



Australian Government

Department of Health
and Aged Care

AUSTRALIAN TECHNICAL ADVISORY
GROUP ON IMMUNISATION (ATAGI)
CLINICAL ADVICE

Issue date: 26 March 2024

STATEMENT ON THE USE OF NIRSEVIMAB FOR PREVENTION OF SEVERE DISEASE DUE TO RESPIRATORY SYNCYTIAL VIRUS (RSV) IN INFANTS

Overview of key points

- Nirsevimab is an injectable, long-acting monoclonal antibody (mAb) that protects against respiratory syncytial virus (RSV) disease for at least 5 months after a single dose. It can be used to protect all infants against severe disease during or entering their first RSV season, and young children aged <24 months who are vulnerable to severe disease during their second RSV season.
- Nirsevimab is newly registered for use in Australia and is anticipated to be supplied in 2024. Some states have introduced state-based programs. Due to international supply shortages, it is anticipated that nirsevimab will not be available for private prescription outside of these state-based programs in 2024.
- Although all infants aged <6 months entering their first RSV season would benefit from nirsevimab, in the setting of supply constraints, it is important to prioritise those with risk conditions that put them at the highest risk of severe RSV disease and hospitalisation (High risk group in Table 1).
- For infants and children up to age 24 months with a high risk of severe RSV disease due to certain medical conditions, use of nirsevimab before their second RSV season can be considered.
- Nirsevimab is safe and well tolerated in infants and young children. Very rare hypersensitivity reactions may occur with use.
- As nirsevimab supply changes and depending on availability of a maternal RSV vaccine to protect infants, guidance on RSV prevention among infants will be updated in the immunisation handbook.
- The RSV season in temperate regions of Australia is usually from April to September. Nirsevimab should be given at birth to infants born just before or during the RSV season. For infants born after the RSV season, take into consideration the likelihood of out-of-season RSV infection and risk of severe disease (Box 1), and consider delaying nirsevimab until just before the next RSV season if appropriate. Older infants and young children who require nirsevimab should receive it just before or early in the RSV season. The pattern of RSV disease in tropical areas is less predictable but may coincide with months of high rainfall. For timing of administration in Australia's tropical regions, seek local advice.
- Palivizumab is an acceptable alternative RSV mAb for high-risk children who are eligible for RSV protection under state and territory provisions; however palivizumab needs to be administered monthly throughout the RSV season.

About nirsevimab

Nirsevimab (Beyfortus, Sanofi-Aventis) is an injectable, long-acting monoclonal antibody (mAb) that protects against RSV disease in infants and young children. It provides protection for at least 5 months.

RSV mAbs, such as nirsevimab, provide passive immunisation directly to the infant or young child and work immediately after injection. RSV is neutralised when the mAbs bind to the RSV fusion protein and prevent virus entry into host cells.¹ Infants can also be protected through passive immunisation if their mother receives an RSV vaccine during pregnancy. In contrast to RSV mAbs, an RSV vaccine administered during pregnancy produces neutralising antibodies in the mother which are transferred across the placenta to the baby *in utero*. This process requires at least 2 weeks after vaccination for a baby to be adequately protected at birth. At the time of publication, a single RSV vaccine, Abrysvo, was registered for use during pregnancy in Australia.

[The Therapeutic Goods Administration \(TGA\)](#) has approved nirsevimab for use in Australia to prevent RSV lower respiratory tract disease in 2 groups:^{2,3}

- newborns and infants born during or entering their first RSV season
- young children up to 24 months of age who are vulnerable to severe RSV disease during their second RSV season

Nirsevimab has an extended duration of protection – a single intramuscular dose protects infants for at least 5 months, which is usually enough for an entire RSV season.⁴

Palivizumab (Synagis, AstraZeneca) is an alternative RSV monoclonal antibody preparation available in Australia⁵ for infants at high risk of RSV disease. Palivizumab is not a long-acting preparation and requires monthly intramuscular injections to provide continuous protection throughout the RSV season. Established guidelines for the use of palivizumab, including funding arrangements by individual states and territories, are available.^{6,7}

From 15 March 2024, immunisation providers can report receipt of nirsevimab to the Australian Immunisation Register.

