therefore not included in the present benefit assessment:

- Children who required concomitant therapeutic measures due to bronchopulmonary dysplasia within the last 6 months prior to the RSV season. These measures included supplemental oxygen, steroids, bronchodilators or diuretics
- Children with haemodynamically relevant congenital heart defects (e.g. relevant left-to-right and right-to-left shunt vitia and patients with pulmonary hypertension or pulmonary venous congestion)
- Children with trisomy 21
- Children aged ≤ 6 months at the start of the RSV season who were born as preterm infants up to the completed 35th week of pregnancy (34 [+ 6 days]).

These were already the subject of the benefit assessment on nirsevimab with a date of resolution of 15 August 2024.

Systematic reviews and a Cochrane review were identified besides the German S2k guideline "On the prevention of severe Respiratory Syncytial Virus (RSV) diseases in at-risk children". Although the guideline does not fulfil the methodological requirements, it is used due to limited higher-quality evidence and its relevance to the healthcare context. Furthermore, the guideline explicitly refers to at-risk children and not to healthy neonates and infants without underlying diseases.

Besides nirsevimab, no other medicinal product is approved for children during their first RSV season, for the prevention of RSV lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies.

Therefore, in the absence of other approved medicinal therapies and due to the lack of other therapy recommendations, the monitoring wait-and-see approach is determined as the appropriate comparator therapy for "Children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies".

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

<u>Children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies</u>

Indication of a considerable additional benefit.

Justification:

For the benefit assessment, the pharmaceutical company submitted results of the HARMONIE and MELODY studies.

The HARMONIE study is an ongoing, open-label, randomised, multicentre study comparing nirsevimab versus no treatment for the prevention of RSV lower respiratory tract disease in children during their first RSV season. Predominantly healthy children ≤ 12 months with a gestational age ≥ 29 weeks who were not eligible for palivizumab therapy were enrolled.

A total of 8,057 children were enrolled in the study and randomised in a 1:1 ratio. Nirsevimab was used according to the product information.

The primary endpoint of the study was the RSV-related hospitalisation. Patient-relevant secondary endpoints include endpoints in the categories of morbidity and side effects. Endpoints on health-related quality of life were not collected.

The MELODY study is a completed, double-blind RCT comparing nirsevimab versus placebo for the prevention of RSV lower respiratory tract infections in children. 3,012 children aged ≤ 12 months with a gestational age ≥ 35 weeks, with no indication for palivizumab were enrolled. The children were randomised in a 2:1 ratio. Randomisation took place in two cohorts at different times. The primary cohort comprises 1,490 children enrolled in the study for the 2019/2020 RSV season of the northern hemisphere and the 2020 RSV season of the southern hemisphere. Nirsevimab was used according to the product information.

The primary endpoint was the occurrence of an RSV-related lower respiratory tract infection. Secondary endpoints included endpoints on morbidity and side effects, but no data on health-related quality of life. The benefit assessment refers to the total population.

<u>On the evaluation time points</u>

For the HARMONIE study, evaluations are available at various evaluation time points (cut-off date of the data cut-off from 28 February 2023, day 151 and day 366) for the endpoint category of morbidity, each of which has limitations. The evaluation on the cut-off date of the data cut-off, which the pharmaceutical company refers to as the end of the RSV season, only covers an observation period of approx. 2 months on average, as the majority of the children were enrolled during the RSV season and were therefore only under observation for a relatively short time until the data cut-off. This evaluation time point is therefore not used for the benefit assessment.

For the MELODY study, results are available at the evaluation time points on day 151 and day 361. In the MELODY study, the evaluations on day 151 primarily assess RSV infections within the RSV season defined by the pharmaceutical company. However, the evaluation on day 361 shows that relevant infections also occur outside this period, so that a more comprehensive picture of the incidence of infection can be obtained by taking this evaluation time point into account.

For the benefit assessment, the evaluation time points on day 151 and on day 361 or 366 for the morbidity endpoints of the HARMONIE and MELODY studies are therefore summarised in a meta-analysis in each case, and for the side effects the data on day 361 or 366.

