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Physician FAQ on Medications Available for the 2023-24 Respiratory Syncytial Virus (RSV) Season

Texas Medical Association
Physicians Caring for Texans

During Texas' 2023-24 RSV season, physicians may choose to treat their patients who may be vulnerable to severe RSV disease by offering various prophylactic medications. TMA has compiled this FAQ with information from the Centers for Disease Control and Prevention (CDC), American Academy of Pediatrics (AAP), CDC Advisory Committee on Immunization Practices (ACIP), the U.S. Food and Drug Administration (FDA), and other resources to cover some of the basic questions on the RSV medications currently available. This FAQ does not address all the information contained in those resources, and physicians should review the underlying resources in full before treating their patients.

Palivizumab (Synagis)

Palivizumab is a monoclonal antibody product approved by FDA for children under 24 months of age with certain conditions that place them at high risk for severe RSV disease.

What are the indications and usage for palivizumab?

Per FDA, palivizumab is indicated for the prevention of serious lower respiratory tract disease caused by RSV in children at high risk of RSV disease. Safety and efficacy were established for:

- Infants born prematurely (at or before 35 weeks) at the beginning of RSV season;
- Infants who have bronchopulmonary dysplasia, a chronic lung condition, that needed medical treatment within the past six months, and who are aged 24 months or less at the beginning of RSV season; and
- Infants born with certain types of heart disease and who are aged 24 months or less at the beginning of RSV season.

AAP provides additional at-risk population-focused guidance for palivizumab.

What are the dosing recommendations, and how is palivizumab administered?

According to FDA, the recommended dose for palivizumab is 15 mg per kg of body weight given monthly by intramuscular injection. FDA says the first dose for palivizumab should be administered before the beginning of the RSV season, and the remaining doses should be administered monthly throughout the RSV season. Children who develop an RSV infection should continue to receive monthly doses throughout the RSV season.

Palivizumab has been FDA-approved since 1998. See FDA's prescribing information.

An FAQ addressing the administration of both palivizumab and nirsevimab can be found later in this document.

Nirsevimab (Beyfortus)

Nirsevimab is a long-acting monoclonal antibody product approved by FDA that is used in a similar manner to routine vaccinations and provides passive immunization.

Who is recommended to receive nirsevimab?

- Infants born before/during RSV season: CDC recommends nirsevimab for infants aged less than 8 months who are born shortly before or entering their first RSV season (typically fall through spring) if:
  - » The mother did not receive RSV vaccine during pregnancy;
  - » The mother's RSV vaccination status is unknown; or
  - » The infant was born within 14 days of maternal RSV vaccination.
- At-risk infants and children: ACIP also recommends nirsevimab for infants and children aged 8-19 months who are at increased risk for severe RSV disease. Per ACIP, those considered at an increased risk are:
  - » Children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the six month period before the start of the second RSV season;
  - » Children with severe immunocompromise;
  - » Children with cystic fibrosis who have either (1) manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable), or (2) weight-for-length under the 10th percentile; and
  - » American Indian or Alaska Native children.
- Infants in rare circumstances: Per CDC, even when the mother received an RSV vaccine, nirsevimab can be considered in rare circumstances when the physician believes the potential benefit of giving it is warranted. Those in such circumstances include, but are not limited to:
  - » Infants born to mothers who may not mount an adequate immune response to RSV vaccination (e.g., people with immunocompromising conditions);
  - » Infants born to mothers who have medical conditions associated with reduced transplacental antibody transfer (e.g., people living with HIV infection);
  - » Infants who have undergone cardiopulmonary bypass or extracorporeal membrane oxygenation (ECMO), leading to loss of maternal antibodies; and

- » Infants with substantial increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease, intensive care admission with a requirement of oxygen at discharge).

Note, there are currently no studies of infants who have been given nirsevimab after their mother received an RSV vaccine, according to CDC. However, the available evidence does not suggest a higher risk for adverse events in that situation, CDC says. Children and adults (including those who are pregnant) are frequently exposed to circulating RSV viruses. Following RSV infection, pregnant individuals produce antibodies that are transferred to infants across the placenta, and many of the babies in the nirsevimab study had maternal RSV antibody. CDC says it and FDA will monitor safety of both products.