About RSV

RSV causes infection in most children by 2 years of age, often presenting as bronchiolitis with breathing difficulty. During the first 6 months of life, infection can be more severe, and children in this age group have the highest rate of RSV hospitalisation compared to all other age groups, including adults.⁸ Most children hospitalised with RSV are otherwise healthy. However, infants born prematurely or with certain medical conditions (Box 1) are at a particularly high risk of severe RSV disease, which can result in the need for hospitalisation, respiratory support or intensive care unit admission.⁹⁻¹¹

Box 1: Risk conditions for severe RSV disease in infants and young children

- Prematurity (particularly infants born <32 weeks gestational age)^{10,11}
- Haemodynamically significant congenital heart disease⁹⁻¹¹
- Significant immunosuppression, e.g. due to solid organ transplant, haematopoietic stem cell transplant,¹² or primary immune deficiencies such as severe combined immunodeficiency (SCID)^{9,10}
- Chronic lung disease that requires oxygen or respiratory support beyond 36 weeks gestation or at hospital discharge^{9,10}
- Neurological conditions that impair respiratory function¹⁰
- Cystic fibrosis with severe lung disease or weight for length <10th percentile¹⁰
- Trisomy 21 or other genetic conditions that increase the risk of RSV¹³

Use of nirsevimab

Nirsevimab protects against RSV disease, such as RSV-associated hospitalisation, in infants, especially those aged <6 months or at increased risk of severe disease (Box 1 in [About RSV](#)).¹¹ Nirsevimab can be given at birth to infants born during or entering their first RSV season. For infants born after the RSV season, take into consideration the likelihood of out-of-season RSV infection and risk of severe disease (Box 1), and consider delaying nirsevimab until just before the next RSV season if appropriate.

Young children up to 24 months of age who have risk factors for severe RSV disease in their second RSV season have also been shown to benefit from nirsevimab given just before or near the start of the RSV season.¹⁴ A higher dose of nirsevimab is required for older infants and young children entering their second RSV season (see [Dosing nirsevimab](#)).

Availability and prioritisation of nirsevimab

The [TGA](#) approved nirsevimab on 22 November 2023.^{2,3} It is not available on the National Immunisation Program and is not currently listed on the Pharmaceutical Benefits Scheme. States and territories may have separate availability and funding arrangements, which will be detailed on their relevant department of health websites where appropriate.¹⁵⁻¹⁷

It is anticipated that the supply of nirsevimab will be limited in coming months to state-based programs. Therefore, the populations that are likely to gain the most benefit should be prioritised to receive nirsevimab according to their risk of severe RSV disease (see Table 1). Those at highest risk prioritised to receive nirsevimab in a setting of constrained supply are infants 0 to <6 months of age with risk conditions for severe disease (shown in the red box in Table 1). For those at moderate risk, different dosage requirements may need to be considered when prioritising who should receive nirsevimab; for example in newborns at birth compared to children 12 to 24 months of age with risk conditions (see [Dosing nirsevimab](#)).

Table 1: Risk of severe RSV disease by age, prematurity and medical risk conditions

Age	Healthy	Prematurity (32 to <37 weeks gestation)	Risk condition listed in Box 1 (includes prematurity <32 weeks gestation)
Birth to <6 months*	Moderate risk	Moderate risk	High risk
6 to <12 months	Low risk	Low-Moderate risk	Moderate risk
12 to 24 months	Low risk. Nirsevimab not recommended	Low risk. Nirsevimab not recommended	Moderate risk

*Risk is particularly increased in infants aged 0 to <3 months.

Other considerations when evaluating the benefit from nirsevimab include:

- Infants with multiple risk factors for severe RSV disease are likely to have an even higher risk of severe outcomes – for example, prematurity and a medical risk condition.
- The risk of hospitalisation from RSV for Aboriginal and Torres Strait Islander infants is approximately 2 times that of other infants of the same age.^{8,18}
- Infants who cannot readily access advanced care for severe RSV because they live in remote regions may have greater benefit.¹⁹
- The availability and eligibility for palivizumab as an alternate RSV mAb.

Dosing nirsevimab

For infants born during or entering their first RSV season, the recommended dose for nirsevimab is:

- 50 mg in 0.5 mL if weight is <5 kg (purple plunger rod)
- 100 mg in 1 mL if weight is ≥5 kg (light blue plunger rod)

by intramuscular injection as a single dose.^{2,3} Do not divide a 100 mg pre-filled syringe into two 50 mg doses.

For children at an increased risk of severe RSV disease in their second season, the recommended dose for nirsevimab is 200 mg administered as 2 × 100 mg (2 mL total) intramuscular injections in different sites (preferably separate limbs, or else separated by 2.5 cm) at the same visit. This is 4 times more than the dose and volume for a newborn.