<u>On the populations under consideration</u>

Children with bronchopulmonary dysplasia or haemodynamically relevant heart defects were excluded from the MELODY study. This was also indirectly the case in the HARMONIE study, as only children without an indication for palivizumab were enrolled in the study. Nevertheless, both studies occasionally include children with an indication for secondary

prevention (e.g. children with trisomy 21 or preterm infants < 36th week of pregnancy). However, the blanket exclusion of all preterm infants below the 36th week of pregnancy by the pharmaceutical company is inappropriate as children born in the 35th week of pregnancy or earlier and were older than 6 months at the start of the RSV season were included in the therapeutic indication to be assessed.

When the HARMONIE and MELODY studies are considered together, the maximum percentage of children who do not correspond to the therapeutic indication to be assessed is 7.8%. Therefore, the respective total populations of both studies are considered for the present assessment.

As part of the written statement procedure, the pharmaceutical company submitted sensitivity analyses on the sub-population, children without trisomy 21 and a gestational age of 36 weeks or more or a gestational age of 35 weeks or less at the age of more than six months. However, these analyses are not taken into account for the present assessment, as the pharmaceutical company only submitted the analyses on the morbidity endpoints. It is considered inappropriate to use the sub-population from the sensitivity analysis for assessment of the morbidity endpoints, while considering the total population for the side effects.

Extent and probability of the additional benefit

Mortality

Four deaths occurred in the intervention arm of the MELODY study alone. There was no statistically significant difference between the treatment groups in this case.

Morbidity

RSV-related lower respiratory tract infection

The composite endpoint RSV-related lower respiratory tract infection was only assessed in the MELODY study. The endpoint comprises the components of RSV-related hospitalisation and RSV-related outpatient care.

Defined criteria had to be met for both components. In addition to a medical examination to determine whether the lower respiratory tract is affected and respiratory sounds are present, a positive RT-PCR test result for RSV must be available. In addition, at least one clinical criterion (increased respiratory rate, hypoxaemia, clinical sign of severe respiratory disease or dehydration with necessary intravenous fluid intake due to dyspnoea) had to be fulfilled.

Hospitalisation was defined as primary or nosocomial. Primary hospitalisation occurred when a child was admitted to hospital due to a respiratory infection and tested positive for RSV by RT-PCR within 2 days of admission. A nosocomial hospitalisation occurred when the respiratory condition of an already hospitalised child deteriorated (e.g. need for or increased oxygen administration or ventilation) and a new RSV infection confirmed by RT-PCR was present. Prerequisite for collection as nosocomial hospitalisation was that the child had to have previously recovered from the first respiratory tract infection or have returned to the initial state.

The sub-component RSV-related outpatient care was defined as medical care due to RSV infection in an outpatient clinic, acute care or accident and emergency department.

For the composite endpoint of RSV-related lower respiratory tract infection, the evaluation on day 361 and on day 151 each showed a statistically significant difference to the advantage of nirsevimab compared to the monitoring wait-and-see approach.

However, there was an effect modification in terms of age: For children ≤ 6 months, there was a statistically significant advantage of nirsevimab over the monitoring wait-and-see approach, but not for children > 6 months. However, a complete analysis is not possible, as no subgroup analyses are available for day 361 and the endpoint was not assessed in the HARMONIE study.

In contrast, suitable data from both studies are available for the endpoint of severe RSV-related lower respiratory tract infection (on day 151). A homogeneous data basis was observed here. Since this endpoint is included in the endpoint of RSV-related lower respiratory tract infection and is also based on the more reliable meta-analysis, no separate assessment by age is performed.

Severe RSV-related lower respiratory tract infection

The endpoint of severe RSV-related lower respiratory tract infection is operationalised as hospitalisation due to RSV-related lower respiratory tract infection.

In the HARMONIE study, hospitalisation due to RSV-related respiratory tract infection was the primary endpoint. Such an infection was considered confirmed if RSV was detected (predominantly by RT-PCR) in combination with at least one clinical criterion (respiratory sounds, increased respiratory rate or hypoxaemia).

