



# HARMONIE Study: Impact on Incidence of Respiratory Syncytial Virus (RSV) Hospitalisation

RSV is one of the most common causes of Lower Respiratory Tract Infections (LRTI) in young children and can cause morbidity <sup>1,2</sup>

## HARMONIE Study



A Phase 3b open-label, multi-centre, parallel 2-arm study performed comparing Beyfortus ▼ (nirsevimab) to no preventative RSV intervention (standard of care) in preventing hospitalisations due to RSV in infants <sup>3</sup>



Individually randomised infants ( $\geq 29$  weeks gestational age) received a single intramuscular injection of nirsevimab (50 mg if  $< 5$  kg, 100 mg if  $\geq 5$  kg at time of dosing) or no intervention (standard of care)



4037

randomised to receive nirsevimab



4021

randomised to receive no intervention

## Investigators used an intention-to-treat analysis

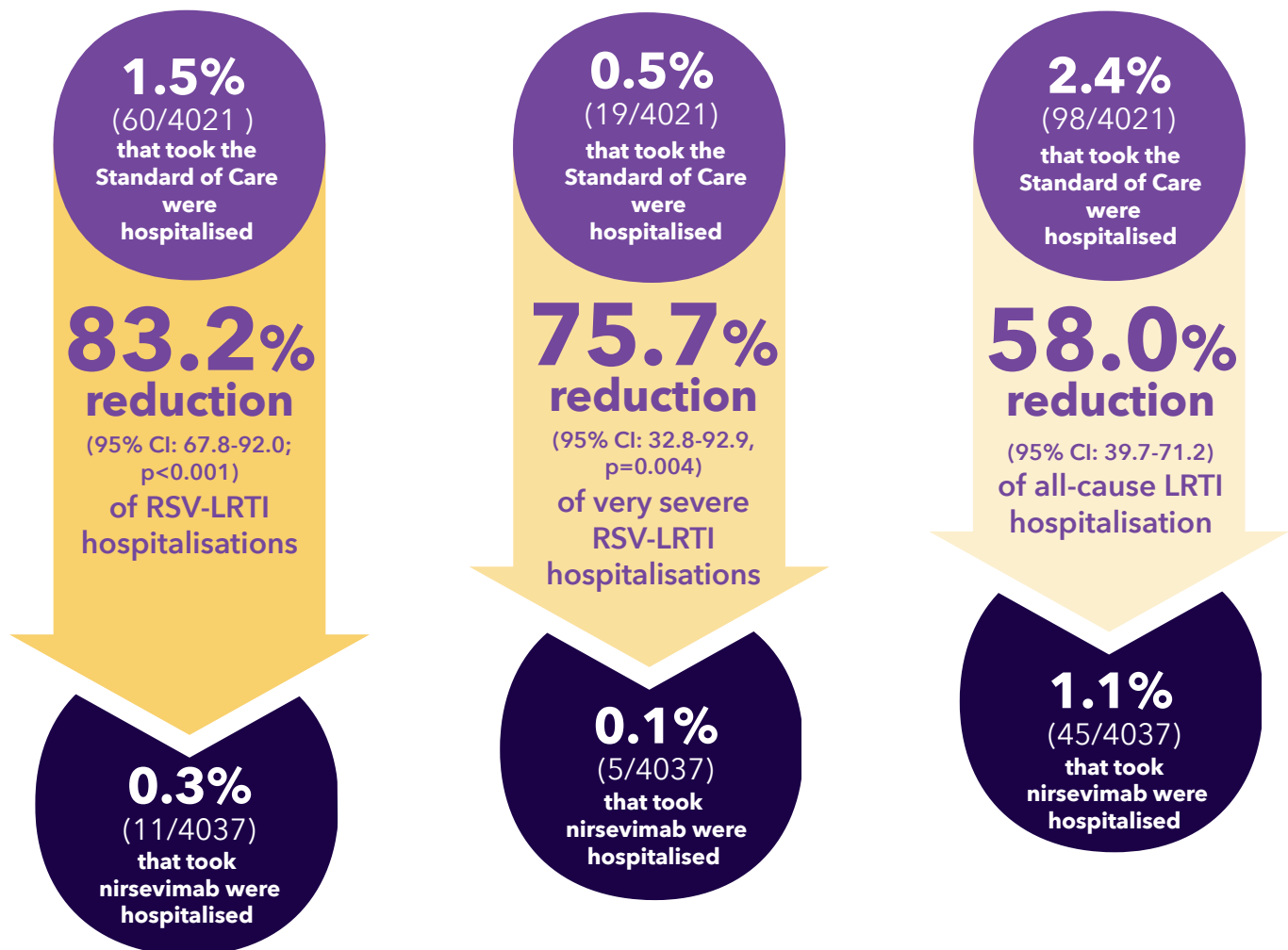


**P** rimary endpoint met: Hospitalisation for RSV-LRTI

- S** econdary endpoints:
- Very severe RSV-LRTI
  - Hospitalisation for RSV-LRTI in each country
  - All-cause LRTI hospitalisation

The efficacy of nirsevimab in preventing RSV-LRTI hospitalisation compared to no intervention; 71 primary end-point events had occurred by 28 February 2023, which was used as the data-cut off date for the initial event-driven primary analysis <sup>3</sup>

