RSV Prevention Update: ACIP/AAP Recommendations for Nirsevimab in Infants and RSV Vaccine in Pregnancy



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Disclosures

Advisory Panels – Pfizer, Avalere, Sobi

Advisory Councils – Moderna, Valneva

Site PI, multicenter clinical trials – Regeneron, Pfizer, GSK

Site Sub-I, multicenter clinical trials – Novavax

Objectives

 Discuss ACIP/AAP recommendations for use of nirsevimab and RSV vaccine for prevention of serious LRT RSV disease in infants



Respiratory Syncytial Virus

- Most common cause of hospitalization in U.S. infants
 - 1-2% of all infants under 12 mos of age
 - 58,000 to 80,000 hospitalizations and 200-300 deaths in <5 y/o each year
 - 2-3% of young infants
 - Risk declines by month with increasing age in infancy and early childhood
- Prematurity and certain chronic diseases increase hospitalization risk
- 79% of hospitalizations are in children with no underlying medical conditions





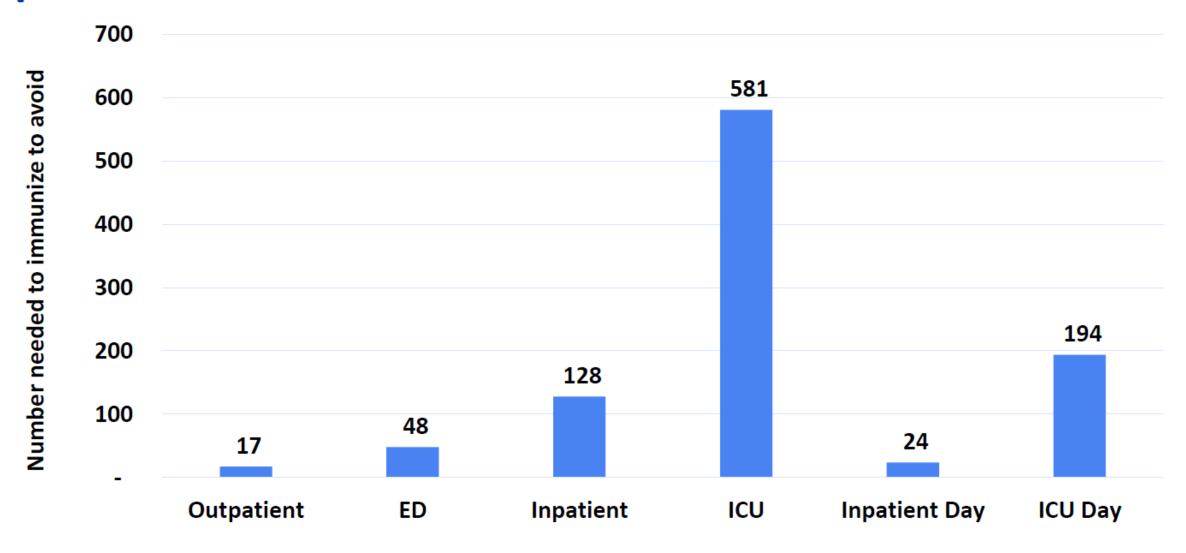
- Long-acting monoclonal antibody
 - Passive immunity
 - Binds to F/Fusion glycoprotein and blocks RSV entry into cells
 - Provides ~ 150 days of protection
- FDA licensed July 17th
- ACIP recommendations August 3rd
 - Included in VFC program
- AAP guidance and resources Red Book Online

Nirsevimab: Clinical Trials Results

- Clinical trial results for >35 wGA^{1,2,3,4} (pooled results)
 - Preventing medically attended RSV-associated LRTI 79.0%
 - Preventing RSV-associated LRTI hospitalization 80.6%
- Preventing RSV-associated LRTI with ICU admission 90.0%
- SAEs similar in nirsevimab and placebo arms

