



National Immunisation Advisory Committee

RECOMMENDATIONS FOR THE PASSIVE IMMUNISATION OF INFANTS AGAINST
RESPIRATORY SYNCYTIAL VIRUS (RSV) DURING THE 2024/2025 SEASON

NIAC | 16.04.2024

About NIAC

NIAC membership includes nominees from the Royal College of Physicians in Ireland, its Faculties and Institutes, the Royal College of Surgeons in Ireland, the Irish College of General Practitioners, the National Immunisation Office, the Nursing and Midwifery Board of Ireland, the Infectious Diseases Society of Ireland, the Travel Medicine Society, the National Virus Reference Laboratory and lay members. Meetings are attended by representatives from the Department of Health and the HSE. Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

[NIAC](#) considers the evidence about vaccines and provides advice to the Chief Medical Officer and the Department of Health. The Department and the Minister for Health make policy decisions on vaccines which are implemented by the Health Service Executive.

RECOMMENDATIONS FOR THE PASSIVE IMMUNISATION OF INFANTS AGAINST RSV DURING THE 2024/2025 SEASON

1. NIAC recommends the passive immunisation with nirsevimab of all infants who are born during the RSV season. These infants should receive nirsevimab ideally prior to discharge home from a maternity hospital.
2. NIAC recommends the passive immunisation with nirsevimab of all [*high-risk infants](#) aged ≤ 12 months at the start of their first RSV season. These infants should receive nirsevimab prior to the start of the RSV season.
3. NIAC recommends the passive immunisation with nirsevimab of all infants who are aged ≤ 6 months at the start of the RSV season. These infants should receive nirsevimab prior to the start of the RSV season.
4. NIAC recommends the passive immunisation with nirsevimab of all ex-preterm infants under 24 months of age with [†] Chronic Lung Disease in their second season RSV season. Infants who will be severely immunocompromised during the RSV season may also be considered for nirsevimab in consultation with their treating specialist. These infants should receive nirsevimab prior to the start of the RSV season.
5. In the event of short supply or programmatic limitations youngest infants (those born during the RSV season) and [*high-risk infants](#) in their first RSV season should be prioritised.
6. [‡] Neonates with prolonged hospitalisation from birth due to prematurity or other reasons should receive nirsevimab shortly before discharge from hospital if they are being discharged during or shortly before the RSV season.
7. The RSV season in Ireland typically starts in calendar weeks 38-40 and ends around calendar week 8 of the following year. Assuming the 24/25 season follows a similar pattern, the programme should start in late September 2024 and finish at the end of February 2025. If no catch-up program is planned, an earlier start to the programme (September 1st) should be considered to capture those who will be aged under three months at the peak of the RSV season. The definitive end date for the program should be determined by levels of circulating RSV and may need to be adjusted.
8. [§]Nirsevimab should be administered as follows:
 - Infants < 5 kg: A single dose of 50 mg administered intramuscularly
 - Infants ≥ 5 kg: A single dose of 100mg administered intramuscularly
 - Children up to 24 months entering their second season: 200 mg given as 2 x 100mg intramuscular injections.

Recommendations may be updated when more information becomes available.

* Infants currently eligible for palivizumab as outlined in Chapter 18a of NIAC Immunisation Guidelines of Ireland.

† Children with CLD (defined as those who required at least 28 days of supplemental oxygen after birth) and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid, or diuretic therapy) for 6 months preceding the RSV season.

‡ Earlier inpatient administration may be considered if infant is considered at risk of RSV exposure in hospital. 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.

§ For additional dosing recommendations in those post cardiac surgery requiring cardiopulmonary bypass please consult the [SPC](#).