## Primary Endpoint Results of HARMONIE Trial (2022-2023)



Prescribing Information can be found on the final page of this infographic.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Adverse events should be reported. Reporting forms and information can be found at [www.hpra.ie](http://www.hpra.ie); email: [medsafety@hpra.ie](mailto:medsafety@hpra.ie). Adverse events should also be reported to Sanofi Ireland Ltd: Tel: 014035600. Alternatively, send via email to [IEpharmacovogilance@sanofi.com](mailto:IEpharmacovogilance@sanofi.com)

# HARMONIE Study: Impact on Incidence of RSV Hospitalisation

## Country-Specific Efficacy Against RSV-LRTI Hospitalisation

United Kingdom

**83.4%**

Efficacy in preventing hospitalisation for RSV-LRTI (Adjusted 95% CI: 34.3-97.6; HR\*: 0.16) multiplicity-adjusted p=0.003<sup>4</sup>  
N=4092

Germany

**74.2%**

Efficacy in preventing hospitalisation for RSV-LRTI (Adjusted 95% CI: 27.9-92.5; HR\*: 0.25) multiplicity-adjusted p=0.006<sup>4</sup>  
N=1789

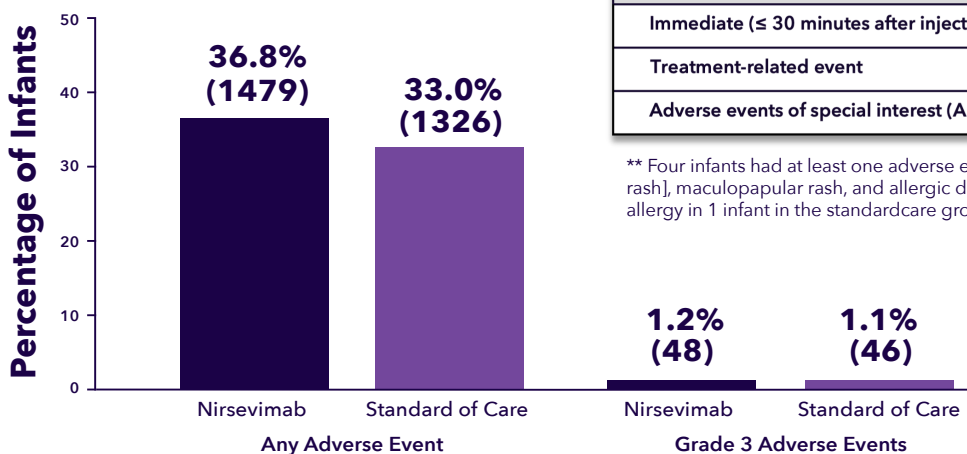
France

**89.6%**

Efficacy in preventing hospitalisation for RSV-LRTI (Adjusted 95% CI: 58.8-98.7; HR\*: 0.10) multiplicity-adjusted p<0.001<sup>4</sup>  
N=2177

\* The efficacy were calculated as 1 minus the hazard ratio (expressed as a percentage)  
CI: Confidence Interval; HR: Hazard Ratio