- Preterms, infants with CLD of prematurity and CHD who are currently recommended to receive palivizumab by AAP
 - Non-inferior to palivizumab⁵
 - Limited data; non-inferior or greater efficacy than palivizumab^{3,4}

Number needed to immunize with nirsevimab to prevent one health outcome



Nirsevimab: Adverse Events

- Most common: rash(0.9%) and injection site reactions (0.3%).
- Infants >34 weeks during first RSV season: similar to placebo
- High-risk infants in first RSV season: similar to infants >34
 weeks without risk factors
- High-risk infants in second RSV season: similar to safety profile during first RSV season

ACIP/AAP Recommendations for Nirsevimab

- All infants < 8 mos born during or entering their first RSV season
- 8 through 19 mos who are at increased risk of severe RSV disease and entering their 2nd RSV season

Morbidity and Mortality Weekly Report

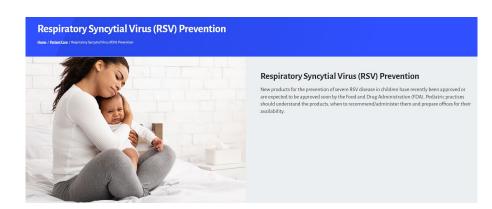
Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

Jefferson M. Jones, MD¹; Katherine E. Fleming-Dutra, MD¹; Mila M. Prill, MSPH¹; Lauren E. Roper, MPH¹; Oliver Brooks MD²; Pablo J. Sánchez, MD³; Camille N. Kotton, MD⁴; Barbara E. Mahon, MD¹; Sarah Meyer, MD⁵; Sarah S. Long, MD⁶; Meredith L. McMorrow, MD¹

Abstract

Respiratory syncytial virus (RSV) is the leading cause of hospitalization among U.S. infants. In July 2023, the Food and Drug Administration approved nirsevimab, a long-acting monoclonal antibody, for passive immunization to prevent

evidence regarding the safety and efficacy of nirsevimab, and assessed the quality of the efficacy and safety evidence using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework (2,3). The Evidence to Recommendation (EtR) Framework was used to develop



ACIP/AAP Recommendations for Nirsevimab: Second RSV Season

- Children with chronic lung disease of prematurity 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.
- Children who are severely immunocompromised.
- •Children with cystic fibrosis who have 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 have weight-for-length that is <10th percentile.
- American Indian and Alaska Native children new group for whom second-season prophylaxis is recommended