What are CDC and AAP recommendations in the context of the 2023-24 RSV season's limited supply of nirsevimab?

On Oct. 23, 2023, CDC issued a Health Alert Network Health Advisory to provide options for clinicians to protect infants from RSV in the context of a limited supply of nirsevimab:

- Prioritize available nirsevimab 100 mg doses for infants at the highest risk for severe RSV disease:
  - » Young infants (aged younger than 6 months); and
  - » Infants with underlying conditions that place them at highest risk for severe RSV disease:
    - Premature birth at less than 29 weeks' gestation;
    - Chronic lung disease of prematurity;
    - Hemodynamically significant congenital heart disease;
    - Severe immunocompromise;
    - Severe cystic fibrosis (either manifestations of severe lung disease or weight-for-length less than the 10th percentile);
    - Neuromuscular disease; or
    - Congenital pulmonary abnormalities that impair the ability to clear secretions.
- Note that recommendations for using 50 mg doses remain unchanged at this time. Avoid using two 50 mg doses for infants weighing 5 kg or more (11 pounds or more) to preserve supply of 50 mg doses for infants weighing less than 5 kg (less than 11 pounds). Physicians should be aware that some insurers may not cover the cost of two 50 mg doses for an individual infant.
- Suspend using nirsevimab in palivizumab-eligible children aged 8-19 months for the 2023-24 RSV season. These children should receive palivizumab according to AAP recommendations.
- Continue to offer nirsevimab to American Indian and Alaska Native children aged 8-19 months who are not palivizumab-eligible and who live in remote regions, where transporting children with severe RSV for escalation of medical care is more challenging or in communities with known high rates of RSV among older infants and toddlers.
- During prenatal care, discuss potential nirsevimab supply concerns when counseling pregnant patients about RSVpreF vaccine (ABRYSVO, Pfizer) as maternal vaccination is effective and will reduce the number of infants requiring nirsevimab during the RSV season.

What are the CDC dosing recommendations, and how is nirsevimab administered?

- For infants younger than 8 months: One dose of 50 mg for infants weighing less than 5 kg (less than 11 pounds) and 100 mg for infants weighing 5 kg or more (11 pounds or more) given as a single injection.
- For infants aged 8-19 months who are at increased risk for severe RSV disease: One dose of 200 mg, administered as two 100 mg injections given at the same time at different injection sites (per ACIP).

When is the recommended time to start administering nirsevimab?

ACIP and AAP recommend administration "shortly before or during the season," which usually occurs between October and March. However, it may be given to eligible infants and toddlers who have not yet received a dose at any time during the season.

AAP recommends that infants born shortly before and during the RSV season receive nirsevimab within the first week of life, including in hospital settings. Eligible children not born during the season should be recalled to receive nirsevimab towards the beginning of the season to avoid them becoming ineligible (per AAP, Wisconsin Chapter).

Month of birth and recommended timing of nirsevimab immunization (CDC)	
October-March	Within one week of birth
April-September	Beginning in October, for example at a 2-, 4-, or 6-month well-child visit

What is the efficacy of nirsevimab, and how long does the RSV protection conferred by nirsevimab last?

According to CDC, the protection from one dose of nirsevimab is expected to last at least five months, about the length of an RSV season.

CDC's *Morbidity and Mortality Weekly Report* (*MMWR*) reported 79% efficacy against RSV-associated lower respiratory tract infection (LRTI); 80% efficacy in preventing

RSV-associated LRTI with hospitalization; and 90% efficacy in preventing RSV-associated LRTI with ICU admission.

How can nirsevimab be ordered?

ACIP has included nirsevimab in the Vaccines for Childrens (VFC) program. However, for the 2023-24 season, demand for nirsevimab is outpacing expectations. The manufacturer, Sanofi, is working with CDC on expediting release of additional doses and equitable distribution.

According to an AAP FAQ, nirsevimab is being distributed to state immunization programs using an allocation system. Physicians can contact their state immunization program for details about VFC ordering and anticipated supply for the 2023-24 RSV season.