## Summary of Adverse Events



## HARMONIE Trial Adverse Events through the Data-Cutoff Date (Safety Analysis Population)<sup>3</sup>

Adverse Events Category	Nirsevimab (N=4015) n (%)	Standard Care (N=4020) n (%)
Immediate (≤ 30 minutes after injection)	26 (0.6)	0 (0.0)
Treatment-related event	86 (2.1)	0 (0.0)
Adverse events of special interest (AESI)**	3 (0.1)	1 (<0.1)

\*\* Four infants had at least one adverse event of special interest (drug reaction [reported as fever and rash], maculopapular rash, and allergic dermatitis in 1 infant each in the nirsevimab group and food allergy in 1 infant in the standardcare group), all of which were assessed to be grade 1 or 2 in severity.

The safety profile of nirsevimab was consistent with data from previous trials.<sup>3</sup>

- Most adverse events were grade 1 or grade 2 in severity.<sup>3</sup>

## Nirsevimab Safety Information

The most frequent adverse reaction was rash (0.7%), occurring within 14 days post dose.<sup>5</sup> The majority of cases were mild to moderate in intensity.<sup>5</sup> Additionally, pyrexia and injection site reactions were reported at a rate of 0.5% and 0.3% within 7 days post dose, respectively.<sup>5</sup> Injection site reactions were non-serious.<sup>5</sup> Serious hypersensitivity reactions have been reported following Beyfortus administration. If signs and symptoms of anaphylaxis or other clinically significant hypersensitivity reaction occur, immediately discontinue administration and initiate appropriate medicinal products and/or supportive therapy.<sup>5</sup>

For full adverse reaction information, please refer to the Beyfortus® IE (nirsevimab) Summary of Product Characteristics.

## Conclusions

HARMONIE demonstrated that nirsevimab prevented hospitalisation for RSV-LRTI in a broad population of healthy preterm and term infants.

- Consistent efficacy of nirsevimab across subgroups, all of which are at risk of RSV-LRTI
- Nirsevimab efficacy in preventing RSV-LRTI hospitalisations of **83.2%**
- Nirsevimab efficacy in preventing very severe RSV disease of **75.7%**
- Reduction in all-cause LRTI hospitalisations was **58.0%**
- The safety profile of nirsevimab was consistent with data from previous trials<sup>3</sup>

**Prescribing Information: Beyfortus (nirsevimab) solution for injection in pre-filled syringe**  
Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

**Presentation: Beyfortus 50 mg solution for injection in pre-filled syringe.** Each pre-filled syringe contains 50 mg of nirsevimab in 0.5 mL (100 mg/mL).

**Beyfortus 100 mg solution for injection in pre-filled syringe.** Each pre-filled syringe contains 100 mg of nirsevimab in 1 mL (100 mg/mL).

Nirsevimab is a human immunoglobulin G1 kappa (IgG1k) monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. Excipients with known effect: This medicine contains 0.1 mg of polysorbate 80 (E433) in each 50 mg (0.5 mL) dose and 0.2 mg in each 100 mg (1 mL) dose (see SmPC).

**Indication:** Beyfortus is indicated for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in: i. Neonates and infants during their first RSV season. ii. Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season (see SmPC). Beyfortus should be used in accordance with official recommendations.

**Dosage and Administration: Infants during their first RSV season:** Beyfortus is recommended as a single dose of 50 mg administered intramuscularly for infants with body weight <5 kg and a single dose of 100 mg administered intramuscularly for infants with body weight ≥5 kg. Beyfortus should be administered from birth for infants born during the RSV season. For others born outside the season Beyfortus should be administered ideally prior to the RSV season. Dosing in infants with a body weight from 1 kg to <1.6 kg is based on extrapolation, no clinical data are available. Exposure in infants <1 kg is anticipated to yield higher exposures than in those weighing more. The benefits and risks of nirsevimab use in infants <1 kg should be carefully considered. There are limited data available in extremely preterm infants (Gestational Age [GA] <29 weeks) less than 8 weeks of age. No clinical data available in infants with a postmenstrual age (gestational age at birth plus chronological age) of less than 32 weeks (see SmPC).