Timing of nirsevimab

Nirsevimab offers protection for at least 5 months. Administration should be timed to maximise protection during peak RSV season, which is usually April to September in most temperate parts of Australia. The pattern of RSV disease in tropical areas is less predictable but may coincide with months of high rainfall.²⁰ In tropical regions, seek local advice on RSV transmission patterns to guide timing of administration. Overall, administration is likely to be most effective when given shortly after birth for infants born just before or during the RSV season. For infants born after the RSV season, take into consideration the likelihood of out-of-season RSV infection and risk of severe disease (Box 1), and consider delaying nirsevimab until just before the next RSV season if appropriate. For older infants and young children, nirsevimab should be given just before or early in the RSV season.

Co-administration with other vaccines

Nirsevimab can be co-administered with other routine childhood vaccines. Limited data on co-administration of nirsevimab with routine vaccines has shown a similar rate of adverse events compared with administration of vaccines alone.²¹ Additionally, since nirsevimab provides passive immunisation through an RSV-specific mAb, it is not expected to interfere with the active immune response to other vaccines that are co-administered, based on first principles.²²

Safety of nirsevimab

In 2 clinical trials, nirsevimab showed a favourable safety profile overall (Table 2).^{4,23} The frequencies of adverse events, including grade 3 and serious adverse events, were similar among recipients of nirsevimab compared to placebo, and no serious adverse events were considered related to nirsevimab.

There is a risk of rare hypersensitivity reactions, including urticaria, dyspnoea, cyanosis, hypotonia and/or anaphylaxis after receiving nirsevimab.²⁴ Immunisation providers should monitor recipients for 15 minutes after administration and have appropriate equipment and protocols to initiate treatment for adverse events if required. Carers of infants and young children should be informed about potential signs and symptoms of hypersensitivity reactions, including anaphylaxis, and advised to seek immediate care if these occur.

Table 2: Frequency of adverse events after nirsevimab administration compared to placebo^{4,23}

Population	Adverse event (AE)	Nirsevimab (%)	Placebo (%)
Preterm (born 29 to ≤35 weeks)	Any	86.2	86.8
	Grade ≥3	8.0	12.5
	Severe AE	11.2	16.9
Late preterm or at term (born ≥35 weeks)	Any	83.7	81.8
	≥Grade 3	3.1	3.8
	Severe AE	6.3	7.4

Efficacy and effectiveness of nirsevimab

In clinical trials, among healthy infants born preterm (defined in the clinical trials as gestational age between 29 weeks and <35 weeks) or late preterm to term (gestational age ≥35 weeks), and entering their first RSV season, nirsevimab administered predominantly at <3 months of age reduced the incidence of hospitalisation for RSV-associated lower respiratory tract infection (LRTI) by 78.4% and 76.8%, respectively, compared to placebo, over 150 days post-administration.^{4,23} Across these two trials, the incidence of medically attended RSV-associated lower respiratory tract infection was reduced by 70.1% and 76.4%, respectively, compared to placebo, over 150 days post-administration.

In a randomised study of more than 8,000 healthy infants, born at ≥29 weeks gestational age, without underlying immunosuppressive conditions and who were ineligible to receive palivizumab, nirsevimab administered at a mean age of 4.5 months reduced the incidence of hospitalisation for RSV-associated LRTI and very severe RSV-related LRTI by 83.2% and 75.7%, respectively, compared to no intervention.²⁵

Early data on the real-world effectiveness of nirsevimab as used in Northern Hemisphere countries in 2023 and early 2024 are beginning to emerge. These data also suggest good protective effectiveness in infants (up to 90% effectiveness) and substantial reductions in cases hospitalised or admitted to the intensive care unit.²⁶⁻²⁸

References

1. Zhu Q, McLellan JS, Kallewaard NL, et al. A highly potent extended half-life antibody as a potential RSV vaccine surrogate for infants. *Science Translational Medicine* 2017;9:eaaj1928.
2. Therapeutic Goods Administration. [BEYFORTUS nirsevimab 100 mg in 1 mL solution for injection prefilled syringe \(397899\)](#). Australian Government Department of Health and Aged Care; 2023. (Accessed November 2023).
3. Therapeutic Goods Administration. [BEYFORTUS nirsevimab 50 mg in 0.5 mL solution for injection prefilled syringe \(397898\)](#). Australian Government Department of Health and Aged Care; 2023. (Accessed December 2023).
4. Griffin MP, Yuan Y, Takas T, et al. Single-dose nirsevimab for prevention of RSV in pre-term infants. *New England Journal of Medicine* 2020;383:415-25.
5. Therapeutic Goods Administration. [SYNAGIS palivizumab \(rmc\) 100 mg / 1 mL solution for injection vial \(231139\)](#). 2015. (Accessed February 2024).
6. Osborn D, Bolisetty S. [Palivizumab: newborn use only](#). ANMF Consensus Group; 2020. (Accessed December 2023).
7. The Royal Children's Hospital Melbourne. [Palivizumab for at-risk patients](#). 2023. (Accessed March 2024).
8. Saravanos GL, Sheel M, Homaira N, et al. Respiratory syncytial virus-associated hospitalisations in Australia, 2006-2015. *Med J Aust* 2019;210:447-53.
9. UK Health Security Agency. [Respiratory syncytial virus: the green book, chapter 27a](#). 2015. (Accessed January 2024).