1. EXECUTIVE SUMMARY

- In October 2023 NIAC recommended the passive immunisation of all infants against RSV.
- NIAC assessed two products, nirsevimab, a monoclonal antibody and RSV Pre-F vaccine given in pregnancy. Both products have acceptable safety and efficacy profiles.
- Nirsevimab, was recommended and given to infants in Spain, France, Luxembourg, and the United States during the 2023/2024 RSV season.
- Early real-world effectiveness data from Spain, Luxembourg, and the US suggest that nirsevimab is 80-90% effective in preventing RSV hospitalisation in infants.
- No safety concerns for nirsevimab have emerged post-marketing.
- Uptake of nirsevimab in Galicia in Spain was: 93% in infants born during the season; and 80% in infants who were ≤ 6 months old at the start of the season and offered catch-up immunisation.
- Maternal RSV Pre-F vaccine was also recommended in the United States.
- There are no real-world effectiveness data yet available for the RSV Pre-F maternal vaccine.
- RSV again circulated in high levels in Ireland in the 2023/2024 season. Between week 40 2023 and week 9 2024 there were 1,397 RSV hospitalisations in infants under one year of age. Hospitalisation rate was highest in those under 6 months of age. There were 118 paediatric intensive care unit (PICU) admissions in infants under one year of age attributed to RSV.
- The 2023/2024 season started around week 38 and peaked at week 48. This was similar to the 2022/2023 season. Prior to the COVID-19 pandemic, season onset and peak were later, typically peaking at week 51 or 52.
- There are some children that may benefit from nirsevimab in their second RSV season. The safety of nirsevimab when given to children under two years of age with chronic lung disease (CLD) or congenital heart disease (CHD) in their second RSV season was demonstrated in a phase 3 clinical trial. There are no clinical efficacy or effectiveness data for nirsevimab administration in the second RSV season for any patient cohort.
- In Ireland, palivizumab is currently recommended for children in their second RSV season with CLD who continue to require medical treatment for six months prior to the start of the RSV season. Palivizumab may also be considered for children who will be profoundly immunocompromised during their second RSV season.
- Certain other cohorts of patients such as those with haemodynamically significant congenital heart disease (HS-CHD) and those with certain neuromuscular disorders are also at increased risk of severe RSV during their second season and may benefit from nirsevimab. The evidence for benefit of RSV passive immunisation in these patient cohorts is uncertain and thus international practice varies.

2. INTRODUCTION

In October 2023, NIAC recommended the passive immunisation of all infants against RSV during their first RSV season. The Committee reviewed the available evidence on two forms of passive immunisation for infants against RSV which are authorised in the EU; a long-acting monoclonal antibody nirsevimab (Beyfortus, Sanofi) which can be administered to the infant directly, and a maternal vaccine RSVpreF (Abrysvo, Pfizer) which can provide infant protection through transplacental antibody transfer. NIAC concluded that both products have acceptable safety and efficacy profiles but that further analysis of cost effectiveness and programmatic considerations including likely uptake were required to determine the most appropriate RSV passive immunisation strategy for Irish infants.

Nirsevimab was implemented in Spain, France and Luxembourg in the 2023/2024 season. In the US both options, nirsevimab and RSV preF maternal vaccine were recommended. A healthcare technology assessment to examine the optimal long-term strategy for RSV prevention in Ireland has been requested. However, such assessments take time and the significant burden of infection in young infants warrants interim specific recommendations for the coming 2024/2025 season. The Committee reviewed available real-world data from the 2023/2024 season with a view to making specific recommendations for the 2024/2025 season.

3. EPIDEMIOLOGY

The epidemiology of RSV in Ireland is described in detail in the 2023 [recommendations](#) for RSV passive immunisation and vaccination. RSV continued to circulate in high levels during the 2023/2024 season. There was a total of 1,397 hospital admissions and 118 PICU admissions in infants under one year of age. Rates of hospitalisation were highest in those under 6 months of age. (Table 1) 107/118 (91%) of notified RSV ICU admission under 12 months of age were under 6 months of age and 88/118 (81%) were under 3 months of age. This is consistent with international data that demonstrates increased risk of RSV hospitalisation in those under 6 months of age.^{1,2}

Table 1. RSV hospitalization rates in children under 2 years of age in Ireland. Source: HPSC.

