Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee 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

At their session on 21 August 2025, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. In Annex XII, the following information shall be added after No. 5 to the information on the benefit assessment of Nirsevimab in accordance with the resolution of 20 February 2025:

Nirsevimab

Resolution of: 21 August 2025
Entry into force on: 21 August 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 31 October 2022):

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

- 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 August 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.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

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:

Monitoring wait-and-see approach

Extent and probability of the additional benefit of nirsevimab compared to monitoring wait-and-see approach:

Indication of a considerable additional benefit.

Study results according to endpoints:[1]

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

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant differences for the benefit assessment.
Morbidity	↑↑	Advantages in (severe) RSV-related lower respiratory tract infections
Health-related quality of life	∅	No data available.
Side effects	↔	No relevant differences for the benefit assessment.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference
∅: No data available.
n.a.: not assessable

HARMONIE study: RCT, direct comparison, nirsevimab vs no intervention

MELODY study: RCT, direct comparison, nirsevimab vs placebo

Mortality

Endpoint	Nirsevimab		no treatment or placebo		Nirsevimab vs no treatment or placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Relative risk [95% CI] p value
Overall mortality[a]					
HARMONIE (Day 366)	4016	0 (0)	4018	0 (0)	–
MELODY (Day 361)	1997	4 (0.2)	997	0 (0)	4.50 [0.24; 83.42]; 0.175[b]

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A25-33) unless otherwise indicated.

Morbidity

Endpoint	Nirsevimab		No intervention or placebo		Nirsevimab vs no intervention or placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Relative risk [95% CI] p value
RSV-related lower respiratory tract infection (composite endpoint)					
HARMONIE (Day 366)	Endpoint not assessed				
MELODY (Day 361)	2009	40 (2.0)	1003	67 (6.7)	0.30 [0.20; 0.44]; < 0.001[c]
Hospitalisation[d]	2009	11 (0.5)[e]	1003	22 (2.2)[e]	0.25 [0.12; 0.51]; < 0.001[c]
Primary	2009	11 (0.5)[e]	1003	22 (2.2)[e]	
Nosocomial	2009	0 (0)[e]	1003	0 (0)[e]	
Outpatient care	2009	n.d.	1003	n.d.	
Accident and emergency department	2009	n.d.	1003	n.d.	
Acute care	2009	n.d.	1003	n.d.	
Outpatient clinic	2009	n.d.	1003	n.d.	
RSV-related lower respiratory tract infection (composite endpoint)					
HARMONIE (Day 151)	Endpoint not assessed				
MELODY (Day 151)	2009	24 (1.2)	1003	54 (5.4)	0.22 [0.13; 0.35]; < 0.001[f]
Hospitalisation[d]	2009	9 (0.4)	1003	20 (2.0)	0.22 [0.10; 0.48]; < 0.001[f]
Primary	2009	9 (0.4)[e]	1003	20 (2.0)[e]	
Nosocomial	2009	0 (0)[e]	1003	0 (0)[e]	
Outpatient care	2009	n.d.	1003	n.d.	
Accident and emergency department	2009	n.d.	1003	n.d.	
Acute care	2009	n.d.	1003	n.d.	
Outpatient clinic	2009	n.d.	1003	n.d.	
Severe RSV-related lower respiratory tract infection					
HARMONIE (Day 366)	4038	43 (1.1)[e]	4019	96 (2.4)[e]	0.45 [0.31; 0.64]; < 0.001[c]

MELODY (Day 361)	2009	11 (0.5)[e]	1003	22 (2.2)[e]	0.25 [0.12; 0.51]; < 0.001[c]
Total[g]					0.40 [0.29; 0.55]; < 0.001
Severe RSV-related lower respiratory tract infection					
HARMONIE (Day 151)	4038	12 (0.3)	4019	67 (1.7)	0.18 [0.10; 0.33]; < 0.001[c]
MELODY (Day 151)	2009	9 (0.4)	1003	20 (2.0)	0.22 [0.10; 0.49]; < 0.001[f]
Total[g]					0.19 [0.12; 0.31]; < 0.001

Health-related quality of life

No data available.

Side effects

Endpoint	**Nirsevimab**		**no intervention or placebo**		**Nirsevimab vs no intervention or placebo**
	N	Patients with event n (%)	N	Patients with event n (%)	Relative risk [95% CI] p value
Adverse events *(presented additionally)*					
HARMONIE (Day 366)	4016	3212 (80.0)	4018	3192 (79.4)	-
MELODY (Day 361)	1997	1722 (86.2)	997	843 (84.6)	-
Serious adverse events (SAE)					
HARMONIE[h] (Day 366)	4016	262 (6.5)	4018	222 (5.5)	1.18 [0.99; 1.40]; 0.071[b]
MELODY (Day 361)	1997	149 (7.5)	997	83 (8.3)	0.90 [0.69; 1.16]; 0.450[b]
Total[i]					1.09 [0.94; 1.25]; 0.264
Severe adverse events					
HARMONIE (Day 366)	4016	151 (3.8)	4018	143 (3.6)	1.06 [0.84; 1.32]; 0.681[b]
MELODY[j] (Day 361)	1997	79 (4.0)	997	41 (4.1)	0.96 [0.66; 1.39]; 0.888[b]

Total[i]					1.03 [0.85; 1.25]; 0.745
Study discontinuation due to adverse events					
HARMONIE (Day 366)	4016	1 (< 0.1)	4018	1 (< 0.1)	1.00 [0.06; 15.99]; > 0.999
MELODY (Day 361)	1997	0 (0)	997	0 (0)	–

a. The results on overall mortality are based on the data on fatal AEs.
b. Own calculation, unconditional exact test
c. RR, 95% CI and p value from own calculation, p value unconditional exact test
d. Corresponds to severe RSV-related lower respiratory tract infections
e. IQWiG's own calculation
f. Poisson regression model with logarithm of duration of observation as offset, stratified by hemisphere (northern vs southern hemisphere), age at randomisation (age ≤ 3 months vs age > 3 to ≤ 6 months vs age > 6 months) and cohort (primary cohort vs safety cohort).
g. IQWiG's own calculation from meta-analysis, fixed-effect model, Mantel-Haenszel method
h. The evaluation considers SAEs that occurred in children in the United Kingdom between day 366 and the data cut-off of the 1-year analysis (26.04.2024). This was 1 SAE per treatment arm in each case.
i. Calculated from meta-analysis, fixed-effect model using the inverse variance method
j. Operationalised as CTCAE grade ≥ 3

Abbreviations used:
n.d.: no data available; CI: confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; RR: relative risk; RSV: Respiratory Syncytial Virus; SAE: serious adverse event; AE: adverse event

2. Number of patients or demarcation of patient groups eligible for treatment

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

Approx. 541,000 – 555,000 patients

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

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nirsevimab	€ 427.56
Appropriate comparator therapy:	
Monitoring wait-and-see approach	Not calculable

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2025)

Costs for additionally required SHI services: not applicable

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

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

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.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. 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.

II. **The resolution will enter into force on the day of its publication on the website of the G-BA on 21 August 2025.**

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 21 August 2025

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

Prof. Hecken