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 (secondary prevention of RSV infections; children during their 1st RSV season)

of 15 August 2024

At its session on 15 August 2024, 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. Annex XII shall be amended in alphabetical order to include the active ingredient Nirsevimab as follows:

Benefit assessment procedure comprises several resolutions.
Please note the current version of the Pharmaceuticals Directive/Annex XII.

Courtesy translation – only the German version is legally binding.

Nirsevimab

Resolution of: 15 August 2024
Entry into force on: 15 August 2024
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.

Beyfortus should be used in accordance with official recommendations.

Therapeutic indication of the resolution (resolution of 15 August 2024):

Prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants with an indication for secondary prevention during their first RSV season.

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

a) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is indicated

Appropriate comparator therapy:

Palivizumab

Extent and probability of the additional benefit of nirsevimab compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is not indicated

Appropriate comparator therapy:

Monitoring wait-and-see approach

Extent and probability of the additional benefit of nirsevimab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

[1] Data from the dossier assessment of the IQWiG (A24-27) and from the addendum (A24-75), unless otherwise indicated.

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a) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is indicated

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	↔	No relevant differences for the benefit assessment.
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

MEDLEY study: RCT, nirsevimab vs palivizumab

Mortality

Study Endpoint	Nirsevimab		Palivizumab		Nirsevimab vs palivizumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
MEDLEY (day 361)					
Overall mortality	614	5 (0.8)	304	1 (0.3)	2.48 [0.29; 21.10]; 0.449[a)]

Please note that the assessment procedure comprises several resolution steps. Only the German version of the Pharmaceuticals Directive/Annex XII.

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Morbidity

Study Endpoint	Nirsevimab		Palivizumab		Nirsevimab vs palivizumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI[a)]]; p value[a)]
MEDLEY (day 151)					
RSV-related infection of the lower respiratory tract (composite endpoint)					
Total	616	4 (0.6[a)])	309	3 (1.0[a)])	0.67 [0.15; 2.97]; 0.625
Hospitalisation	616	2 (0.3[a)])	309	2 (0.6[a)])	0.50 [0.07; 3.54]; 0.599
Primary	616	2 (0.3[a)])	309	2 (0.6[a)])	0.50 [0.07; 3.54]; 0.599
Nosocomial	616	0 (0[a)])	309	0 (0[a)])	–
Outpatient care	616	4 (0.6 [a)])	309	1 (0.3[a)])	2.01 [0.23; 17.88]; 0.617
Accident and emergency department	616	1 (0.2[a)])	309	0 (0[a)])	1.51 [0.06; 36.89]; 0.573
Acute care	616	2 (0.3[a)])	309	1 (0.3[a)])	1.00 [0.09; 11.02]; > 0.999
Outpatient clinic	616	1 (0.2[a)])	309	0 (0[a)])	1.51 [0.06; 36.89]; 0.573
MEDLEY (day 361)					
RSV-related infection of the lower respiratory tract (composite endpoint)					
Total	616	12 (1.9)	309	7 (2.3)	0.86 [0.34; 2.16][a)]; 0.791[a)]
Hospitalisation	616	5 (0.8)	309	3 (1.0)	0.84 [0.20; 3.48][a)]; 0.866[a)]
Primary	616	–	309	–	–
Nosocomial	616	–	309	–	–
Outpatient care	616	11 (1.8[a)])	309	4 (1.3[a)])	1.38 [0.44; 4.30][a)]; 0.617[a)]
Accident and emergency department	616	6 (0.1[a)])	309	0 (0.0[a)])	6.53 [0.37; 115.57][a)]; 0.089[a)]
Acute care	616	3 (0.5[a)])	309	1 (0.3[a)])	1.50 [0.16; 14.41][a)]; 0.791[a)]
Outpatient clinic	616	5 (0.8[a)])	309	3 (0.1[a)])	0.84 [0.20; 3.48][a)]; 0.866[a)]

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Health-related quality of life

No endpoints on health-related quality of life were collected.

Side effects

Study Endpoint	Nirsevimab		Palivizumab		Nirsevimab vs palivizumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value;
MEDLEY (day 361)					
Total adverse events (presented additionally)					
	614	444 (72.3)	304	215 (70.7)	–
Serious adverse events (SAE)					
	614	80 (13.0)	304	38 (12.5)	1.04 [0.73; 1.50] 0.870[a)]
Severe adverse events (CTCAE grade 3 or 4)					
	614	50 (8.1)	304	25 (8.2)	0.99 [0.63; 1.57] 0.979[a)]
Therapy discontinuation due to adverse events					
	614	1 (0.2)	304	0 (0.0)	1.49 [0.06; 36.41] 0.599[a)]

a) IQWiG's own calculation

Abbreviations used:

CTCAE = Common Terminology Criteria for Adverse Events; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; RR = relative risk; RSV = Respiratory Syncytial Virus; vs = versus; SAE = serious adverse event; AE = adverse event

b) <u>Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is not indicated</u>

No adequate data are available to allow an assessment of the additional benefit.

Benefit assessment procedure comprises several resol... Pharmaceuticals Directive
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Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	∅	No data available.
Side effects	n.a.	There are no assessable data.
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		

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

a) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is indicated

Approx. 52,000 – 66,000 patients

b) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is not indicated

Approx. 450 patients

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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) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 28 March 2024):

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

4. Treatment costs

Annual treatment costs:

a) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is indicated

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nirsevimab	€ 427.33
Appropriate comparator therapy:	
Palivizumab	€ 5,560.14 - € 13,335.20

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2024)

Costs for additionally required SHI services: not applicable

b) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is not indicated

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nirsevimab	€ 427.33
Appropriate comparator therapy:	
Monitoring wait-and-see approach	Not calculable

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2024)

Costs for additionally required SHI services: not applicable

Please note: The assessment procedure contains several resolutions. The present version of the pharmaceuticals Directive/Annex XII.

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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:

a) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is indicated

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

b) Children with an indication for secondary prevention of lower respiratory tract infections caused by Respiratory Syncytial Virus (RSV) in whom palivizumab is not indicated

- 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.

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II. **The resolution will enter into force on the day of its publication on the website of the G-BA on 15 August 2024.**

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

Berlin, 15 August 2024

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

Prof. Hecken

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