Age	2022/2023 season (week 40 2022-39)			2023/2024 season (week 40 2023-9)		
	Number	Rate per 100,000 population	Denominator	Number	Rate per 100,000 population	Denominator
< 6 months	834	2886.0	28898	1017	3519.3	28898
≥ 6 months	290	1003.5	28898	380	1315.0	28898
1-2 years	500	432.4	115630	623	538.8	115630

Infants at increased risk of severe RSV infection

Infants born before 30 weeks' gestation, preterm infants with CLD of prematurity, certain infants with HS-CHD, infants with a pulmonary abnormality or neuromuscular disease that impairs their ability to clear upper airways secretions and those with severe immunocompromise are at increased risk of severe RSV disease in their first season and are currently offered RSV prophylaxis with palivizumab in their first RSV season.³

Risk of RSV in the second year of life

There are limited data on the epidemiology of RSV in infants during their second RSV season in Ireland. During the 2023/2024 season there were 134 RSV ICU admissions notified to the HPSC in children under 4 years of age. Sixteen (12%) of these were aged 1-4 years. Data on comorbidities in those admitted to ICU during the 2023/2024 is currently being collected and will be shared with NIAC once available. Infants with Chronic Lung Disease and infants with severe immunocompromise are currently offered RSV prophylaxis with palivizumab in their second RSV season.³

Timing of the RSV season

In 2023/2024, the RSV season followed a similar pattern to the 2022/2023 season. The season started around week 36 and peaked at week 48 with 984 notified cases. Since week 9 of 2024 there have been less than 30 notified cases per week. Prior to the COVID-19 pandemic, the RSV season peaked and ended slightly later, and it is likely that there may be a drift back to prior patterns over time.

4. SAFETY

Nirsevimab was authorised in the European Union (EU) based on safety and efficacy data from three clinical trials. Since authorisation, a pragmatic randomised controlled trial (HARMONIE) assessed safety and efficacy in healthy infants. Nirsevimab displayed an acceptable safety profile in all trials. Safety data were previously described in detail in the 2023 [recommendations](#). No additional safety concerns have emerged during roll out for the 2023/2024 season in Spain, France, Luxembourg, or the United States.

Nirsevimab is currently authorised for use in the EU in infants in their first RSV season. The Food and Drug Administration (FDA) has approved its use in children up to 24 months who remain vulnerable to severe RSV disease through their second RSV season. The European Medicines Authority (EMA) is reviewing such an extension of indication to include the second RSV season, with the outcome anticipated in advance of the 2024/2025 season.

The MEDLEY trial enrolled infants with CLD or CHD who were eligible for palivizumab in the second RSV season according to local and national protocols. Those randomised to receive nirsevimab in the first season, received 200mg of nirsevimab in their second season followed by four once monthly doses of placebo (N/N). Those randomised to receive palivizumab in the first season, were re-randomized 1:1 to receive 200mg of nirsevimab followed by placebo (P/N) or five once monthly doses of palivizumab (P/P) in the second season. Adverse events (AE) and antidrug antibodies (ADA) were the primary safety outcomes. The incidence of AEs during the second season was similar across treatment groups (P/P: 29 [69.0%]; P/N: 29 [72.5%]; N/N: 126 [70.0%]), with no deaths or AEs of special interest reported. The ADA incidence was low in participants who received (N/N), occurring in 1/90 participants (1.1%) at Day 31 and in 0/158 participants at Day 151; no participant with post baseline ADA in the first season had detectable ADA in the second season.⁴

Coadministration with Routine Childhood Vaccines

Based on limited data from clinical trials, coadministration of nirsevimab with routine vaccines resulted in a similar rate of adverse events compared with administration of routine vaccines alone. Nirsevimab is not expected to interfere with the immune response to other routine childhood immunizations.⁵

