Proposed clinical considerations for clesrovimab

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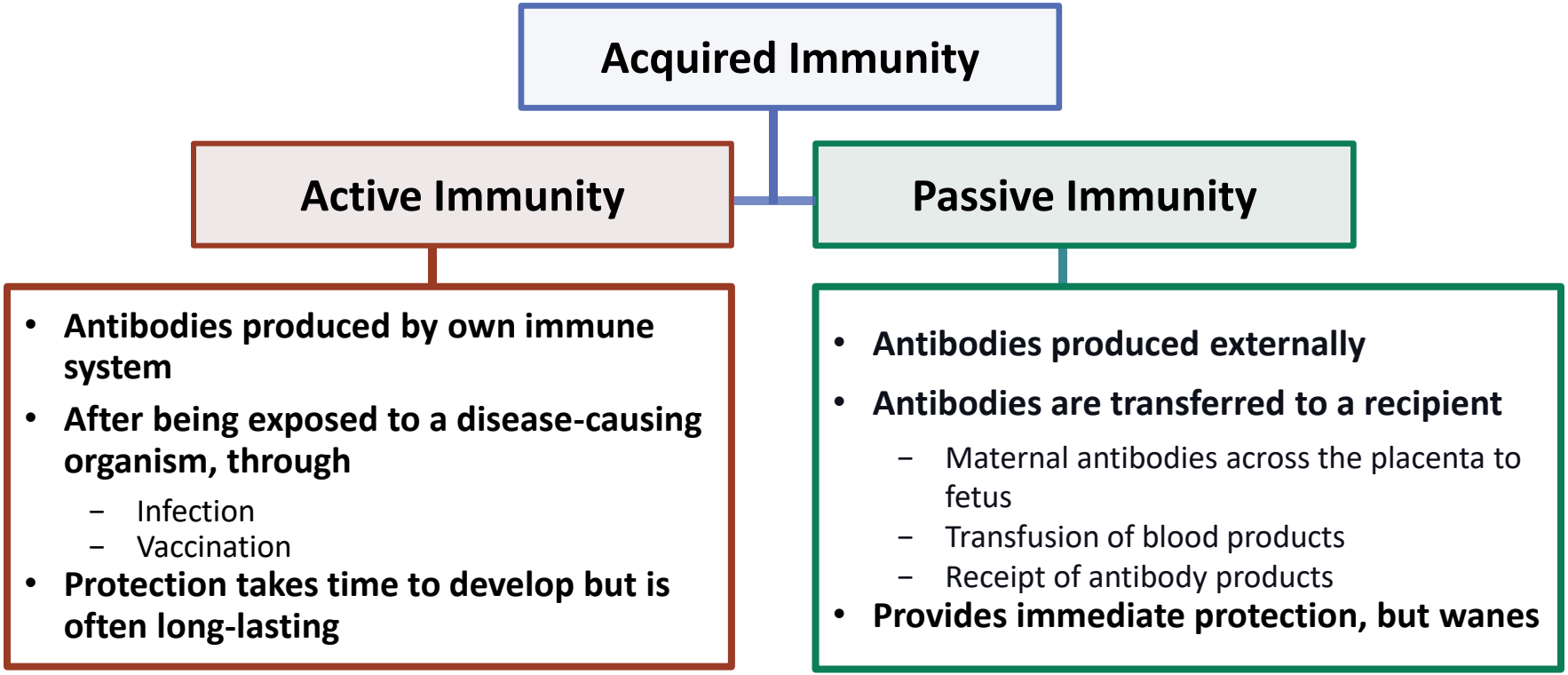
Outline

- Similarities and differences in use of clesrovimab vs nirsevimab
- Review of indications, timing, and dosing
- Storage, handling, and administration

Active and Passive Immunity



Chapter 1: Principles of Vaccination | Pink Book | CDC

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** 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

Proposed Recommendations for Use of RSV Antibody Immunizations (nirsevimab or clesrovimab*) in Infants

- **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

*Clesrovimab is not currently approved by FDA or recommended by ACIP

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

- 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

Timing of Infant RSV Antibody Administration

- **For infants born October through March**
  - Administer in the first week of life—*ideally during the birth hospitalization*.
  - Infants with prolonged birth hospitalizations due to prematurity or other causes should be immunized shortly before or promptly after discharge.
  - If not given in the hospital, administer in outpatient settings.
- **For infants born April through September**
  - *Optimal timing is shortly before the RSV season begins* (i.e., October through November)

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; Beyfortus Prescribing Information (fda.gov)

Infant RSV Antibody Timing by Birth Month: First RSV Season in Most of Continental U.S.

