Nirsevimab (secondary prophylaxis of RSV lower respiratory tract disease)

Addendum to Project A24-27 (dossier assessment)[1]

ADDENDUM

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[1] Translation of the addendum *Nirsevimab (Sekundärprophylaxe von RSV-Erkrankungen der unteren Atemwege) – Addendum zum Projekt A24-75 (Dossierbewertung)*. Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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List of abbreviations

Abbreviation	Meaning
BPD	bronchopulmonary dysplasia
CHD	congenital heart defect
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RSV	respiratory syncytial virus
SGB	Sozialgesetzbuch (Social Code Book)

1 Background

On 9 July 2024, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Project A24-27 (Nirsevimab – Benefit assessment according to §35a Social Code Book V) [1].

The commission comprises the assessment of the data of the MEDLEY study on morbidity at Day 151 presented by the pharmaceutical company (hereinafter referred to as "the company") in the dossier [2], taking into account the information from the commenting procedure [3].

The responsibility for the present assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

The MEDLEY study was included for the benefit assessment A24-27 [1] of nirsevimab for secondary prophylaxis of respiratory syncytial virus (RSV) lower respiratory tract disease in children during their 1st RSV season in whom palivizumab is indicated (research question 1 of the benefit assessment). A detailed description of the MEDLEY study can be found in dossier assessment A24-27 [1].

A total of 3 data cut-offs were planned for the MEDLEY study. The 1st data cut-off on 3 May 2021 was performed after all children had completed 150 days of follow-up after the 1st dose. The 2nd data cut-off on 30 April 2022 was performed after all children in the cohort with bronchopulmonary dysplasia (BPD) or haemodynamically significant congenital heart defect (CHD) had completed the Day 151 Visit of the 2nd RSV season; it included analyses of benefit and harm outcomes up to 360 days after the 1st dose. A 3rd data cut-off (final analysis) was performed on 20 January 2023, after all children in the BPD/CHD cohort had completed 360 days of follow-up after the 1st dose of the 2nd season. This 3rd data cut is not relevant, as the 2nd RSV season is not part of the research question considered here.

As described in dossier assessment A24-27, the 2nd data cut-off was used for the benefit assessment because it covers the longest available observation period within the 1st RSV season. Since after the end of the 5-month RSV season, RSV lower respiratory tract infections still occurred to a relevant extent; the analyses on Day 361 are more informative than those on Day 151 and are relevant for the benefit assessment. As already noted in dossier assessment A24-27, the results of the comparison between intervention and comparator arm are not statistically significant on the analysis dates Day 151 and Day 361.

In compliance with the commission, the results for the outcome of RSV lower respiratory tract infection at the analysis date Day 151 are presented in Appendix A as supplementary information.

2.1 Summary

The present addendum does not change the conclusion on the added benefit of nirsevimab from dossier assessment A24-27.

The following Table 1 shows the result of the benefit assessment of nirsevimab, taking into account dossier assessment A24-27 and the present addendum.

Table 1: Nirsevimab – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
1	Children during their 1st RSV season with indication for secondary prophylaxis[c] of lower respiratory tract infections caused by RSV in whom palivizumab is indicated[d]	Palivizumab	Added benefit not proven
2	Children during their 1st RSV season with indication for secondary prophylaxis[c] of lower respiratory tract infections caused by RSV in whom palivizumab is not indicated[d]	Watchful waiting	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. No ACT is determined for nirsevimab for the prevention of lower respiratory tract infections caused by RSV in paediatric patients at the beginning of their 1st RSV season that is not a secondary prophylaxis, as this therapeutic indication currently does not fall within the scope of §35 a SGB V.
c. For certain children, the intervention is a secondary prophylaxis:
- Children who required accompanying therapeutic measures for bronchopulmonary dysplasia within the last 6 months before the onset of the RSV season. These measures included supplemental oxygen, steroids, bronchodilators or diuretics.
- Children with haemodynamically significant congenital heart defect (e.g. relevant left-to-right and right-to-left shunt diseases, and patients with pulmonary hypertension or pulmonary venous congestion)
- Children with trisomy 21
- Children ≤ 6 months of age at the onset of the RSV season who were born prematurely up to the completed 35th week of gestation (34 weeks [+ 6 days])

d. The therapeutic advice on RSV antibodies (AM-RL Appendix IV - Therapeutic advice in accordance with §92 [para.2 2, sentence 7] SGB V) dated 2 November 2023 [4] must be taken into account. With regard to research question 2, the G-BA specified that this patient group currently comprises only patients with trisomy 21 (without bronchopulmonary dysplasia, without haemodynamically significant congenital heart defect, who were not born prematurely up to the completed 35th week of gestation (34 weeks [+ 6 days]).

