A Quick Guide to Nirsevimab SmPC

A human Immunoglobulin G1 kappa (IgG1κ) monoclonal antibody

This document is based on the approved Nirsevimab EU Summary of Product Characteristics (SmPC)

and follows the same layout to allow for easy reference to the full document as required.

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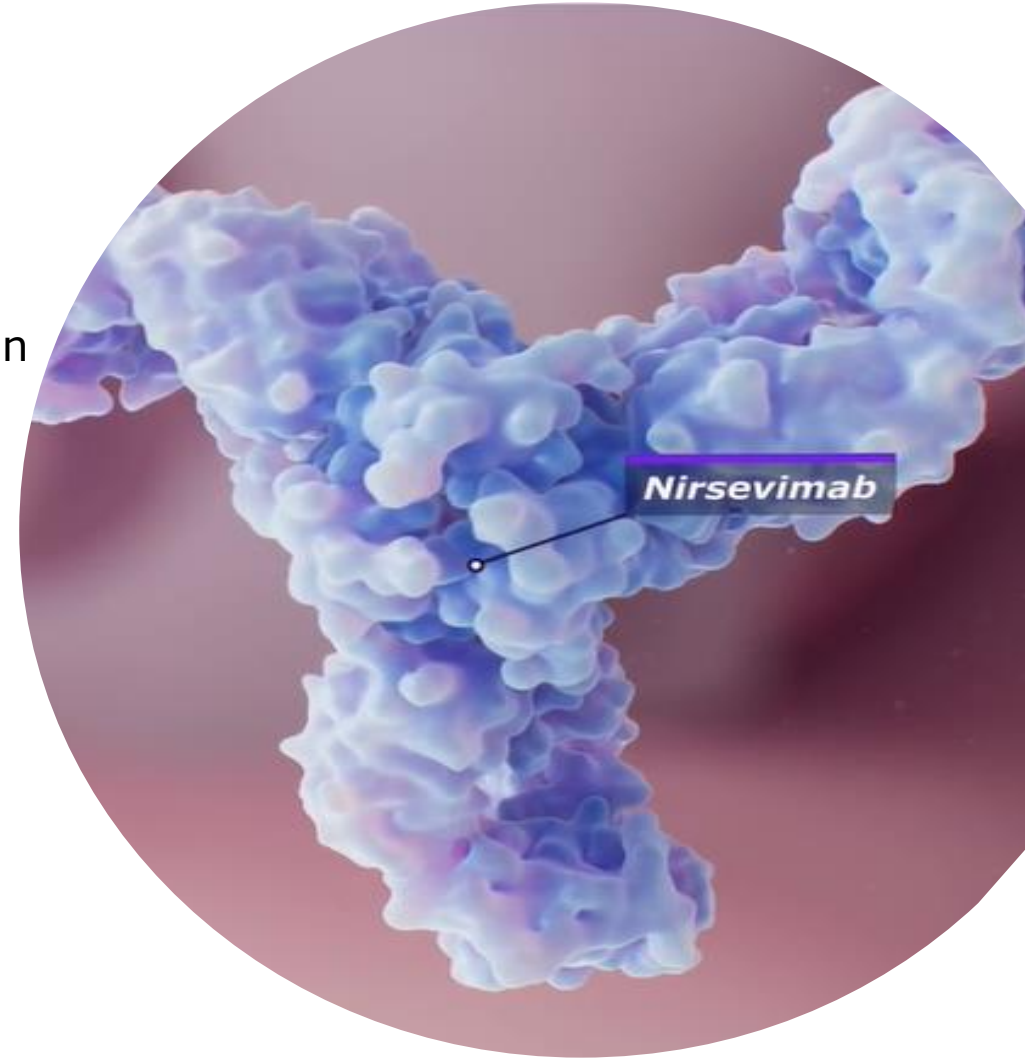
What is Nirsevimab?

- Nirsevimab is a **Recombinant Neutralizing Human IgG1κ long-acting monoclonal antibody** to the prefusion conformation of the RSV F protein

- Nirsevimab has been **modified with a triple amino acid substitution (YTE)** in the Fc region to extend serum half-life.

- Nirsevimab **binds to a highly conserved epitope in antigenic site Ø** on the prefusion protein hence inhibits the essential membrane fusion step in the viral entry process, neutralizing the virus and blocking cell-to-cell fusion.

- Nirsevimab is produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.



What is the composition of Nirsevimab?

Nirsevimab 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).

Nirsevimab 100 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 100 mg of nirsevimab in 1 mL (100 mg/mL).

What is the pharmaceutical form of Nirsevimab?

Solution for injection (injection).

Clear to opalescent, colourless to yellow, pH 6.0 solution.

What is Nirsevimab indicated for?

Nirsevimab is indicated for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants during their first RSV season.