**Children who remain vulnerable to severe RSV disease through their second RSV season:** The recommended dose is a single dose of 200 mg given as two intramuscular injections (2 x 100 mg). Beyfortus should be administered ideally prior to the start of the second RSV season. For individuals undergoing cardiac surgery with cardiopulmonary bypass, an additional dose may be administered as soon as the individual is stable after surgery to ensure adequate nirsevimab serum levels. If within 90 days after receiving the first dose of Beyfortus, the additional dose during the first RSV season should be 50 mg or 100 mg according to body weight, or 200 mg during the second RSV season. If more than 90 days have elapsed since the first dose, the additional dose could be a single dose of 50 mg regardless of body weight during the first RSV season, or 100 mg during the second RSV season, to cover the remainder of the RSV season.

Beyfortus is for intramuscular injection only. It is administered intramuscularly, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve. If two injections are required, different injection sites should be used.

The safety and efficacy of nirsevimab in children aged 2 to 18 years have not been established. No data are available.

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in SmPC.

**Warnings and precautions: Hypersensitivity including anaphylaxis:** Serious hypersensitivity reactions have been reported following Beyfortus administration. Anaphylaxis has been observed with human immunoglobulin G1 (IgG1) monoclonal antibodies. If signs and symptoms of anaphylaxis or other clinically significant hypersensitivity reaction occur, immediately discontinue administration and initiate appropriate medicinal products and/or supportive therapy. **Clinically significant bleeding disorders:** As with any other intramuscular injections, nirsevimab should be given with caution to individuals with thrombocytopenia or any coagulation disorder. **Immunocompromised children:** In some immunocompromised children with protein-losing conditions, a high clearance of nirsevimab has been observed in clinical trials (see SmPC), and nirsevimab may not provide the same level of protection in those individuals. **Polysorbate 80 (E433):** This medicine contains 0.1 mg of polysorbate 80 in each 50 mg (0.5 mL) dose and 0.2 mg in each 100 mg (1 mL) dose. Polysorbates may cause allergic reactions.

**Interactions:** No interaction studies have been performed. Nirsevimab does not interfere with reverse transcriptase polymerase chain reaction (RT-PCR) or rapid antigen detection RSV diagnostic assays that employ commercially available antibodies targeting antigenic site I, II, or IV on the RSV fusion (F) protein. **Concomitant administration with vaccines:** Since nirsevimab is a monoclonal antibody, a passive immunisation specific for RSV, it is not expected to interfere with the active immune response to co-administered vaccines. There is limited experience of co-administration with vaccines. In clinical trials, when nirsevimab was given with routine childhood vaccines, the safety and reactogenicity profile of the co-administered regimen was similar to the childhood vaccines given alone. Nirsevimab can be given concomitantly with childhood vaccines. Nirsevimab should not be mixed with any vaccine in the same syringe or vial (see SmPC). When administered concomitantly with injectable vaccines, they should be given with separate syringes and at different injection sites.

**Fertility, pregnancy and lactation:** Not applicable.

**Adverse Reactions: Uncommon (≥1/1,000 to <1/100):** The most frequent adverse reaction was rash (0.7%) occurring within 14 days post dose. Additionally, within 7 days post-dose, pyrexia and injection site reactions were reported in 0.5% (0.6% in placebo) and 0.3% (0% in placebo) of nirsevimab recipients, respectively. **Other Serious Adverse Drug Reactions: Not known** (cannot be estimated from available data): hypersensitivity. Prescribers should consult the SmPC in relation to other adverse reactions.

**Legal Category:** POM

**Marketing Authorisation Number:**

EU/1/22/1689/001-002, EU/1/22/1689/004-005

**Marketing Authorisation Holder:**

Sanofi Winthrop Industrie, 82 avenue Raspail, 94250, Gentilly, France

**Further information is available from: IE:** Sanofi, 18 Riverwalk, Citywest Business Campus, Dublin 24 or contact [IEmedinfo@sanofi.com](mailto:IEmedinfo@sanofi.com)

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Alternatively, send via email to [IEPharmacovigilance@sanofi.com](mailto:IEPharmacovigilance@sanofi.com)