Synagis® (Palivizumab)

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➲ Instructions for Use

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Community Plan Policy

- Synagis® (Palivizumab)

Coverage Rationale

➲ See Benefit Considerations

Synagis (palivizumab) is proven and medically necessary to prevent serious lower respiratory tract disease caused by respiratory syncytial virus disease (RSV) in high risk infants and young children when all of the following are met:

- Administered during RSV "season" as defined by Centers for Disease and Prevention (CDC) surveillance reports (NREVSS Interactive Dashboard) or state or local health departments to confirm the start of the respiratory syncytial virus (RSV) "season"; **and**
- Monthly dose of Synagis does not exceed 15 mg/kg per dose; **and**
- Dosage of Synagis does not exceed 5 monthly doses per single RSV "season"
  Note: Infants in a neonatal intensive care unit who qualify for prophylaxis may receive the first dose 48 to 72 hours before discharge to home or promptly after discharge. If the first dose is administered in the hospital, this dose will be considered the first dose of the maximum 5 dose series for the "season". Any subsequent doses received in the hospital setting are also considered as part of the maximum 5 dose series. For infants born during the RSV "season," fewer than 5 monthly doses may be needed.
  and
- **One** of the following clinical situations:
  - **Prematurity:**
    - Infants born before 29 weeks, 0 day's gestations who are < 12 months of age at the start of RSV "season"
  - **Chronic Lung Disease (CLD):**
    - **Age 0 to < 12 months:** Prophylaxis may be considered during the RSV "season" during the first year of life for preterm infants who develop chronic lung disease (CLD) of prematurity defined as gestational age < 32 weeks, 0 days, and a requirement for > 21% oxygen for at least the first 28 days after birth.
    - **Age ≥ 12 to < 24 months:** Synagis is proven for use in pre-term infants born at < 32 weeks, 0 day's gestation who are ≥ 12 to < 24 months of age who required at least 28 days of oxygen after birth and who continue to require supplemental oxygen, diuretics, or chronic systemic corticosteroid therapy within 6 months of the start of the second RSV "season".
  - **Congenital Heart Disease (CHD):**
    - **Age 0 to < 12 months:** Infants and children with hemodynamically significant CHD who are born within 12 months of onset of RSV "season" and who will most likely benefit from immunoprophylaxis include:
      - Infants and children with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures
      - Infants and children with moderate to severe pulmonary hypertension

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        - Documentation that decisions regarding Synagis prophylaxis for infants with cyanotic heart defects in the first year of life were made in consultation with a pediatric cardiologist
        - **Age < 24 months:** A postoperative dose for children who still require prophylaxis and who have undergone surgical procedures should be administered Synagis prophylaxis after cardiac bypass or at the conclusion of extracorporeal membrane oxygenation.
            - Children who undergo cardiac transplantation during the RSV "season" may be considered for Synagis prophylaxis.
    - **Congenital abnormalities of the airway or neuromuscular disease:**
        - **Age 0 to < 12 months:** Infants and children with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the lower airway because of ineffective cough may be considered for prophylaxis during the first year of life.
    - **Immunocompromised children < 24 months of age:**
        - Synagis may be administered when used for prophylaxis in children who are receiving cancer chemotherapy or are severely immunocompromised although the efficacy of prophylaxis in this population is unknown (e.g., children who are receiving chemotherapy or undergo hematopoietic stem cell transplantation or solid organ transplantation).
    - **Cystic fibrosis (CF) with other qualifying indications:**
        - **Age 0 to < 12 months:** Infants and children with cystic fibrosis with clinical evidence of CLD and/or nutritional compromise in the first year of life may be considered for prophylaxis.
            - Failure to thrive defined as weight for length less than the 10th percentile on a pediatric growth chart
        - **Age ≥ 12 to < 24 months:** Continued use of Synagis prophylaxis in the second year may be considered for infants and children with manifestations of severe lung disease including:
            - Previous hospitalization for pulmonary exacerbation in the first year of life
            - Abnormalities on chest radiography or chest computed tomography that persists when stable
            - Weight for length less than the 10th percentile on a pediatric growth chart

and

- Patient has not previously received treatment with Beyfortus (nirsevimab-alip) or Enflonsia (clesrovimab-cfor) during or entering the current RSV "season"