ACIP/AAP Nirsevimab Recommendations

< 8 months at the start of RSV season or 8-19 months, high risk



shortly before season/ any time during season

Born during RSV season

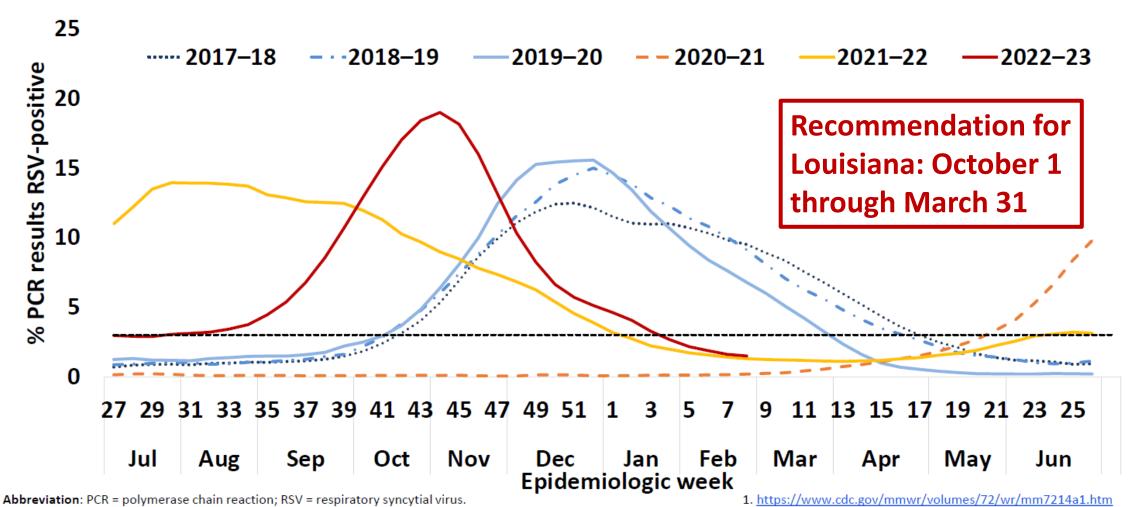


First week of life

In nursery or in outpatient setting

*RSV season varies by year and geography but generally considered October-March

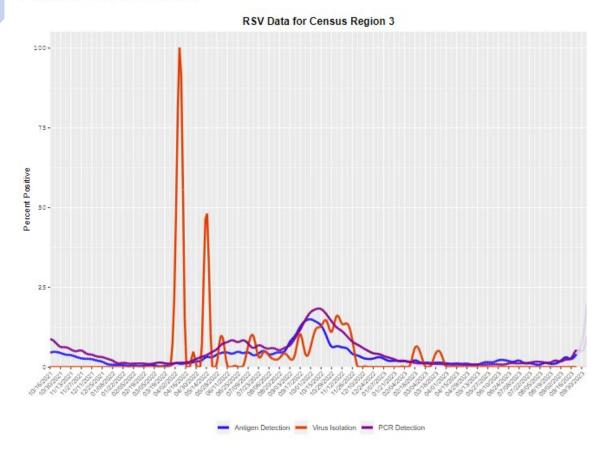
Changes in seasonality of RSV transmission following SARS-CoV2 introduction— NREVSS¹, 2017–2023



* 3-week centered moving averages of percentage of RSV-positive PCR results nationwide. The black dotted line represents the threshold for a seasonal epidemic (3% RSV-positive laboratory PCR results).

Region 3: South

Percent Positive



Detections

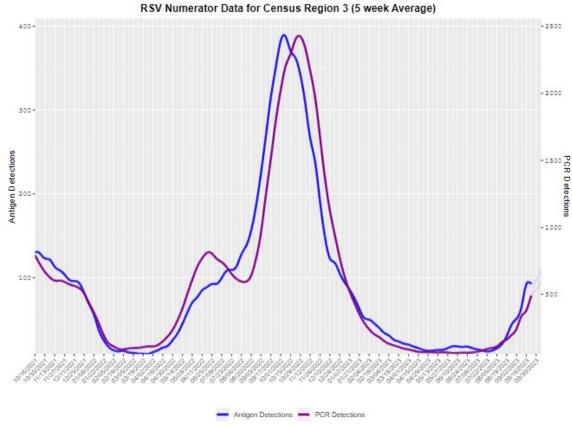


Table: South United States percent positive RSV tests, by week

Table: South United States RSV detections, by week

National Respiratory and Enteric Virus Surveillance System (NREVSS): https://www.cdc.gov/surveillance/nrevss/rsv/region.html#south

Nirsevimab Formulations

- Single dose, packaged in pre-filled syringes of either:
 - 50mg (0.5mL) with purple plunger rod (for infants weighing <5 kg)
 - 100 mg (1mL) with light blue plunger rod (weighing ≥5kg)
 - 200 mg (2, 100 mg injections at separate sites)





- Palivizumab will be needed until nirsevimab is available
 - When available, if additional palivizumab doses are indicated, give nirsevimab 1 month after last palivizumab dose
 - Once nirsevimab is given, no additional doses of palivizumab are needed

ACIP RSVpreF Vaccine Recommendations for Pregnancy

- Single dose at 32-36 weeks gestation
- Seasonal: September January
 - Jurisdiction flexibility regarding start/stop
 - Most infants will be born during RSV season
- May be administered with other indicated vaccines
- Additional data needed to inform whether additional doses indicated in subsequent pregnancies



Phase 3 trial vaccine efficacy against severe medically attended RSV-associated LRTI, co-primary trial endpoint