5. EFFICACY AND EFFECTIVENESS

Efficacy of nirsevimab and RSV Pre-F was detailed in the 2023 [recommendations](#). Direct comparisons could not be made due to differences in trial design and outcomes. Early effectiveness data for nirsevimab has been reported in the US and Spain. In the US, effectiveness of nirsevimab was calculated using data from the New Vaccine Surveillance Network (NVSN), a population-based, prospective surveillance platform for acute respiratory illness (ARI) in infants, children, and adolescents aged <18 years. Infants were eligible for analysis if they were aged <8 months as of October 1, 2023, or born after October 1, 2023, were hospitalised with ARI during October 1, 2023– February 29, 2024, and had verified nirsevimab status. Six hundred and ninety-nine infants across four sites met inclusion criteria. Nirsevimab effectiveness was 90% (95% CI: 75–96) against RSV-associated hospitalisation. This result may not accurately reflect effectiveness in the general population, as due to supply issues in the US, receipt of nirsevimab was more frequent among infants with high-risk medical conditions than those without these conditions (46% versus 6%, $p<0.001$). Additionally, this is an early estimate, in this analysis, the median interval from receipt of nirsevimab was 45 days. Effectiveness over the full season may be lower due to waning levels of protective antibody over time.⁶

In Catalonia in Spain, a retrospective cohort study, using routinely collected electronic health data from October 1, 2023 to January 31, 2024, included all infants born between April and September 2023. Eighty seven percent of infants received nirsevimab by the end of the study period. The

incidence rate of hospital admissions due to RSV bronchiolitis was 9.55 per 100,000 person days for those who did not receive nirsevimab versus 2.16 for those who received nirsevimab. Effectiveness against hospitalisation and ICU admission for bronchiolitis due to RSV was calculated at 87.6% and 90.1% respectively.⁷

In Luxembourg, nirsevimab was recommended to all those born during the RSV season and those born from 1 January 2023. Rates of hospitalisation during the 2022/2023 and 2023/2024 seasons were compared. Uptake of nirsevimab was estimated at 84% (1,277 doses for 1,524 births). There was a reduction of 69% in RSV hospitalisation in infants under 6 months of age. (232 vs 72)⁸

6. UPTAKE

NIAC previously highlighted that vaccine uptake will be a critical consideration in determining the best approach for delivering passive RSV immunisation to Irish infants. Prior to implementation in Europe during the 2023/2024 season it was unknown if a novel monoclonal antibody would be acceptable to parents. The experience in the 2023/2024 season in Spain suggests that very good uptake of nirsevimab is achievable. Uptake of nirsevimab in Galicia in Spain was 93% in infants born during the season and 80% in infants who were ≤6 months old at the start of the season and offered catch up immunisation during an intensive three-week program ran at the start of the season. An information campaign commenced in March 2022 and was considered critical to the success of the program.⁹ Historically uptake of neonatal vaccines in Ireland has been good. BCG vaccine was removed from the schedule in 2015 due to lack of availability but prior to this time uptake of BCG at birth was greater than 95%. While not a vaccine, vitamin K is an intramuscular injection given to all babies at birth in Ireland. National vitamin K uptake is not available, but data examined in the Rotunda Hospital where there are approximately 9,000 births annually estimates vitamin K uptake at 99.5%. While there has been a concerning decline in uptake of the primary childhood immunisation schedule, vaccine uptake in the first year of life is at least 85%. On the other hand, population-based sampling in Ireland from 2017-2018 estimated influenza vaccine uptake in pregnancy to be 61.7% (95% CI: 55.3-67.8) and pertussis uptake to be 49.9% (95% CI: 43.3–56.6).¹⁰ There is typically a lead in time for uptake of novel vaccines in pregnancy, and the relative lack of post-marketing safety data associated with the maternal vaccine, compared with nirsevimab may be an additional barrier to acceptance for the 2024/2025 season.

7. INTERNATIONAL POSITIONS

Table 2. Recommendations for nirsevimab use in the first and second RSV season in countries that implemented a programme for the 23/24 season.