Synagis is unproven for the following situations:

- Infants with chronic lung disease (CLD) who do not continue to require medical support in the second year of life
- Infants and children with hemodynamically insignificant heart disease (e.g., secundum atrial septal defect, small ventricular septal defect, pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and patent ductus arteriosus)
- Infants with cardiac lesions adequately corrected by surgery unless they continue to require medication for congestive heart failure
- Infants with cardiomyopathy sufficiently mild that they do not require pharmacotherapy
- Children in the second year of life unless otherwise indicated as proven above
- Routine use of prophylaxis in children with Down syndrome [unless qualifying heart disease, CLD, airway clearance issues (the inability to clear secretions from the upper airway because of ineffective cough), or prematurity (< 29 weeks, 0 day's gestation)] is present
- Routine use of prophylaxis in children with cystic fibrosis (unless indications noted in proven indications above are present)
- Administration of monthly Synagis prophylaxis **after** an infant or child has experienced a breakthrough RSV hospitalization during the current season if child had met criteria for palivizumab
- Prophylaxis for primary asthma prevention or to reduce subsequent episodes of wheezing in infants and children
- Synagis prophylaxis for prevention of nosocomial disease
- When Synagis prophylaxis is administered in **any** of the following scenarios:
    - Outside of the RSV "season"
    - In doses greater than needed to provide protection in the RSV "season"
    - In excess of 5 doses per single RSV "season"
    - To persons other than those at defined high risk, as specified above
- Treatment of symptomatic RSV disease

Additional Information

Because the timing of the onset, peak, and decline of RSV activity might vary geographically, providers can adjust administration schedules based on local epidemiology. RSV seasonality in tropical climates (including southern Florida, Guam, Hawaii, Puerto Rico, U.S.-affiliated Pacific Islands, and U.S. Virgin Islands) might differ from that of most of the

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continental United States or be unpredictable. In Alaska, RSV seasonality is less predictable, and the duration of RSV activity is often longer than the national average duration.[9]

For analysis of National Respiratory and Enteric Virus Surveillance System (NREVSS) reports in the CDC Morbidity and Mortality Weekly Report, season onset is defined as the first of 2 consecutive weeks during which the mean percentage of specimens testing positive for RSV antigen is ≥ 10% or the mean percentage of specimens testing positive for RSV by PCR is ≥ 3%, whichever occurs first. RSV "season" offset is defined as the last week during which the mean percentage of positive specimens by antigen is ≥ 10%, or the mean percentage of positive specimens by PCR is ≥ 3%, whichever occurs last. Use of specimens to determine the start of the RSV "season" requires that the number of specimens tested be statistically significant.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
90378	Respiratory syncytial virus, monoclonal antibody, recombinant, for intramuscular use, 50 mg, each

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Diagnosis Code	Description
D81.0	Severe combined immunodeficiency [SCID] with reticular dysgenesis
D81.1	Severe combined immunodeficiency [SCID] with low T- and B-cell numbers
D81.2	Severe combined immunodeficiency [SCID] with low or normal B-cell numbers
D81.6	Major histocompatibility complex class I deficiency
D81.7	Major histocompatibility complex class II deficiency
D81.82	Activated Phosphoinositide 3-kinase Delta Syndrome [APDS]
D81.89	Other combined immunodeficiencies
D81.9	Combined immunodeficiency, unspecified
D83.0	Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function
D83.2	Common variable immunodeficiency with autoantibodies to B- or T-cells
D83.8	Other common variable immunodeficiencies
D83.9	Common variable immunodeficiency, unspecified
D84.81	Immunodeficiency due to conditions classified elsewhere
D84.821	Immunodeficiency due to drugs
D84.822	Immunodeficiency due to external causes
D84.89	Other immunodeficiencies
D84.9	Immunodeficiency, unspecified
P07.21	Extreme immaturity of newborn, gestational age less than 23 completed weeks
P07.22	Extreme immaturity of newborn, gestational age 23 completed weeks
P07.23	Extreme immaturity of newborn, gestational age 24 completed weeks
P07.24	Extreme immaturity of newborn, gestational age 25 completed weeks
P07.25	Extreme immaturity of newborn, gestational age 26 completed weeks
P07.26	Extreme immaturity of newborn, gestational age 27 completed weeks
P07.31	Preterm newborn, gestational age 28 completed weeks
P26.0	Tracheobronchial hemorrhage originating in the perinatal period
P26.1	Massive pulmonary hemorrhage originating in the perinatal period
P26.8	Other pulmonary hemorrhages originating in the perinatal period