Time period after birth	Trial dosing interval (24–36 weeks gestation) Vaccine efficacy¹ (99.5% or 97.58% CI)	Approved dosing interval (32–36 weeks gestation) Vaccine efficacy ² (95% CI)
o–90 days after birth	81.8% (40.6, 96.3)	91.1% (38.8, 99.8)
o–180 days after birth	69.4% (44.3, 84.1)	76.5% (41.3, 92.1)

Within o-180 days after birth

- Among 81 infants with severe medically attended RSV LRTI, 50 (62%) were hospitalized
- Among 63 infants
 hospitalized with RSV, 50
 (79%) had severe medically
 attended RSV LRTI

¹ Vaccine efficacy was calculated as 1–(P/[1–P]), where P is the number of cases of illness in the RSVpreF group divided by the total number of cases of illness. At 90 days, 99.5% confidence intervals (CIs) were used (determined by the alpha-spending function and adjusted with the use of the Bonferroni procedure), and at later intervals, 97.58% CIs were used (based on a two-sided alpha level of 0.0483 adjusted with the use of the Bonferroni procedure).

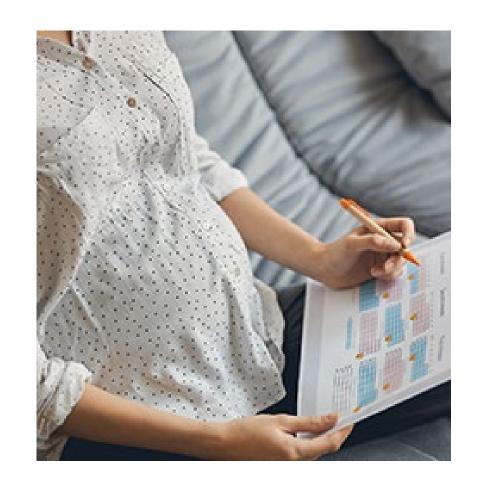
² Vaccine efficacy was calculated as 1-(hP/[1-P]), where P is the number of cases in the RSVpreF group divided by the total number of cases and h is the ratio of number of participants at risk in the placebo group to the number of participants at risk in the RSVpreF group.

^{1.} Kampmann et al. Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants - PubMed (nih.gov)

^{2.} Vaccines and Related Biological Products Advisory Committee May 18, 2023 Meeting Briefing Document-FDA

Maternal RSVpreF Vaccine

- Advantages: protection immediately after birth, avoids infant injection
- Disadvantages: inadequate antibody transfer, potential for preterm birth (5.7% vs 4.7% in placebo group @ 24-36wks admin; 4.2% vs 3.7% at 32-36 wks admin), nirsevimab may provide longer protection
- 14 days following maternal vaccination or more likely needed for transplacental transfer of significant maternal antibody for infant protection



Modified Nirsevimab Recommendations Now that RSV Vaccine is Recommended for Pregnant Women

- Infants aged <8 months born during or entering their first RSV season if
 - Mother did not receive RSV vaccine or status
 - Infant born within 14 days of maternal vaccination
 - Recommendations are the same for infants with prior RSV infection
- Can be considered in rare circumstances where potential incremental benefit is warranted
 - e.g.; maternal immunocompromising conditions, conditions which potentially reduce transplacental antibody transport, infants with substantial risk for severe RSV
- Children 8-19 months at increased risk for severe RSV and entering their second RSV season

Patient Care

Early Childhood Gun Safety & Injury Prevention Mental Health Initiatives

Respiratory Syncytial Virus (RSV) Prevention

Home / Patient Care / Respiratory Syncytial Virus (RSV) Prevention



Respiratory Syncytial Virus (RSV) Prevention

New products for the prevention of severe RSV disease in children have recently been approved. Pediatric practices should understand the products, when to recommend/administer them and prepare offices for their availability.

Education Opportunities: Fall Respiratory Season Webinar Series

Prevention of RSV in Children - Clinical Updates

Tuesday, October 10th, from 6:00 - 7:00 PM CT

Register here.