Infants[1] born October through March are recommended to receive an RSV antibody within one week of birth, ideally during birth hospitalization.

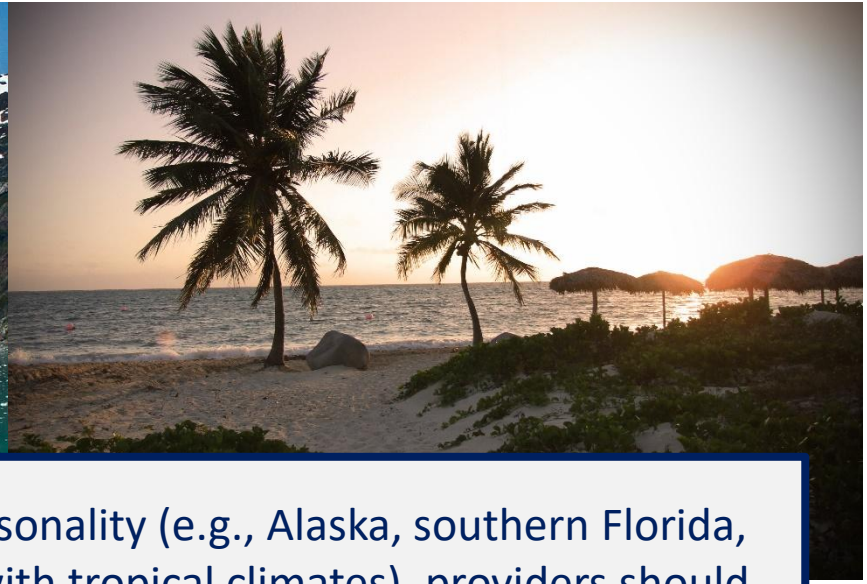
October | November | December | January | February | March | April | May | June | July | August | September

Infants[1] born April through September are recommended to receive an RSV antibody shortly before the RSV season begins.

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,

[1] **Most infants born to vaccinated mothers are not recommended to receive an RSV antibody**

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

Seasonal Administration Exceptions

- **Recommendations for the timing of infant RSV antibody administration are flexible**
- **Health care providers may use clinical judgment to determine when to give infant RSV antibodies outside of October through March.**
- **Special circumstances to consider:**
  - Travel to areas with increased RSV activity
  - Concern that patient may not return for a visit when RSV antibodies should ideally be administered

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

Work group considerations on RSV antibody administration flexibility

- Recommended that CDC provide national recommendations with flexibility for state and local jurisdictions but avoid providing region-specific recommendations due to the complexity of implementation
- Supported current CDC recommendations on flexibility, but desired additional guidance on how to support decisionmakers for implementing flexibility
- Making annual changes to the timing of RSV antibody administration would be complicated for jurisdictions and providers
  - Before 2020, the RSV season was fairly predictable with only minor year-to-year variations. RSV seasonality appears to be returning to pre-pandemic patterns, but additional years of data are needed to verify this
  - Since real-time RSV data trends can be difficult to interpret, state or local jurisdictions may also choose to alter the timing of RSV antibody administration based on local historical patterns of RSV seasonality

Work group considerations on RSV antibody administration flexibility (2)

- Not all RSV disease can be prevented, and for most of the Unites States, administration of RSV antibody to newborns during October through March will protect infants in their first few months of life during the peak of the RSV season
- There is no evidence-based test positivity threshold above which RSV antibody is recommended
  - 3% is used to define the RSV season for surveillance purposes using the National Respiratory and Enteric Virus Surveillance System (NREVSS) PCR test positivity
  - 3% is not a threshold to guide RSV antibody administration
- Use of local RSV data may be the best source to guide action
  - Test positivity can differ by system based on testing practices and patient population
  - Other sources of data, including trends in RSV hospitalizations or the total numbers of positive tests can be considered

Considerations for starting RSV antibody administration prior to October

- Potential advantages
  - Can provide more time for infants to receive an RSV antibody prior to the start of the RSV season
  - Potentially useful for jurisdictions with early seasonality
- Potential disadvantages
  - Protection is expected to be greatest shortly after administration and decrease over time, but it is unknown how quickly protection decreases
  - Infants who receive an antibody in September could have reduced protection by the peak of the season and towards the end of the season