For ordering commercial/private stock nirsevimab, the 100 mg formulation of nirsevimab is unavailable for new orders through Sanofi, AAP says. Ordering is not anticipated to reopen during the 2023-24 RSV season, although Sanofi has indicated it plans to fulfill all orders that have been placed successfully.

Sanofi reopened ordering for 50 mg dosage using an allocation system on Nov. 16, AAP says. According to its FAQ:

- Customers should have heard about allocated amounts from their regional representative or via their account on VaccineShop.com.
- Customers are able to place a direct order up to their allocation amount for a 30-day period (by Dec 15).
- If allocations are not accepted/ordered, Sanofi will offer declined doses to customers without allocations first.

Current CDC guidance prioritizes the 100 mg dose for those at highest risk for infection; recommendations for the 50 mg formulation remain unchanged at this time.

What are the contraindications to receiving nirsevimab?

Per AAP, nirsevimab is contraindicated in children and infants with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose of nirsevimab or to a product component.

While neither a contraindication nor a precaution, CDC also notes that nirsevimab should be used with caution in infants and children with bleeding disorders. CDC recommends using a 23-gauge or smaller caliber needle and steady pressure to the site for one to two minutes.

What are the adverse events associated with nirsevimab?

Adverse reactions might occur after administration of nirsevimab and should be reported. ACIP says that if an adverse reaction occurs after administration of nirsevimab alone, the reaction may be reported online to MedWatch, and if an adverse reaction occurs after the co-administration of nirsevimab with a vaccine, the reaction should be reported online to the Vaccine Adverse Event Reporting System.

Can nirsevimab be co-administered with other routine vaccines?

Nirsevimab can be administered without regard to timing of routine childhood vaccines, according to CDC. This includes simultaneous administration (i.e., same clinic day) with vaccine products. No interval between nirsevimab and live vaccines (such as MMR and varicella) is necessary.

CDC states that nirsevimab is not expected to interfere with the immune response to vaccine products, although experience with administering nirsevimab with vaccine products is limited. In clinical trials, when nirsevimab was given concomitantly with routine childhood vaccines, the safety and reactogenicity profile of the co-administered regimen was similar to the childhood vaccines given alone, the agency says.

If an infant has been diagnosed with RSV this season, should they still receive nirsevimab?

Per CDC, nirsevimab recommendations are the same regardless of prior RSV infection or RSV-associated hospitalization.

If an infant's mother has received maternal RSV vaccine, should the infant receive nirsevimab?

Per CDC, except in rare circumstances, nirsevimab is not needed for most infants younger than age 8 months who are born 14 or more days after their mother received RSV vaccine during pregnancy (see ACIP's section on special population and situations).

Can a patient receive both nirsevimab and palivizumab within the same RSV season?

Per AAP:

- If nirsevimab is administered, palivizumab should not be administered later that season.
- If palivizumab was administered initially for the season and fewer than five doses were administered, the infant should receive one dose of nirsevimab as soon as it is available, regardless of the time since the last palivizumab dose. No further palivizumab should be administered.
- If palivizumab was administered in season 1, and the child is eligible for RSV prophylaxis in season 2, the child should receive nirsevimab in season 2, if available. If nirsevimab is not available, palivizumhab should be administered as previously recommended.

However, in the context of limited supply during the 2023-24 RSV season, suspend using nirsevimab in palivizumab-eligible children aged 8-19 months for the 2023-24 RSV season, AAP says. These children should receive palivizumab according to AAP recommendations.

Will a vaccine information statement (VIS) be available for nirsevimab?

CDC has developed a "VIS-like" document – called an immunization information sheet – on nirsevimab, and encourages physicians to share this document with parents/families when administering nirsevimab. Physicians can download a copy from CDC.

What are the costs, codes, and payment for nirsevimab?

According to AAP coding guidance, report product codes for nirsevimab based on the dose administered:

- **90380**: Respiratory syncytial virus, monoclonal antibody, seasonal dose; **0.5 mL** dosage, for intramuscular use
- **90381**: Respiratory syncytial virus, monoclonal antibody, seasonal dose; **1 mL** dosage, for intramuscular use

Follow state specifications for reporting the immunization when the immunoglobulin product is provided through the Vaccines for Children program. For example, report **90380 SL** to indicate state-supplied product.