Nirsevimab should be used in accordance with official recommendations.

What is the schedule of administration for Nirsevimab?

- **Recommended Dose**

- Single dose of 50 mg administered intramuscularly for infants with body weight <5 kg
- Single dose of 100 mg administered intramuscularly for infants with body weight ≥5 kg.

- Nirsevimab should be administered prior to commencement of the RSV season, or from birth for infants born during the RSV season.

- **For infants undergoing cardiac surgery with cardiopulmonary bypass, an additional dose may be administered** as soon as the infant is stable after surgery to ensure adequate nirsevimab serum levels.
  - If within 90 days after receiving the first dose of Nirsevimab, the additional dose should be 50 mg or 100 mg according to body weight.
  - 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, to cover the remainder of the RSV season.

What is the schedule of administration for Nirsevimab?

- Dosing in infants with a body weight from 1.0 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 section 5.1).

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

How is Nirsevimab administered?

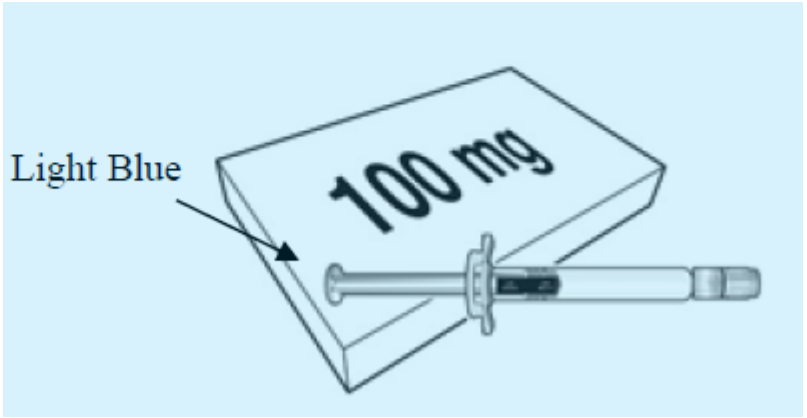
- Nirsevimab is for **Intramuscular injection** only.
- Preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve.

Instructions for administration

Nirsevimab is available in a 50 mg and a 100 mg pre-filled syringe. Check the labels on the carton and pre-filled syringe to make sure you have selected the correct 50 mg or 100 mg presentation as required.

Nirsevimab 50 mg (50 mg/0.5 mL) pre-filled syringe with a purple plunger rod.

Nirsevimab 100 mg (100 mg/1 mL) pre-filled syringe with a light blue plunger rod.



What are the contraindications of Nirsevimab?

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of SmPC

What are the special warnings and precautions for use?

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity including anaphylaxis

Serious hypersensitivity reactions, including anaphylaxis, have been observed with monoclonal antibodies. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis 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 infants with thrombocytopenia or any coagulation disorder.

Special Populations

Race

There was **no clinically relevant effect** of race.

Renal impairment

No clinical studies have been conducted to investigate the effect of renal impairment.

As a typical IgG monoclonal antibody, **nirsevimab is not cleared renally** due to its large molecular weight, change in renal function is not expected to influence nirsevimab clearance.

Hepatic impairment

No clinical studies have been conducted to investigate the effect of hepatic impairment.

As IgG monoclonal antibodies are **not primarily cleared via the hepatic pathway**, change in hepatic function is not expected to influence Nirsevimab clearance.

Infants at higher risk for severe RSV disease

There was **no significant influence** of chronic lung disease or congenital heart disease on the pharmacokinetics of nirsevimab.

Does Nirsevimab interact with other medicinal products?

- No interaction studies have been performed.
- Monoclonal antibodies do not typically have significant interaction potential, as they **do not directly affect cytochrome P450 enzymes** and are not substrates of hepatic or renal transporters.
- Indirect effects on cytochrome P450 enzymes are unlikely as the target of nirsevimab is an exogenous virus.
- They are **not substrates for renal or hepatic transporters**

Can Nirsevimab be administered with other pediatric vaccines?

- Since nirsevimab is a monoclonal antibody, a **passive immunization 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 section 6.2 SmPC).
- When administered concomitantly with injectable vaccines, they should be given with separate syringes and at different injection sites

What information is not applicable to the administration of Nirsevimab?

Fertility, pregnancy and lactation

Effects on ability to drive and use machines

Summary of Nirsevimab Safety profile (4.8)? Uncommon

- **Rash** (0.7%)

  occurring within 14 days post dose.

  The majority of cases were mild to moderate in intensity.