Considerations for extending RSV antibody administration past March

- Potential advantages
  - Infants born in April could be immunized shortly after birth, providing protection during their first few months of life when they are highest risk for severe disease
- Potential disadvantages
  - The risk of exposure and infection during the tail end of the RSV season might be low
  - Most infants born to unvaccinated mothers are recommended to receive only one dose of an RSV antibody
  - Most infants who receive a dose in April would not be recommended to receive a dose in October; a dose in October could provide protection for an entire RSV season

Considerations for administration of infant RSV antibody outside of October through March

- Because the timing of the onset, peak, and decline of RSV activity varies geographically, public health authorities or regional medical centers may provide additional guidance for infant RSV antibody administration for their jurisdictions or patient populations
- In areas with clear increases in RSV transmission prior to October, administration prior to October can be considered
- In areas with high RSV transmission through the end of March, administering to newborns past March can be considered
- In areas with historical data suggesting consistent RSV transmission beginning prior to October or consistent high RSV transmission past the end of March, the standard months of seasonal administration can be modified according to expected annual patterns

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.

*Proposed: clesrovimab is not currently approved by FDA or recommended by ACIP

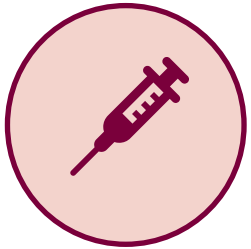
Considerations for Counseling Patients Regarding Maternal RSV Vaccine and Infant RSV Antibodies

Maternal RSV vaccine 	Immediate protection for baby after birth No injection for the infant Potentially reduced protection in some situations (e.g., mother is immunocompromised or infant born soon after vaccination) Potential risk for hypertensive disorders of pregnancy
Infant RSV antibody 	Direct receipt of antibodies rather than relying on transplacental transfer Protection may wane more slowly than maternal RSV vaccine Side effects are usually mild and resolve quickly; hypersensitivity reactions are uncommon but have been reported Delayed administration could leave the infant unprotected[1]

[1] Infants born during October through March should be administered RSV antibody in the first week of life – ideally during the birth hospitalization.
Use of the Pfizer Respiratory Syncytial Virus Vaccine During Pregnancy for the Prevention of Respiratory Syncytial Virus–Associated Lower Respiratory Tract Disease in Infants: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023 | MMWR ; Evaluation of Preterm Birth and SGA at Birth - October 2024 ACIP meeting

Clesrovimab (or Nirsevimab) and Palivizumab

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



Clesrovimab* or nirsevimab

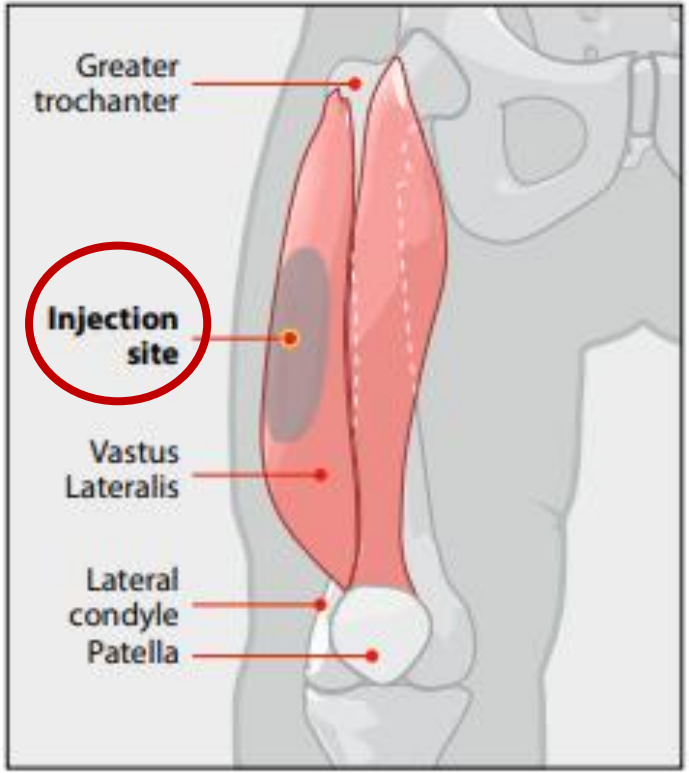
…then do *not* give palivizumab during the same RSV season.

Palivizumab

*Proposed: clesrovimab is not currently approved by FDA or recommended by ACIP

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)

Expected 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.

*Not final as clesrovimab has not yet been approved. It is expected that storage and handling of clesrovimab will be similar the requirements of nirsevimab; Nirsevimab Package Insert (fda.gov)

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 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 is not currently approved by FDA or recommended by ACIP

Proposed Recommendation on 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.