AM-RL: Pharmaceutical Directive; G-BA: Federal Joint Committee; RSV: respiratory syncytial virus; SGB: Social Code Book V

3 References

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Nirsevimab (Sekundärprophylaxe von RSV-Erkrankungen der unteren Atemwege); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2024 [Accessed: 22.07.2024]. URL: https://doi.org/10.60584/A24-27.

2. Sanofi-Aventis Deutschland. Nirsevimab (Beyfortus); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2024 [Accessed: 03.06.2024]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/998/#dossier.

3. Sanofi Aventis Deutschland. Stellungnahme zum IQWiG-Bericht Nr. 1796: Nirsevimab (Sekundärprophylaxe von RSV-Erkrankungen der unteren Atemwege); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung. 2024: [Soon available under: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/998/#beschluesse in the document "Zusammenfassende Dokumentation"].

4. Gemeinsamer Bundesausschuss. Anlage IV zum Abschnitt H der Arzneimittel-Richtlinie; Verordnungseinschränkungen und -ausschlüsse in der Arzneimittel-versorgung; Therapiehinweise gemäß § 92 Abs. 2 Satz 7 SGB V i. V. m. § 17 AM-RL zur wirtschaftlichen Verordnungsweise von Arzneimitteln [online]. 2024 [Accessed: 02.04.2024]. URL: https://www.g-ba.de/downloads/83-691-867/AM-RL-IV-Therapiehinweise_2024-01-18.pdf.

5. Martín Andrés A, Silva Mato A. Choosing the optimal unconditioned test for comparing two independent proportions. Computat Stat Data Anal 1994; 17(5): 555-574. https://doi.org/10.1016/0167-9473(94)90148-1.

Appendix A Results for the outcome of RSV lower respiratory tract infection at the analysis date Day 151

Table 2: Results (morbidity) on Day 151 (supplementary information) – RCT, direct comparison: nirsevimab vs. palivizumab

Study Outcome category Outcome	Nirsevimab		Palivizumab		Nirsevimab vs. palivizumab
	N	Patients with event n (%[a])	N	Patients with event n (%[a])	RR [95% CI][b]; p-value[c]
MEDLEY (Day 151)					
Morbidity					
RSV lower respiratory tract infection (composite outcome)	616	4 (0.6)	309	3 (1.0)	0.67 [0.15; 2.97]; 0.625
Hospitalization	616	2 (0.3)	309	2 (0.6)	0.50 [0.07; 3.54]; 0.599
Primary	616	2 (0.3)	309	2 (0.6)	0.50 [0.07; 3.54]; 0.599
Nosocomial	616	0 (0)	309	0 (0)	–
Outpatient care	616	4 (0.6)	309	1 (0.3)	2.01 [0.23; 17.88]; 0.617
Emergency outpatient clinic	616	1 (0.2)	309	0 (0)	1.51 [0.06; 36.89]; 0.573
Acute care	616	2 (0.3)	309	1 (0.3)	1.00 [0.09; 11.02]; > 0.999
Outpatient clinic	616	1 (0.2)	309	0 (0)	1.51 [0.06; 36.89]; 0.573

a. Institute's calculation.
b. Institute's calculation of RR (in case of 0 events in one study arm with correction factor of 0.5 in both study arms) and CI (asymptotic).
c. Institute's calculation (unconditional exact test, CSZ method according to [5]).

CI: confidence interval; CSZ: convexity, symmetry, z-score; n: number of patients with (at least one) event; N: number of analysed patients; RCT: randomized controlled trial; RR: relative risk