Work group considerations and clinical considerations for clesrovimab

Maternal and Pediatric RSV Session
Coronavirus and Other Respiratory Viruses Division

June 25, 2025

Outline

- Work group considerations and interpretations of uptake, safety, effectiveness, and impact studies
- Review of clinical considerations
  - Clesrovimab recommendations compared with nirsevimab
  - Clesrovimab storage, handling, and administration

Summary of RSV immunization effectiveness, uptake, and impact for the 2024-25 RSV season

- Nirsevimab was effective against RSV-associated emergency department encounters, hospitalization, and critical illness among infants in their first RSV season
- Maternal vaccination was effective against RSV-associated ED encounters and hospitalizations
- An estimated 57% of infants were either born to vaccinated mother or received nirsevimab
- Compared with prior to RSV immunization introduction, RSV-associated hospitalization rates were reduced by ~30–40% among eligible infants and by half among infants aged 0–2 months

Workgroup considerations on RSV immunization effectiveness, uptake, and impact

- The impact of RSV immunizations to decrease severe RSV disease in infants during the 2024–25 RSV season in the RSV-NET and NVSN networks is clear[1]
- Increasing uptake is important in order to further reduce burden of RSV disease
  - Higher impact has been seen in other countries that have attained higher uptake of these immunizations[2–6]
  - Important to maximize availability of RSV immunizations, including providing infant RSV antibody during birth hospitalization
  - The increase in birthing hospital enrolled in the Vaccine For Children (VFC) program is important, but challenges remain

RSV-NET RSV-Associated Hospitalization Surveillance Network; NVSN: New Vaccine Surveillance Network

[1]Patton 2025 MMWR [2] Bloomfield 2025 Medical Journal of Australia;[3]Dessers 2025 Belgian Journal of Paediatrics; [4]García-García 2025 Influenza and Other Respiratory Viruses; [5]Ares-Gomez 2024 Lancet ID; [6]Mazagatos 2024 Influenza Other Respir Viruses;

Summary of FAERS[1] postmarketing adverse events and medication errors reporting with nirsevimab

- During the reporting period since approval until March 31, 2025, the most frequently reported adverse events involved patients who developed RSV infections despite prior receipt of nirsevimab, and included signs, symptoms, or complications of these infections (e.g., bronchiolitis).
- No product safety labeling updates have been made since serious hypersensitivity reactions with nirsevimab were added on February 23, 2024.
- No additional safety signals have been identified at this time.
- Errors involving incorrect nirsevimab dose or incorrect product (e.g., adult vaccine being given to infant) continue to be reported.
- FDA will continue routine pharmacovigilance for nirsevimab.

[1]FDA Adverse Event Reporting System (FAERS) Database | FDA

Summary interpretation of Vaccine Safety Datalink nirsevimab study

- Study of 37,909 infants that received nirsevimab during 2024-2025 season using self-controlled risk interval
- No increased risk observed for seizures, immune thrombocytopenia (ITP), drug reactions, sepsis, or fever
- No cases of anaphylaxis and 18 (~0.05% of doses) cases of allergic reaction reported, primarily hives

Workgroup interpretation of nirsevimab safety

- FAERS and VSD safety data are reassuring
- Continued monitoring of safety important

FAERS: FDA Adverse Event Reporting System; VSD: Vaccine Safety Datalink; CSF: cerebrospinal fluid

Vaccine Safety Datalink maternal vaccine study summary

- Matched cohort with ~14,000 pairs of vaccinated-unvaccinated pregnant women
- No increased risk observed for most outcomes, including fever, fatigue, stroke, seizure, Bell's palsy, ITP, pulmonary embolism, preterm birth, infant being born small for gestational age, stillbirth
- Association of maternal RSV vaccine and HDP overall (adjusted odds ratio [aOR]: 1.09 [95% CI, 1.03–1.15]) and preeclampsia (aOR: 1.12 [95% CI, 1.03–1.21])
  - Severity of HDP similar among vaccinated and unvaccinated
  - Potential residual confounding (e.g., including parity in the propensity matching) and outcome misclassification due the difficulty in determining the timing of when HDP first occurs and lack of chart review