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Diagnosis Code	Description
P26.9	Unspecified pulmonary hemorrhage originating in the perinatal period
P27.0	Wilson-Mikity syndrome
P27.1	Bronchopulmonary dysplasia originating in the perinatal period
P27.8	Other chronic respiratory diseases originating in the perinatal period
P27.9	Unspecified chronic respiratory disease originating in the perinatal period
P29.30	Pulmonary hypertension of newborn
P29.38	Other persistent fetal circulation
Q20.0	Common arterial trunk
Q20.1	Double outlet right ventricle
Q20.2	Double outlet left ventricle
Q20.3	Discordant ventriculoarterial connection
Q20.4	Double inlet ventricle
Q20.5	Discordant atrioventricular connection
Q20.6	Isomerism of atrial appendages
Q20.8	Other congenital malformations of cardiac chambers and connections
Q20.9	Congenital malformation of cardiac chambers and connections, unspecified
Q21.0	Ventricular septal defect
Q21.10	Atrial septal defect, unspecified
Q21.11	Secundum atrial septal defect
Q21.12	Patent foramen ovale
Q21.13	Coronary sinus atrial septal defect
Q21.14	Superior sinus venosus atrial septal defect
Q21.15	Inferior sinus venosus atrial septal defect
Q21.16	Sinus venosus atrial septal defect, unspecified
Q21.19	Other specified atrial septal defect
Q21.20	Atrioventricular septal defect, unspecified as to partial or complete
Q21.21	Partial atrioventricular septal defect
Q21.22	Transitional atrioventricular septal defect
Q21.23	Complete atrioventricular septal defect
Q21.3	Tetralogy of Fallot
Q21.4	Aortopulmonary septal defect
Q21.8	Other congenital malformations of cardiac septa
Q21.9	Congenital malformation of cardiac septum, unspecified
Q22.0	Pulmonary valve atresia
Q22.1	Congenital pulmonary valve stenosis
Q22.2	Congenital pulmonary valve insufficiency
Q22.3	Other congenital malformations of pulmonary valve
Q22.4	Congenital tricuspid stenosis
Q22.5	Ebstein's anomaly
Q22.6	Hypoplastic right heart syndrome
Q22.8	Other congenital malformations of tricuspid valve
Q22.9	Congenital malformation of tricuspid valve, unspecified
Q23.0	Congenital stenosis of aortic valve
Q23.1	Congenital insufficiency of aortic valve
Q23.2	Congenital mitral stenosis

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Diagnosis Code	Description
Q23.3	Congenital mitral insufficiency
Q23.4	Hypoplastic left heart syndrome
Q23.81	Bicuspid aortic valve
Q23.82	Congenital mitral valve cleft leaflet
Q23.88	Other congenital malformations of aortic and mitral valves
Q24.1	Levocardia
Q24.2	Cor triatriatum
Q24.3	Pulmonary infundibular stenosis
Q24.4	Congenital subaortic stenosis
Q24.5	Malformation of coronary vessels
Q24.6	Congenital heart block
Q24.8	Other specified congenital malformations of heart
Q25.0	Patent ductus arteriosus
Q25.1	Coarctation of aorta
Q25.21	Interruption of aortic arch
Q25.29	Other atresia of aorta
Q25.3	Supravalvular aortic stenosis
Q25.40	Congenital malformation of aorta unspecified
Q25.41	Absence and aplasia of aorta
Q25.42	Hypoplasia of aorta
Q25.43	Congenital aneurysm of aorta
Q25.44	Congenital dilation of aorta
Q25.45	Double aortic arch
Q25.46	Tortuous aortic arch
Q25.47	Right aortic arch
Q25.48	Anomalous origin of subclavian artery
Q25.49	Other congenital malformations of aorta
Q25.5	Atresia of pulmonary artery
Q25.6	Stenosis of pulmonary artery
Q25.71	Coarctation of pulmonary artery
Q25.72	Congenital pulmonary arteriovenous malformation
Q25.79	Other congenital malformations of pulmonary artery
Q25.8	Other congenital malformations of other great arteries
Q25.9	Congenital malformation of great arteries, unspecified
Q26.0	Congenital stenosis of vena cava
Q26.1	Persistent left superior vena cava
Q26.2	Total anomalous pulmonary venous connection
Q26.3	Partial anomalous pulmonary venous connection
Q26.4	Anomalous pulmonary venous connection, unspecified
Q26.8	Other congenital malformations of great veins
Q26.9	Congenital malformation of great vein, unspecified
Q31.1	Congenital subglottic stenosis
Q31.2	Laryngeal hypoplasia
Q31.3	Laryngocele
Q31.5	Congenital laryngomalacia