As of Oct. 6, 2023, two new CPT codes were released specific for reporting the administration and counseling of monoclonal antibodies for RSV. Report administration code for nirsevimab based on whether or not physician counseling was performed:

- **96380**: Administration of respiratory syncytial virus, monoclonal antibody, seasonal dose by intramuscular injection, with counseling by physician or other qualified health care professional
- **96381**: Administration of respiratory syncytial virus, monoclonal antibody, seasonal dose by intramuscular injection. If counseling was not performed on the date of administration, 96381 is the correct code to report.

In its FAQ, AAP reports:

- Payment terms for this season for those ordering direct from Sanofi are 150 days from time of shipment.
- There is no minimum order size. Nirsevimab is packaged as five single-dose, prefilled syringes per carton in both formulations.
- Nirsevimab is fully returnable upon expiration. Sanofi offers credit (based on exact amount returned and the invoice purchase price that is net of prompt pay or other discounts) upon expiration on all full and open-box Sanofi products directly purchased from Sanofi that are returned within one year after the expiration date.

Respiratory Syncytial Virus Vaccine (ABRYSVO)

ABRYSVO is an FDA-approved vaccine indicated for active immunization of pregnant individuals at 32 through 36 weeks gestational age for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by RSV in infants from birth through age 6.

Who is recommended to receive the maternal RSV vaccine and when?

CDC recommends pregnant individuals get a single dose of Pfizer's bivalent RSVpreF vaccine (ABRYSVO) during weeks 32 through 36 of pregnancy during September through January.

To prevent severe RSV disease in infants, CDC recommends either maternal RSV vaccination or infant immunization with RSV monoclonal antibody. Most infants will not need both, CDC says.

What are the dosing recommendations, and how is the maternal RSV vaccine administered?

According to CDC, the maternal RSV vaccine is supplied as a single-dose vial of 120 µg of lyophilized preF antigen component (60 µg from RSV-A, 60 µg from RSV-B) to be reconstituted with the accompanying vial of sterile water diluent component. A single dose after reconstitution is approximately 0.5 mL. Consult the package insert for proper storage and handling details, shelf life, and reconstitution instructions.

CDC recommends administering the RSVpreF vaccine (ABRYSVO) intramuscularly in the deltoid region of the upper arm. Do not administer RSV vaccine intravenously, intradermally, or subcutaneously.

What is the efficacy of the maternal RSV vaccine, and how long does the RSV protection conferred by the maternal RSV vaccine last?

According to CDC, clinical trials showed the maternal RSV vaccine reduced the risk of severe RSV disease by 82% within three months and by 69% within six months after birth.

How can the maternal RSV vaccine be ordered?

Information on how to order the maternal RSV vaccine is available on the ABRYSVO website.

What are the contraindications to receiving the maternal RSV vaccine?

FDA says the maternal RSV vaccine is contraindicated in individuals with a history of severe allergic reaction (e.g., anaphylaxis) to any component of the product.

CDC says that while adults with a minor acute illness, such as a cold, can receive RSV vaccination, moderate or severe acute illness, with or without fever, is a precaution to vaccination; vaccination should generally be deferred until the patient improves.

To learn more, see ACIP's Contraindications and Precautions, General Best Practice Guidelines for Immunization.

What are the adverse events associated with the maternal RSV vaccine?

CDC says that in the clinical trials, the adverse events most often reported by people who received the maternal RSV vaccine during pregnancy were pain at the injection site, headache, myalgia, and nausea.

- Preterm birth: People in the clinical trial who received the maternal RSV vaccine got it during weeks 24 through 36 of pregnancy. More preterm births were observed among maternal RSV vaccine recipients than among placebo recipients. However, this difference was not statistically different, CDC says.

  Among people in the clinical trial who received either the maternal RSV vaccine or a placebo during weeks 32 through 36 of pregnancy, preterm birth occurred in 4.2% who received the RSV vaccine compared with 3.7% who received a placebo.

  CDC says available data are insufficient to establish or exclude a causal relationship between preterm birth and RSVpreF (ABRYSVO). To reduce the potential risk of preterm birth when administering maternal RSV vaccine, FDA approved the vaccine for use during weeks 32 through 36 of pregnancy. The vaccine studies did not include people who already had a higher risk of preterm births.