ITP: Immune Thrombocytopenic Purpura; HDP: hypertensive disorders of pregnancy

Work group interpretation of maternal vaccine Vaccine Safety Datalink study findings

- Overall study findings were reassuring, including lack of association of preterm birth and vaccination
- WG continues to feel that the benefits of maternal RSV vaccination clearly outweigh the potential risks
- WG was split on importance of the association of vaccination and HDP
  - Some were concerned that an imbalance of HDP was seen in multiple studies (phase 3 clinical trial, published retrospective cohort study, postmarketing study), and felt it was important that healthcare providers discuss the potential risk of HDP with pregnant women
  - Some were not concerned about this association since the effect size was small, and there was no increased severity in vaccinated vs. unvaccinated women with HDP and no overall association of vaccination with preterm birth; American College of Obstetricians and Gynecologists was in agreement with this opinion

HDP: hypertensive disorders of pregnancy

Infant RSV Antibody–Clesrovimab

- **Long-acting, monoclonal antibody manufactured by Merck**
- **Passive immunization**
- **Single-dose, manufacturer-filled syringe**
  - 105 mg/0.7 mL
  - Same dose for all infants regardless of weight

Proposed use of clesrovimab versus nirsevimab

- **Clesrovimab and nirsevimab** recommendations would be the same for use in **infants younger than 8 months of age** born during or entering their first RSV season
  - No preferential recommendation for use of clesrovimab versus nirsevimab
- **Only nirsevimab**[1] recommended for **children ages 8 through 19 months who are at increased risk of severe RSV disease** and entering their second RSV season
  - Infants eligible to receive nirsevimab when entering second RSV season could have received nirsevimab or clesrovimab for first RSV season
  - No effectiveness or safety concerns for using clesrovimab for first RSV season and nirsevimab for second RSV season

[1] Clesrovimab not recommended for this age group because it is not approved by FDA for this indication

Proposed recommendations for use of RSV antibody immunizations (nirsevimab or clesrovimab) in infants < 8 months

- **One dose for infants younger than 8 months of age born during or entering their first RSV season (administration during October through March in most of the continental U.S.) if:**
  - The mother did not receive RSV vaccine during pregnancy
  - The mother's RSV vaccination status is unknown
  - The infant was born less than 14 days after maternal RSV vaccination

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 | MMWR

When RSV antibody may be considered for infants born to vaccinated mothers[1]

- Born to mothers who may not mount an adequate immune response to vaccination (e.g., immunocompromising conditions)
- Born to mothers who have conditions associated with reduced transplacental antibody transfer (e.g., living with HIV infection)
- Infants who have procedures leading to loss of maternal antibodies (e.g., cardiopulmonary bypass, extracorporeal membrane oxygenation [ECMO], exchange transfusion)
- Infants with substantially increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease, ICU admission with oxygen requirement at discharge)

RSV Immunization Guidance for Infants and Young Children | RSV | CDC | ICU: intensive care unit; [1] For infants aged <8 months during their first RSV season