Nirsevimab Implementation Strategies in Outpatient Pediatric Practices

Tuesday, October 17th, from 7:00 - 8:00 PM CT

Register here.

RSV Overview

Respiratory syncytial virus (RSV) causes acute respiratory tract infections in people of all ages and can cause severe illness in infants and children with certain health conditions. Approximately 58,000-80,000 children under the age of 5 and up to 3% of children in their first year of life are hospitalized due to RSV infection each year in the US. Most children will get an RSV infection before the age of 2 years, and approximately 20-30% of children infected will develop a lower respiratory tract infection, such as bronchiolitis or pneumonia. Reinfection is common and is usually less severe than the primary infection.

In the US, RSV typically circulates from the fall, peaks in December or January and continues through the spring. It is transmitted by direct or close contact with those infected or from touching contaminated surfaces.

AAP Recommendations

Red Book: Respiratory Syncytial Virus Chapter

Red Book Online: ACIP and AAP Recommendations for Nirsevimab

RSV Prevention Products

The following are products to prevent severe RSV infection in children.

Nirsevimab (Beyfortus)

A monoclonal antibody product included in the Vaccines for Children Program and offering long-lasting protection and was recently recommended for all infants in the 2023-2024 RSV season.



Nirsevimab Frequently Asked Questions

Get answers to your questions about nirsevimab.

Ordering & Product Information

Considerations for calcuating and financing your orders, product cost, formulation and storage requirements.

Implementation Resources

View these tools to assess readiness and guide implementation of nirsevimab administration in inpatient and outpatient settings.

Administration, Dosing and Schedule

Find the latest recommendations for nirsevimab, dosing guidance and how it is administered.

Nirsevimab Administration Visual Guide

An algorithm to guide practices and facilities who are administering nirsevimab.

Payment and Coding

Learn more about what codes to use to get paid for administering nirsevimab in your practice.

Palivizumab (Synagis)

A short-acting monoclonal antibody product, available since 1998 and recommended for high-risk infants and young children.

Palivizumab Policy

Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection

Palivizumab Technical Report

Palivizumab Prophylaxis in Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection

Professional Education Resources

Pediatrics in Review: "Implications of Food and Drug Administration Approval of Respiratory Syncytial Virus Prophylactic Medication"

Learn the latest findings for preventing RSV illness and vaccine considerations for your patients to tackle this major public health priority.

Educating Families about RSV and Nirsevimab

The AAP offers resources to help families better understand the risks for severe RSV disease and the benefits of prevention.

HealthyChildren.org – RSV: When It's More Than Just a Cold

AAP - Pediatric Patient Education: RSV

Requires subscription to Pediatric Care Online to access.

Podcasts and Voices Blogs

Learn what others are saying. Listen to our podcasts and read our blog posts.

Immunizations Special: RSV, COVID, Pneumococcal Disease, Influenza – Episode 170

In this episode Sean O'Leary, MD, MPH, FAAP, chair of the AAP Committee on Infectious Diseases, joins hosts David Hill, MD, FAAP, and Joanna Parga-Belinkie, MD, FAAP, for an "immunizations omnibus." He describes newly approved products to protect against RSV, COVID and pneumococcal disease, and he predicts a difficult flu season.

Pediatrics on Call | August 29, 2023





IMMUNIZATION INFORMATION STATEMENT

Respiratory Syncytial Virus (RSV) Preventive Antibody:

What You Need to Know

Why get immunized with a RSV preventive antibody?

A respiratory syncytial virus (RSV) preventive antibody can prevent severe lung disease caused by RSV.

RSV is a common respiratory virus that usually causes mild, cold-like symptoms but can also affect the lungs. Symptoms of RSV infection may include runny nose, decrease in appetite, coughing, sneezing, fever, or wheezing.