In the MELODY study, severe RSV-related lower respiratory tract infections are included in the composite endpoint (RSV-related lower respiratory tract infection) and account for about one third of the events collected there.

A separate consideration of these events is appropriate in the present assessment since the meta-analytic summary of the HARMONIE and MELODY studies offers a higher reliability of data and this endpoint exclusively depicts severe RSV-related infections and thus, a higher severity grade.

For the endpoint of severe RSV-related lower respiratory tract infection, the meta-analysis showed a statistically significant difference to the advantage of nirsevimab compared to the monitoring wait-and-see approach in the evaluation on day 361 or 366 as well as on day 151.

Quality of life

Endpoints in the health-related quality of life category were not assessed in the HARMONIE and MELODY studies.

Side effects

SAEs and severe AEs

For the endpoints of SAEs and severe AEs, there was no statistically significant difference between the treatment groups respectively.

Therapy discontinuation due to AEs

Only in the HARMONIE study did one child in each of the two treatment arms discontinue the study. For the endpoint of discontinuation due to AEs, there was no statistically significant difference between the treatment groups.

Overall assessment

The results of the HARMONIE and MELODY studies were presented by the pharmaceutical company for the assessment of the additional benefit of nirsevimab for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants during

their first RSV season, who are not addressed in the therapeutic information on RSV antibodies. Data on the endpoints in the categories of mortality, morbidity and side effects are available.

In the endpoint category of mortality, there was no statistically significant difference between the treatment groups.

In the endpoint category of morbidity, the MELODY study showed a statistically significant difference to the advantage of nirsevimab compared to the monitoring wait-and-see approach for the composite endpoint of RSV-related lower respiratory tract infection on day 361 and on day 151 respectively. For the endpoint of severe RSV-related lower respiratory tract infection, the meta-analysis of the HARMONIE and MELODY studies showed a statistically significant difference to the advantage of nirsevimab compared to the monitoring wait-and-see approach in the evaluation on day 361 or 366 as well as on day 151.

Endpoints in the health-related quality of life category were not assessed in the HARMONIE and MELODY studies.

There were no statistically significant differences between the treatment groups in the endpoint category of side effects.

In the overall assessment of the results, based on the positive effects in the endpoints on morbidity, i.e. RSV-related lower respiratory tract infection and severe RSV-related lower respiratory tract infection, an additional benefit of nirsevimab can be derived for children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease, who are not addressed in the therapeutic information on RSV antibodies. The extent of the additional benefit derived is classified as considerable.

Reliability of data (probability of additional benefit)

The risk of bias of the results of the patient-relevant endpoints of the HARMONIE study is assessed as low, with the exception of the endpoint of discontinuation due to AEs. In contrast, a high risk of bias can be assumed for the aforementioned endpoint. The reason for this is the lack of blinding in a subjective endpoint survey.

In addition, there are uncertainties in both HARMONIE and MELODY studies with regard to the percentage of enrolled children who do not correspond to the target population of the therapeutic indication to be assessed here. These uncertainties lead to a limitation of the reliability of data of the study results.

However, the meta-analytic summary of the results of the HARMONIE and MELODY studies, taking into account the uncertainties presented, showed an indication of an additional benefit in the overall assessment with regard to the significance of the evidence.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a therapeutic indication to be assessed for the first time for the active ingredient nirsevimab. The therapeutic indication assessed here is as follows: "Beyfortus is indicated for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants during their first RSV season, who are not addressed in the therapeutic information on RSV antibodies."

The monitoring wait-and-see approach was determined as the appropriate comparator therapy. For the assessment of the additional benefit of nirsevimab, the pharmaceutical company presented results from the two randomised controlled trials HARMONIE and

MELODY. Results are available for the endpoint categories of mortality, morbidity and side effects compared to the monitoring wait-and-see approach.

In the endpoint category of mortality, there was no statistically significant difference between the treatment groups.