Choose one product to prevent severe RSV disease in infants

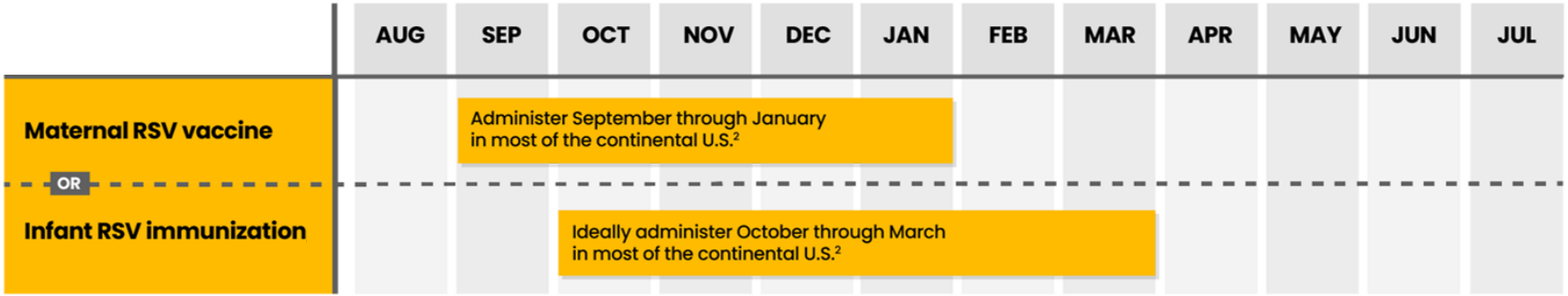
Maternal RSV vaccination
- Pfizer Abrysvo

- or -

Infant RSV antibody
- Nirsevimab
- Clesrovimab

Most infants will *not* need both maternal vaccination and an RSV antibody.

Infant RSV antibody and maternal vaccination have different administration windows to provide optimal protection to the infant



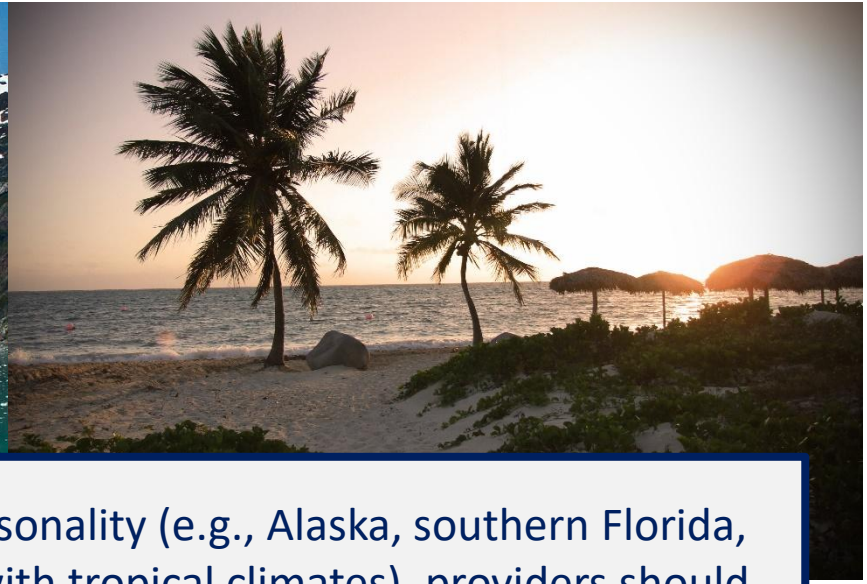
[2] In jurisdictions with RSV seasonality that differs from most of the continental United States, including Alaska, southern Florida, Guam, Hawaii, Puerto Rico, U.S.-affiliated Pacific Islands, and U.S. Virgin Islands, providers should follow state, local, or territorial guidance. However, nirsevimab may be administered outside of routine seasonal administration (ie., October through March) based on local RSV activity and other special circumstances. For infants born during October through March, nirsevimab should be administered in the first week of life—ideally during the birth hospitalization.

Optimal timing for infant RSV administration is shortly before the RSV season

Administration should be targeted shortly before the start of their first RSV season and continued during the season for those who have not received a dose

For infants born shortly before or during the RSV season, immunize within 1 week of birth, ideally during the birth hospitalization

RSV seasonality differs based on climate



In jurisdictions with differing RSV seasonality (e.g., Alaska, southern Florida, Puerto Rico, and other jurisdictions with tropical climates), providers should follow state, local, or territorial guidance on the timing of administration.

RSV Immunization Guidance for Infants and Young Children | RSV | CDC

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 | MMWR

Administer the correct RSV immunization product

Infants and Some Young Children

Infant RSV antibody* only

⚠ Do not administer Abrysvo, Arexvy, or mResvia to infants or children.