- **Pyrexia** (0.5%)

  Occurring within 7 days post dose

- **Injection site reactions** (0.3%)

  Occurring within 7 days post dose

  Injection site reactions were non-serious

Infants at higher risk

Infants at higher risk for severe RSV disease

Safety was also evaluated in MEDLEY in 918 infants at higher risk for severe RSV disease, including 196 extremely preterm infants (GA <29 weeks) and 306 infants with chronic lung disease of prematurity, or haemodynamically significant congenital heart disease entering their first RSV season, who received nirsevimab (614) or palivizumab (304). The safety profile was comparable to the palivizumab comparator and consistent with the safety profile in term and preterm infants GA ≥29 weeks (D5290C00003 and MELODY).

Efficacy summary for Nirsevimab

In clinical trials, the Efficacy of Nirsevimab has been demonstrated

See section 5.1 & Table 2 of the Nirsevimab SmPC for results.

Clinical Efficacy

Table 2: Efficacy in term and preterm infants against MA RSV LRTI, MA RSV LRTI with hospitalisation and very severe MA RSV LRTI through 150 days post dose, D5290C00003 and MELODY (Primary cohort)

Group	Treatment	N	Incidence % (n)	Efficacy[a] (95% CI)
Efficacy in infants against MA RSV LRTI through 150 days post dose				
Very and moderately preterm GA ≥29 to <35 weeks (D5290C00003)[b]	Nirsevimab	969	2.6 (25)	70.1% (52.3, 81.2)[c]
	Placebo	484	9.5 (46)	
Term and late preterm GA ≥35 weeks (MELODY Primary cohort)	Nirsevimab	994	1.2 (12)	74.5% (49.6, 87.1)[c]
	Placebo	496	5.0 (25)	
Efficacy in infants against MA RSV LRTI with hospitalisation through 150 days post dose				
Very and moderately preterm GA ≥29 to <35 weeks (D5290C00003)[b]	Nirsevimab	969	0.8 (8)	78.4% (51.9, 90.3)[c]
	Placebo	484	4.1 (20)	
Term and late preterm GA ≥35 weeks (MELODY Primary cohort)	Nirsevimab	994	0.6 (6)	62.1% (-8.6, 86.8)
	Placebo	496	1.6 (8)	
Efficacy in infants against very severe MA RSV LRTI through 150 days post dose				
Very and moderately preterm GA ≥29 to <35 weeks (D5290C00003)[b]	Nirsevimab	969	0.4 (4)	87.5% (62.9, 95.8)[d]
	Placebo	484	3.3 (16)	
Term and late preterm GA ≥35 weeks (MELODY Primary cohort)	Nirsevimab	994	0.5 (5)	64.2% (-12.1, 88.6)[d]
	Placebo	496	1.4 (7)	

[a] Based on relative risk reduction versus placebo.

[b] All subjects who received 50 mg irrespective of weight at the time of dosing.

[c] Prespecified multiplicity controlled; p-value =<0.001.

[d] Not multiplicity controlled.

Medley in 5.1

Efficacy against MA RSV LRTI in infants at higher risk for severe RSV disease (MEDLEY)

MEDLEY randomised a total of 925 infants at higher risk for severe RSV disease including infants with chronic lung disease or congenital heart disease and preterm infants GA <35 weeks, entering their first RSV season. Infants received a single intramuscular dose (2:1) of nirsevimab (50 mg nirsevimab if <5 kg weight or 100 mg nirsevimab if ≥5 kg weight at the time of dosing) or 5 monthly intramuscular doses of 15 mg/kg palivizumab. At randomisation, 21.6% were GA <29 weeks; 21.5% were GA≥29 to <32 weeks; 41.9% were GA ≥32 to <35 weeks; 14.9% were GA ≥35 weeks. Of these infants 23.6% had chronic lung disease; 11.2% had congenital heart disease; 53.5% were male; 79.2% were White; 9.5% were of African origin; 5.4% were Asian; 56.5% weighed <5 kg (6.4% were <2.5 kg); 11.4% of infants were ≤1.0 month of age, 33.8% were >1.0 to ≤3.0 months 33.6% were >3.0 months to ≤6.0 months, and 21.2% were >6.0 months.

The efficacy of nirsevimab in infants at higher risk for severe RSV disease is extrapolated from the efficacy of nirsevimab in D5290C00003 and MELODY based on pharmacokinetic exposure (see

Practical considerations for Nirsevimab

What excipients does Nirsevimab contain?

- L-histidine
- L-histidine hydrochloride
- L-arginine hydrochloride
- Sucrose
- Polysorbate 80
- Water for injections

How do I store Nirsevimab?

- Store in a refrigerator (2°C - 8°C).
- Do not freeze.
- Do not shake or expose to direct heat.
- Keep the pre-filled syringe in the outer carton in order to protect from light.
- Nirsevimab may be kept at room temperature (20°C - 25°C) when protected from light for a maximum of 8 hours. After this time, the syringe must be discarded.

What is the shelf life of Nirsevimab?

3 years

Thank you

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