Anyone can become infected by RSV, and almost all children get an RSV infection by the time they are 2 years old. While most children recover from an RSV infection in a week or two, RSV infection can be dangerous for infants and some young children, causing difficulty breathing, low oxygen levels, and dehydration. In the United States, RSV is the most common cause of bronchiolitis (inflammation of the small airways in the lungs) and pneumonia (infection of the lungs) in children younger than 1 year of age. Children who get sick from RSV may need to be hospitalized, and some might even die.

RSV Preventive Antibodies

The RSV preventive antibody (generic name nirsevimab, trade name Beyfortus) is a shot that prevents severe RSV disease in infants and young children. Antibodies are proteins that the body's immune system uses to fight off harmful germs. Like traditional vaccines, preventive antibodies are immunizations that provide protection against a specific pathogen. While both are immunizations, the way they provide immunity is different. Nirsevimab is an immunization that provides antibodies directly to the recipient. Traditional vaccines are immunizations that stimulate the recipient's immune system to produce antibodies.

Infants born during the RSV season (typically fall through spring) should receive a single dose of the RSV Immunization within 1 week after birth. Most infants whose mothers got the RSV vaccine don't need to get nirsevimab, too. Both protect infants from severe RSV by providing antibodies, either from the mother to the infant or directly to the infant. Most infants will likely only need protection from either the maternal RSV vaccine or nirsevimab (not both). However, there may be some situations in which nirsevimab would be recommended for an infant after the mother received an RSV vaccine.

Infants born outside of the RSV season who are younger than 8 months should receive a single dose of the RSV Immunization shortly before their first RSV season (typically the fall), but infants who are younger than 8 months who have not yet received a dose may receive a dose at any time during the season.

Some infants and young children who are at increased risk for severe RSV disease may need a single dose of the RSV antibody before or during their second RSV season.

RSV preventive antibodies can be given at the same time as vaccines routinely recommended for infants and young children.



Talk with your health care provider

Tell your health care provider if the person getting the preventive antibody has a:

- · History of serious allergic reactions to an RSV preventive antibody (nirsevimab) or any of its components,
- · Bleeding disorder, or
- Moderate or severe acute illness.

In some cases, your child's health care provider may decide to postpone giving RSV preventive antibodies until a future visit

People who have a minor illness, such as a cold, can safely receive an RSV preventive antibody. People who are moderately or severely ill should usually wait until they recover.

Your health care provider can give you more information.

Risks of a reaction to RSV preventive antibodies

After getting an RSV preventive antibody, your child might have temporary pain, redness, swelling where the injection was given, or a rash.

As with any medicine, there is a very remote chance that RSV Immunization could cause a severe allergic reaction, other serious injury, or death.

An allergic reaction could occur after your child leaves the hospital or clinic. If you see signs of a severe allergic reaction (for example, hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, or weakness), call 9-1-1 and get your child to the nearest hospital.

Call your health care provider if you see any other symptoms that concern you.

What if there is a serious problem?

If your child got an RSV preventive antibody without getting a vaccine at the same time, and you suspect an adverse reaction, you or your health care provider can submit a report through https://www.fda.gov/medwatch or by phone at 1-800-FDA-1088.

If your child got an RSV preventive antibody and a vaccine at the same time and you suspect an adverse reaction, you or your health care provider should report it to the <u>Vaccine Adverse</u>. Event Reporting System (VAERS) https://vaers.hhs.gov/ or call. 1-800-822-7967. In your report, note that your child got an RSV Immunization along with a vaccine.

Note: MedWatch and VAERS are only for reporting reactions. MedWatch and VAERS staff members do not give medical advice.

How can I learn more?

- Ask your health care provider.
- Call your local or state health department.
- Visit U.S. Food and Drug Administration website at <u>Drugs@FDA: FDA-Approved</u> <u>Drugs</u>.
- Contact the Centers for Disease Control and Prevention (CDC):
- o Call 1-800-232-4636 (1-800-CDC-INFO) or
- Visit the CDC website https://www.cdc.gov/rsv/about/ prevention.html





MedWatch: The FDA Safety Information and Adverse Event Reporting Program



MedWatch: The FDA Safety Information and Adverse Event Reporting Program

Subscribe to MedWatch Safety Alerts

Medical Product Safety Educational Resources

Medical Product Safety Information

Reporting Serious Problems to FDA

MedWatch, the FDA's medical product safety reporting program for health professionals, patients and consumers.