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Diagnosis Code	Description
Q31.9	Congenital malformation of larynx, unspecified
Q32.0	Congenital tracheomalacia
Q32.1	Other congenital malformations of trachea
Q32.3	Congenital stenosis of bronchus
Q32.4	Other congenital malformations of bronchus
Q33.0	Congenital cystic lung
Q33.2	Sequestration of lung
Q33.3	Agenesis of lung
Q33.4	Congenital bronchiectasis
Q33.6	Congenital hypoplasia and dysplasia of lung
Z29.11	Encounter for prophylactic immunotherapy for respiratory syncytial virus (RSV)
Z51.11	Encounter for antineoplastic chemotherapy
Z92.21	Personal history of antineoplastic chemotherapy

Background

Palivizumab is a humanized murine monoclonal immunoglobulin produced by recombinant DNA technology which has neutralizing and fusion-inhibitory activity against RSV.

RSV is the leading cause of hospitalization among U.S. infants, with infants aged 0–2 months at the highest risk for hospitalization. To describe RSV seasonality (defined as onset, offset, peak, and duration) nationally, by U.S. Department of Health and Human Services (HHS) regions and for the state of Florida, the Centers for Disease Control and Prevention (CDC) analyzes RSV laboratory detections reported to the National Respiratory and Enteric Virus Surveillance System (NREVSS). This NREVSS surveillance data may be used to identify RSV activity and coordinate timing of immunoprophylaxis with palivizumab.

According to the MMWR, Seasonality of Respiratory Syncytial Virus — United States, 2017–2023, the COVID-19 pandemic disrupted RSV seasonality during 2020–2022. To describe U.S. RSV seasonality during prepandemic and pandemic periods, polymerase chain reaction (PCR) test results reported to the NREVSS during July 2017–February 2023 were analyzed. Seasonal RSV epidemics were defined as the weeks during which the percentage of PCR test results that were positive for RSV was ≥ 3%. Nationally, prepandemic seasons (2017– 2020) began in October, peaked in December, and ended in April. During 2020–21, the typical winter RSV epidemic did not occur. The 2021–22 season began in May, peaked in July, and ended in January. The 2022–23 season started (June) and peaked (November) later than the 2021–22 season, but earlier than prepandemic seasons. In both prepandemic and pandemic periods, epidemics began earlier in Florida and the Southeast and later in regions further north and west. The epidemic lasted 32 weeks until the offset occurred in January. Although the timing of the 2022–23 season suggested that seasonal patterns are returning toward those observed in prepandemic years, off-season RSV circulation might continue.

Benefit Considerations

Benefits for the use of palivizumab to prevent complications of RSV infection in defined high-risk patients are for a maximum of five doses one month apart. Coverage begins at the start of the RSV season, which varies in different parts of the United States. Physicians should consult CDC surveillance reports (NREVSS Interactive Dashboard) or their state or local health departments to confirm the start of the RSV season before administering palivizumab.

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

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Clinical Evidence

Proven

NREVSS is a laboratory-based system that monitors geographical and temporal trends for various respiratory and enteric viruses, including RSV activity, to the CDC.