In the endpoint category of morbidity, the MELODY study showed a statistically significant advantage of nirsevimab compared to the monitoring wait-and-see approach for the composite endpoint of RSV-related lower respiratory tract infection on day 361 and on day 151 respectively. For the endpoint of severe RSV-related lower respiratory tract infection, the meta-analysis of the HARMONIE and MELODY studies showed a statistically significant advantage of nirsevimab compared to the monitoring wait-and-see approach in the evaluation on day 361 or 366 as well as on day 151.

Endpoints in the health-related quality of life category were not assessed in the HARMONIE and MELODY studies.

There were no statistically significant differences between the treatment groups in the endpoint category of side effects.

Uncertainties exist in particular for the endpoint of discontinuation due to AEs in the HARMONIE study, due to the lack of blinding in a subjective endpoint survey. In addition, there are uncertainties in the HARMONIE and MELODY studies in terms of the percentage of enrolled children who do not correspond to the target population of the therapeutic indication being assessed here. Despite these limitations, the reliability of data is still classified as an indication overall in a meta-analytic analysis of both studies.

The overall assessment resulted in an indication of a considerable additional benefit of nirsevimab compared to the monitoring wait-and-see approach in children during their first RSV season, for the prevention of RSV lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies.

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 provided by the pharmaceutical company.

The information provided by the pharmaceutical company on the SHI target population is comprehensible in principle, but the lower limit is underestimated and the upper limit is subject to uncertainties. The pharmaceutical company stated a lower number of live births for 2023 than in the previous procedure for nirsevimab from 2024, in which the average number of live births in the years 2018 to 2022 was taken into account, resulting in a lower estimate. Using the previous reference value would result in a larger target population. In addition, the known uncertainties from the previous procedure continue to exist.

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 Beyfortus (active ingredient: nirsevimab) at the following publicly accessible link (last access: 17 June 2025):

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

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, nirsevimab should be used from birth in infants born during the RSV season. Infants born outside the RSV season should receive nirsevimab prior to the RSV season if possible.

According to the product information for nirsevimab, infants with a body weight < 5 kg receive a 50 mg single dose and infants with a body weight of ≥ 5 kg receive a 100 mg single dose.

Children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies

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				
Nirsevimab	Single dose	1.0	1	1.0
Appropriate comparator therapy				
Monitoring wait-and-see approach	Not calculable			

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					
Nirsevimab	Children < 5 kg				
	50 mg	50 mg	1 x 50 mg	1.0	1.0 x 50 mg
	Children > 5 kg				
	100 mg	100 mg	1 x 100 mg	1.0	1.0 x 100 mg
Appropriate comparator therapy					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Monitoring wait-and-see approach	Not calculable				

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. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

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					
Nirsevimab 50 mg	1 SFI	€ 453.83	€ 1.77	€ 24.50	€ 427.56
Nirsevimab 100 mg	1 SFI	€ 453.83	€ 1.77	€ 24.50	€ 427.56
Appropriate comparator therapy					
Monitoring wait-and-see approach	Not calculable				
Abbreviations: SFI = solution for injection;					

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.

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.

2.5 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:

Children during their first RSV season, for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract diseases, who are not addressed in the therapeutic information on RSV antibodies

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.
References:

Product information for nirsevimab (Beyfortus); Beyfortus 50 mg solution for injection in a pre-filled syringe; Beyfortus 100 mg solution for injection in a pre-filled syringe; last revised: April 2025

3. Bureaucratic costs calculation

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

4. Process sequence

At their session on 26 November 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 17 February 2025, the pharmaceutical company submitted a dossier for the benefit assessment of nirsevimab to the G-BA in due time.

By letter dated 18 February 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit 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 nirsevimab.

The dossier assessment by the IQWiG was submitted to the G-BA on 27 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 2 June 2025. 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 proposed 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	26 November 2024	Determination of the appropriate comparator therapy
Working group Section 35a	1 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	15 July 2025 5 August 2025	Consultation on the dossier evaluation by the IQWiG and 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