During Pregnancy

Abrysvo (Pfizer) only

⚠ Do not administer RSV antibody*, Arexvy, or mResvia during pregnancy.

Older Adults

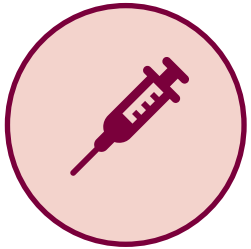
Abrysvo (Pfizer)
Arexvy (GSK)
mResvia (Moderna)

⚠ Do not administer RSV antibody* to older adults.

*Includes nirsevimab, clesrovimab, and palivizumab.

Clesrovimab (or nirsevimab) and palivizumab

- **If clesrovimab or nirsevimab is given to an infant or child…**



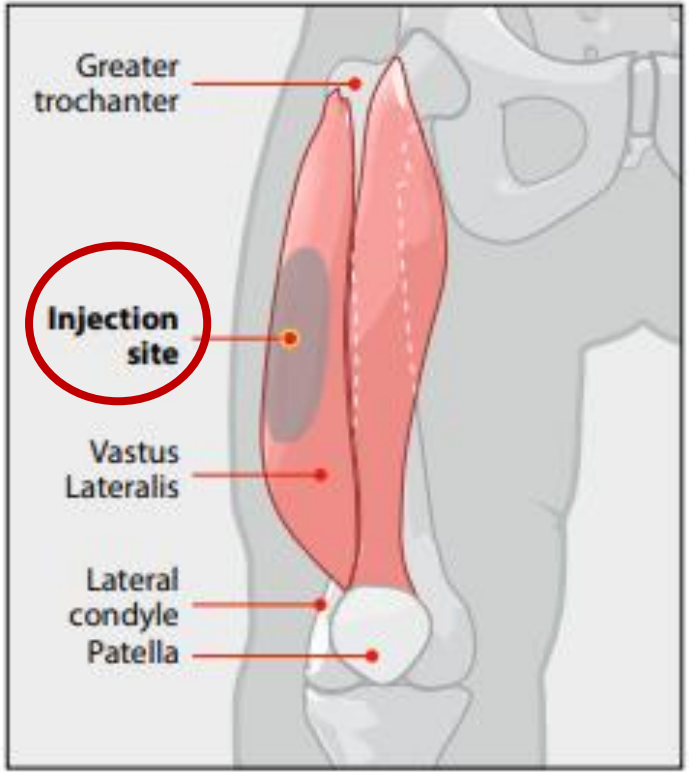
Clesrovimab* or nirsevimab

…then do *not* give palivizumab during the same RSV season.

Palivizumab

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 | MMWR, AAP Recommendations for the Prevention of RSV Disease in Infants and Children | Red Book Online | American Academy of Pediatrics

Infant RSV antibody administration



- **Route**
  - Intramuscular injection
- **Site**
  - Vastus lateralis muscle of anterolateral thigh
  - The gluteal muscle should **not** be used.
- **Coadministration**
  - Simultaneous administration with vaccines is acceptable.

Beyfortus Prescribing Information (fda.gov) Enflonsia Prescribing Information.pdf

Clesrovimab storage and handling

Store refrigerated between 2°C and 8°C (36°F and 46°F).

Use within 48 hours of removing from refrigerator.

- May be kept at room temperature, between 20°C and 25°C (68°F and 77°F), for a maximum of 48 hours

Do *not* freeze.

Do *not* shake.

Protect from light.

Enflonsia Prescribing Information.pdf

How to report adverse events after infant RSV antibody administration

- **If RSV antibody is administered alone:**
  - Report suspected adverse events (AEs) to MedWatch
  - www.fda.gov/medwatch

- **If RSV antibody is administered simultaneously with any vaccine:**
  - Report suspected AEs to Vaccine Adverse Event Reporting System (VAERS)
  - vaers.hhs.gov
  - Additional reporting to MedWatch is not necessary

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.