Researchers in The Cochrane Collaboration conducted a literature review in 2024 to assess the effects of palivizumab in preventing severe RSV infection in children. They reviewed a total of six randomized controlled trials (RCTs) with 3611 children. All studies were parallel RCTs assessing the effects of 15 mg/kg of palivizumab every month for up to five months, compared to placebo or no intervention in an outpatient setting, although one study also included hospitalized infants, and another study administered palivizumab intranasally. Most of the included studies were conducted in children with a high risk of severe RSV infection due to comorbidities like bronchopulmonary dysplasia or congenital heart disease. Systemic palivizumab reduces hospitalization due to RSV infection at two years' follow-up (RR 0.44, 95% CI 0.30 to 0.64; I^2 = 23%; 5 studies, 3343 participants; high-certainty evidence). Based on 98 hospitalizations per 1000 participants in the placebo group, this corresponds to 43 (29 to 62) per 1000 participants in the palivizumab group.

Palivizumab probably results in little to no difference in mortality at two years' follow-up (RR 0.69, 95% CI 0.42 to 1.15; I^2 = 0%; 5 studies, 3343 participants; moderate-certainty evidence due to concerns about imprecision). Based on 23 deaths per 1000 participants in the placebo group, this corresponds to 16 (10 to 27) per 1000 participants in the palivizumab group. Palivizumab probably results in little to no difference in adverse events at 150 days' follow-up (RR 1.08, 95% CI 0.85 to 1.38; I^2 = 0%; 4 studies, 3099 participants; moderate-certainty evidence due to concerns about imprecision). Based on 78 cases per 1000 participants in the placebo group, this corresponds to 84 (66 to 107) per 1000 participants in the palivizumab group. Palivizumab probably results in a slight reduction in hospitalization due to respiratory-related illness at two years' follow-up (RR 0.80, 95% CI 0.65 to 0.99; I^2 = 41%; 6 studies, 3437 participants; moderate-certainty evidence due to concerns about imprecision). Systemic palivizumab may result in a large reduction in RSV infection at two years' follow-up (RR 0.33, 95% CI 0.20 to 0.55; I^2 = 0%; 3 studies, 554 participants; low-certainty evidence due to serious concerns about imprecision). Systemic palivizumab also reduces the number of wheezing days at one-year follow-up (RR 0.39, 95% CI 0.35 to 0.44; 1 study, 429 participants; high-certainty evidence). The risk of bias in outcomes across all studies was similar and predominantly low.

Unproven

MAKI was a multicenter, double-blind, placebo-controlled trial to explore the causal role of RSV infection in the pathogenesis of wheezing during the first year of life using palivizumab. Healthy preterm infants (n = 429) born at a gestational age of 33 to 35 weeks were randomized in a 1:1 ratio to receive either monthly palivizumab (dose = 15 mg/kg) injections (n = 214) or placebo (n = 215) during the RSV season. The primary outcome evaluated was number of parent reported wheezing days in the first year of life. Secondary outcomes assessed included were the number of days with bronchodilator use, the number of RSV infections confirmed by means of a nasopharyngeal swab positive for RSV RNA with or without medical attention, the number of hospitalizations for laboratory-proven RSV infection, the number of wheezing episodes, and the prevalence of recurrent wheeze. Researchers reported that treatment with palivizumab (median number of injections was 4) resulted in a relative reduction of 61% (95% confidence interval, 56 to 65) in the total number of wheezing days during the first year of life [930 of 53,075 days in the RSV-prevention group (1.8%) vs. 2309 of 51,726 days (4.5%) in the placebo group]. Additionally, the proportion of infants with recurrent wheezing was lower in the RSV-prevention group than in the placebo group (11.2% vs. 20.9%, p = 0.005). More co-infections during non-wheezing episodes were reported in the RSV-prevention group than in the placebo group [114 of 291 swabs (39%) vs. 70 of 233 swabs (30%), p = 0.03]. Researchers concluded that in otherwise healthy preterm infants, prophylactic treatment with palivizumab reduced the total number of wheezing days in the first year of life among preterm infants with a gestational age of 33 to 35 weeks. These findings implicate RSV infection as an important mechanism of recurrent wheeze during the first year of life in this population.