Country	First RSV Season	Second RSV season
Spain ¹¹	<p>Infants born during the season.</p> <p>Infants ≤6 months at the start of the season.</p>	<p>Patients with haemodynamically significant congenital heart disease (HS-CHD).</p> <p>Bronchopulmonary dysplasia (BPD).</p> <p>Other pathologies on which one presumes a higher risk of RSV (e.g., severely immunosuppressed, inborn error of metabolism, neuromuscular illness, severe chronic pulmonary conditions, down syndrome, cystic fibrosis and those with palliative conditions).</p>
France ¹²	<p>Infants prior to discharge from maternity hospital from 15 Sept 2023 to end of Jan 2024.</p> <p>Infants born since 6 Feb 2023 at start of season (8 months).</p> <p>Infants and children in whom palivizumab is recommended.</p>	<p>Infants under 2 years of age who required treatment for BPD in the past 6 months or with HS-CHD.</p>
US ¹³	<p>Infants born during the RSV season.</p> <p>Infants ≤8 months at the start of the season.</p>	<p>Children with BPD who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before the start of the second RSV season.</p> <p>Children with severe immunocompromise.</p> <p>Children with cystic fibrosis who have either 1) manifestations of severe lung disease (previous hospitalisation for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable), or 2) weight-for-length <10th percentile.</p> <p>American Indian or Alaska Native children.</p>

Luxembourg ⁸	<p>Infants born between 1 October 2023 and 30 March 2024.</p> <p>Infants born after 1 Jan 2023 at the start of the season.</p>	Infants aged less than 24 months with comorbidities that increase their risk of severe RSV disease.
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8. DISCUSSION

RSV continues to place significant burden on children, their families, and paediatric health services in Ireland. The 2023/2024 season was similar in intensity to previous seasons. There are now two licenced products that could significantly reduce this burden. Following NIAC’s recommendations for the passive immunisation of all infants against RSV, a Health Technology Assessment was commenced to determine the optimal long-term strategy for RSV prevention in Ireland. While awaiting the outcome of this assessment, the burden of RSV in infants is such that all efforts should be made to implement an interim RSV prevention strategy for the coming 2024/2025 season. Given the planning required to implement such a program for the coming season, NIAC considered currently available post-marketing data. There is early real-world safety and effectiveness data available for nirsevimab that demonstrates that the product is effective, and feasible to implement. On the other hand, the maternal vaccine was not implemented in any European country this season, and thus similar effectiveness, real world safety and acceptability data are not yet available. The optimal long-term strategy for prevention of RSV in infants in Ireland is yet to be determined and will be informed by real world data and implementation experience with both nirsevimab and RSV Pre F maternal vaccine. However, there are currently more real-world safety, effectiveness, and acceptability data available for nirsevimab and thus NIAC recommends nirsevimab for the coming 2024/2025 season. NIAC will continue to review emerging data for both nirsevimab and maternal RSV PRE F vaccine and update recommendations accordingly.

NIAC recommends a passive immunisation programme with nirsevimab that includes both a ‘birth cohort’ (those born during the RSV season) and a ‘catch-up cohort’ (those aged under 6 months at the start of the RSV season). If immunisation of a catch-up cohort is not feasible for this season, the youngest infants and those high-risk infants that were previously eligible for palivizumab should be prioritised. The optimal timing of commencing a program for the 2024/2025 season will depend on whether a catch-up cohort is included. Given the duration of protection from nirsevimab is up to 6 months, if a catch-up program cannot be implemented for the 2024/2025 season an earlier start to the program should be considered so that infants who will be under three months at the peak of the season are protected.

Finally, there are a cohort of infants who will benefit from receipt of nirsevimab in their second season. Currently palivizumab use in the second season is restricted to those with chronic lung

disease or severe immunocompromise. NIAC recommends replacing palivizumab with nirsevimab in the second season for these infants. There may be other children such as those with haemodynamically significant congenital heart disease or those with neuromuscular disorders that would also benefit from nirsevimab in their second RSV season. NIAC is currently reviewing the indications for nirsevimab in the second season and will update recommendations once further data from the 2023/2024 season are available.

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