Other safety outcomes noted by CDC.

- Although not common in the clinical trials, hypertensive disorders of pregnancy (including pre-eclampsia) occurred in 1.8% of participants who received the RSV vaccine compared with 1.4% of pregnant people who received a placebo.
- Pre-eclampsia, low birth weight (meaning less than 5.5 pounds), and jaundice in newborns occurred more frequently in infants born to mothers who received the RSV vaccine compared with infants born to mothers who received a placebo. These conditions are often associated with preterm birth.

Adverse events following vaccination should be reported to the Vaccine Adverse Event Reporting System, even if it is unclear that the vaccine caused the adverse event.

Can maternal RSV vaccine be co-administered with other routine vaccines?

Yes. CDC says people can receive maternal RSV, Tdap, COVID-19, and influenza vaccines at the same clinic visit when the vaccines are recommended. CDC's general best practice guidelines for immunization indicate that age-appropriate vaccinations can be given at the same visit, unless there is a specific reason not to.

If an infant's mother has received maternal RSV vaccine, should the infant receive nirsevimab?

CDC says that, except in rare circumstances, nirsevimab is not needed for most infants younger than age 8 months who are born 14 or more days after their mother received RSV vaccine during pregnancy (see ACIP's section on special population and situations).

What are the costs, codes, and payment for the maternal RSV vaccine?

CDC reports the costs and payment for the maternal RSV vaccine vary.

- Private health insurance: Most private health insurance plans cover the maternal RSV vaccine, although there may be a cost to the patient depending on their plan.
- Medicaid: As of Oct. 1, 2023, most people with coverage from Medicaid and the Children's Health Insurance Program will be guaranteed coverage of all vaccines recommended by ACIP at no cost to them.
- Vaccines for Children program: VFC will cover the maternal RSV vaccine. Pregnant teens enrolled in Medicaid will not be charged for the vaccine or administration. VFC-eligible teens not enrolled in Medicaid will get the vaccine at no charge, although they may be charged an administration fee. Children younger than 19 years old are eligible for the VFC program if they belong to one or more of the following groups:
  - » Medicaid-eligible;
  - » Uninsured;
  - » Underinsured; or
  - » American Indian or Alaska Native.

For cost code information, see the Coding Guide for ABRYSVO™ Administration.

Resource

1. AAP: ACIP and AAP Recommendations for Nirsevimab
2. AAP: Nirsevimab Administration
3. AAP: Nirsevimab Coding & Payment
4. AAP: Nirsevimab Frequently Asked Questions
5. AAP: Palivizumab Prophylaxis in Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection
6. AAP: Red Book: 2021–2024 Report of the Committee on Infectious Diseases
7. AAP: Updated Guidance for Palivizumab Prophylaxis
8. CDC: Frequently Asked Questions About RSV Immunization for Children 19 Months and Younger
9. CDC: RSV in Infants and Young Children
10. CDC ACIP: ACIP Evidence to Recommendations for Use of Nirsevimab
11. CDC ACIP: CDC's Vaccines for Children Program Addendum: Special Considerations for Nirsevimab
12. CDC Health Alert Network: Limited Availability of Nirsevimab in the United States—Interim CDC Recommendations
13. CDC: Healthcare Providers: RSV Prevention Information
14. CDC: Healthcare Providers: RSV Vaccination for Pregnant People
15. CDC *Morbidity and Mortality Weekly Report*: 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
16. CDC: Respiratory Syncytial Virus (RSV) Preventive Antibody: Immunization Information Statement (IIS)
17. FDA: ABRYSVO
18. FDA: FDA Approves First Vaccine for Pregnant Individuals to Prevent RSV in Infants
19. FDA: Highlights of Prescribing ABRYSVO™ (Respiratory Syncytial Virus Vaccine)
20. FDA: Highlights of Prescribing BEYFORTUS™ [nirsevimab-alip]
21. FDA: Highlights of Prescribing SYNAGIS® [palivizumab]
22. Pfizer: ABRYSVO™
23. Sanofi: Sanofi Beyfortus™ (nirsevimab-alip) Statement