MedWatch receives reports from the public and when appropriate, publishes safety alerts for FDA-regulated products such as:

- · Prescription and over-the-counter medicines
- Biologics such as blood components, blood/plasma derivatives and gene therapies.
- Medical devices such as hearing aids breast pumps, and pacemakers.
- Combination products such as pre-filled drug syringe, metered-dose inhalers and nasal spray.
- Special nutritional products such as dietary supplements, medical foods and infant formulas.
- Cosmetics such as moisturizers, makeup, shampoos, hair dyes and tattoos.
- Food such as beverages and ingredients added to foods.

Content current as of:

10/10/2023

Regulated Product(s)

Biologics
Cosmetics
Dietary Supplements
Drugs
Medical Devices
Radiation-Emitting Products
Medical Food/Beverage

Topic(s)

Recalls





Introducing Beyfortus™ for RSV Prevention

Office of Public Health Immunization Program

10/20/2023



Immunization Program Updates

- Nirsevimab Availability
- The Vaccines for Children Program (VFC)
- Special Considerations
- The LINKS System
- Q & A



Nirsevimab Availability

- Due to the robust demand for nirsevimab (Beyfortus™) and limited manufacturer supply, nirsevimab is on backorder for many ordering channels.
- VFC ordering for nirservimab (Beyfortus™) has been temporarily paused.
- Ordering will be put on allocations when supplies are replenished.
- Timeframe is currently unknown.



Vaccines for Children Program



Vaccines for Children Program (VFC)

- Federally funded program that provides vaccines at no cost to children who might not otherwise be vaccinated due to inability to pay.
- Federally purchased vaccine is available at no cost to enrolled public and private healthcare providers for eligible children.
- The VFC Program is critical for ensuring that all children have a better chance of getting their recommended vaccinations on schedule.



VFC Program Eligibility

- Children ages 18 and younger
- Children who are Medicaid Eligible, Underinsured, Underinsured, American Indian or Alaskan Native
- The insurance status of infants and children must be documented separately from the parent to determine VFC eligibility.
- Every newborn must be screened for VFC eligibility.
- Birthing facilities will only be required to carry nirsevimab and birth dose Hepatitis B vaccine; however, all ACIP recommended vaccines for children may be ordered through the VFC Program.



Birthing Facility Participation in VFC

- Birthing facilities are key partners in nirsevimab administration for newborns.
- Immunization Program goal is for birthing facilities to co-administer nirsevimab with Hepatitis B birth dose.
- Fourteen out of fifty-two birthing (27%) facilities in Louisiana are enrolled in the VFC Program.
- The Immunization Program hosted a webinar for birthing facilities on 10/10/23 to encourage them to consider VFC enrollment.



Other VFC Considerations

- Louisiana has a no-borrowing policy, restricting "sharing" of VFC and private stock vaccine.
- Screening infants for eligibility at birth is very important.
- Physicians are able to search mother's name in the LINKS system to see if mother was given RSV vaccine during pregnancy.