10. Caserta MT, O'Leary ST, Munoz FM, et al. Palivisumab prophylaxis in infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics* 2023;152.
11. Shi T, Vennard S, Mahdy S, Nair H. Risk factors for poor outcome or death in young children with respiratory syncytial virus-associated acute lower respiratory tract infection: a systematic review and meta-analysis. *Journal of Infectious Diseases* 2022;226:S10-S6.
12. Science M, Akseer N, Asner S, U A. Risk stratification of immunocompromised children, including pediatric transplant recipients at risk of severe respiratory syncytial virus disease. *Pediatric Transplantation* 2019;23:e13336.
13. Chan M, Park J, Shi T, et al. The burden of respiratory syncytial virus (RSV) associated acute lower respiratory infections in children with Down syndrome: a systematic review and meta-analysis. *Journal of Global Health* 2017;7:020413.
14. Domachowske JB, Chang Y, Atanasova V, et al. Safety of re-dosing nirsevimab prior to RSV season 2 in children with heart or lung disease. *Journal of the Pediatric Infectious Diseases Society* 2023;12:477-80.
15. Government of Western Australia. [Western Australian children first to access protection from RSV](#). 2024. (Accessed March 2024).
16. NSW Health. [Respiratory syncytial virus \(RSV\) prevention](#). 2024. (Accessed March 2024).
17. Queensland Government. [Free RSV immunisation program for Queensland infants and young children](#). 2024. (Accessed March 2024).
18. Homaira N, Oei JL, Mallitt KA, et al. High burden of RSV hospitalization in very young children: a data linkage study. *Epidemiology and Infection* 2016;144:1612-21.
19. Canada's Drug and Health Technology Agency. [CADTH Health Technology Review – nirsevimab \(Beyfortus\)](#). Canada's Drug and Health Technology Agency; 2023. (Accessed November 2023).
20. Farquharson KA, Anthony D, Menzies R, Homaira N. Burden of respiratory syncytial virus disease across the lifespan in Australia and New Zealand: a scoping review. *Public Health* 2024;226:8-16.
21. Jones JM, Fleming-Dutra KE, Prill MM, et al. Use of nirsevimab for the prevention of respiratory syncytial virus disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices – United States, 2023. *Morbidity and Mortality Weekly Report* 2023;72:920-5.
22. Esposito S, Abu-Raya B, Bonanni P, et al. Coadministration of anti-viral monoclonal antibodies with routine pediatric vaccines and implications for nirsevimab use: a white paper. *Frontiers in Immunology* 2021;12:708939.
23. Muller WJ, Madhi SA, Seoane Nunez B, et al. Nirsevimab for prevention of RSV in term and late-preterm infants. *New England Journal of Medicine* 2023;388:1533-4.
24. US Food and Drug Administration. [Drug safety-related labeling changes \(SrLC\): Beyfortus](#). 2024. (Accessed February 2024).
25. Drysdale SB, Cathie K, Flamein F, et al. Nirsevimab for prevention of hospitalizations due to RSV in infants. *New England Journal of Medicine* 2023;389:2425-35.
26. Ernst C, Bejko D, Gaasch L, et al. Impact of nirsevimab prophylaxis on paediatric respiratory syncytial virus (RSV)-related hospitalisations during the initial 2023/24 season in Luxembourg. *Eurosurveillance* 2024;29:1.
27. Lopez-Lacort M, Munoz-Quiles C, Mira-Iglesias A, et al. Early estimates of nirsevimab immunoprophylaxis effectiveness against hospital admission for respiratory syncytial virus lower respiratory tract infections in infants, Spain, October 2023 to January 2024. *Eurosurveillance* 2024;29:1.
28. Moline H, Tannis A, Toepfer A, et al. Early estimate of nirsevimab effectiveness for prevention of respiratory syncytial virus-associated hospitalization among infants entering their first respiratory syncytial virus season — New Vaccine Surveillance Network, October 2023–February 2024. *Morbidity and Mortality Weekly Report* 2024;73:209–14.