Immunization Program Contact

Adrienne Mercadel Whitney, VFC Program Manager

Adrienne.Mercadel@La.Gov

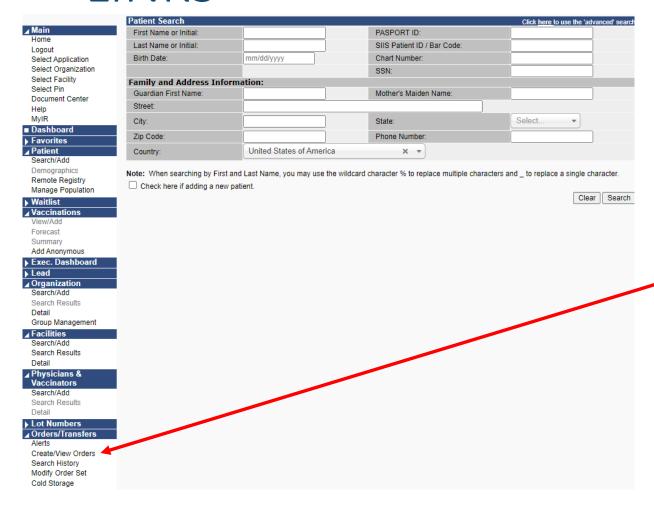
(504) 568-2600



LINKS Overview



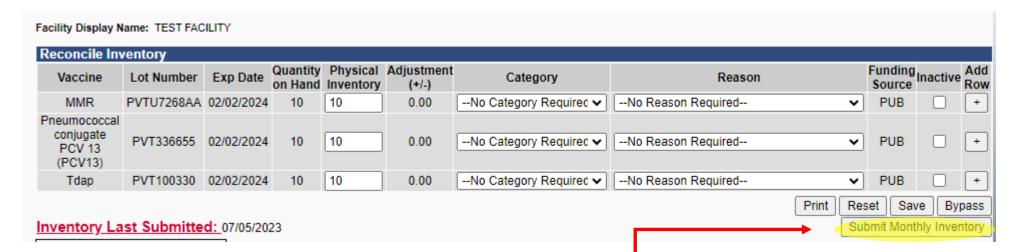
LINKS



Ordering Beyfortus

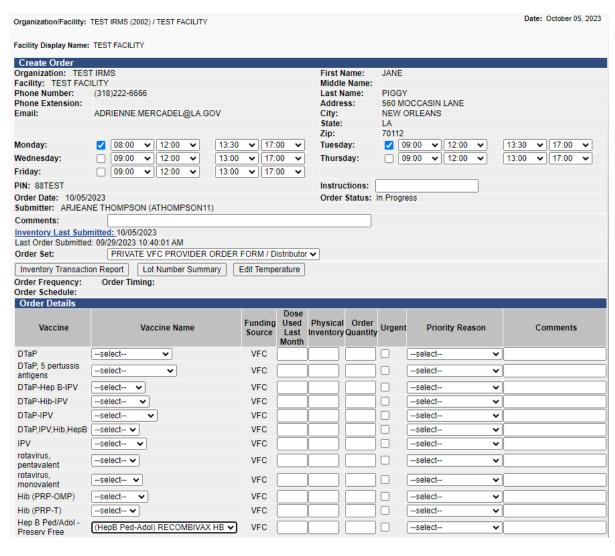
- Go to the section labeled "Orders/Transfers" on the left column menu
- Click "Create/View Orders"
- Once you go to the "Create/View orders screen, please click "Create Order" in the bottom right corner





- Reconcile your inventory by entering the quantity of vaccine you have next to each lot number in the box that says "Physical Inventory"
 - 1. If the "Quantity on Hand" and "Physical Inventory" do not match, select a category and reason.
 - 2. If there is 0 in the "Quantity on Hand" and "Physical Inventory" fields, check the box for inactive
- Click "Submit Monthly Inventory"





- Confirm the Organization, Facility, Address, and Contact Information
- Confirm or click to select that the "Order Set" is selected as "PRIVATE VFC PROVIDER ORDER FORM/Distributor"
- Under the Order Details Section, select the RSV Vaccine.
- Enter the number of doses needed under "Order Quantity"
 - RSV, mAb, nirsevimab-alip, 0.5 mL, neonate to 24 months or RSV, mAb, nirsevimab-alip, 1.0 mL, neonate to 24 months can be ordered in increments of 5.
- Enter any comments if applicable
- Click "Submit Order"
- 5075 doses have been ordered post FDA-approval, and 185 doses have been administered.

THANK YOU