A 2016 Cochrane Review assessed the efficacy and safety of palivizumab compared with placebo, no prophylaxis or other prophylaxis, in preventing hospitalization and mortality from respiratory syncytial virus (RSV) infection in children with cystic fibrosis (CF). A database review identified one randomized controlled trial comparing five monthly doses of palivizumab to placebo in CF infants up to two years old. At six months follow-up, one participant in each group was hospitalized due to respiratory syncytial virus; there were no deaths in either group. In the palivizumab and placebo groups, 86 and 90 children experienced any adverse event, while five and four children had related adverse events respectively. Nineteen children receiving palivizumab and 16 receiving placebo suffered serious adverse events; one participant receiving palivizumab discontinued due to this. At 12 months follow-up, there were no significant differences between groups in number of *Pseudomonas* bacterial colonisations or change in weight-to-height ratio. Authors concluded that while the overall incidence of adverse events was similar in both groups, it is not possible to draw firm conclusions on

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the safety and tolerability of respiratory syncytial virus prophylaxis with palivizumab in CF infants. Six months after treatment, the authors reported no clinically meaningful differences in outcomes. Additional randomized studies are warranted to establish the safety and efficacy of palivizumab in children with cystic fibrosis.

The significance of these conclusions must be validated in additional randomized, controlled trials in order to be considered for inclusion into the recommendations of the Committee on Infectious Diseases (COID) of the American Academy of Pediatrics (AAP) on palivizumab prophylaxis of infants and young children.

Professional Societies

On August 19, 2025, the American Academy of Pediatrics published online recommendations for RSV immunizations. Nirsevimab, clesrovimab, and palivizumab are addressed in these recommendations:

- Nirsevimab and clesrovimab are considered the first-line recommended immunization products for administration to infants to protect against medically attended RSV disease. They are long-acting monoclonal antibody products administered as a single dose for administration during an infant's first RSV season. The AAP recommends any licensed RSV immunization product appropriate for age and health status and does not prefer one product over another.
- Palivizumab is a short-acting monoclonal antibody product that is administered in monthly doses during the RSV season. Palivizumab is no longer routinely recommended for use and will be discontinued as of December 31, 2025.

Federal Advisory Committees

On June 26, 2025, the U.S. Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) voted to recommend clesrovimab as an option for the prevention of RSV lower respiratory tract disease in infants younger than 8 months of age who are born during or entering their first RSV season. This recommendation is provisional and will be official once reviewed and finalized by the CDC Director or the Health and Human Services Secretary (in the absence of a CDC Director).

On August 3, 2023, the Advisory Committee on Immunization Practices recommended nirsevimab for infants aged < 8 months born during or entering their first RSV season and for infants and children aged 8–19 months who are at increased risk of severe RSV disease entering their second RSV season. The recommendations for nirsevimab apply to infants and children recommended to receive palivizumab by AAP. The AAP recommends nirsevimab, consistent with the ACIP, for:

- Infants aged < 8 months born during or entering their first RSV season whose pregnant parent did not receive RSVpreF vaccine, whose pregnant parent's RSVpreF vaccination status is unknown, or who were born < 14 days after the pregnant parent's RSVpreF vaccination.
- Nirsevimab is not needed for most infants aged < 8 months whose pregnant parent received RSVpreF vaccine ≥ 14 days before giving birth. Nirsevimab may be considered for infants born to a vaccinated pregnant parent in rare circumstances when, based on the clinical judgment of the health care provider, the potential incremental benefit of administration is warranted. These situations include, but are not limited to:
    - Infants born to pregnant people who might not have mounted an adequate immune response to vaccination (e.g., persons with immunocompromising conditions) or who have conditions associated with reduced transplacental antibody transfer (e.g., persons living with HIV infection); and
    - Infants who might have experienced loss of transplacentally acquired antibodies, such as those who have undergone cardiopulmonary bypass or extracorporeal membrane oxygenation; and
    - Infants with substantially increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease or intensive care admission requiring oxygen at hospital discharge).
- Infants and children 8 through 19 months of age who are at increased risk of severe RSV disease and entering their second RSV season, including those recommended by the AAP to receive palivizumab, regardless of RSV vaccination status of the pregnant parent. This includes the following:
    - Infants and children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) at any time during the 6-month period before the start of the second RSV season.
    - Infants and children who are severely immunocompromised.
    - Infants and 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 less than the 10th percentile.
    - American Indian and Alaska Native children.

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U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Synagis (palivizumab) is FDA-approved for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients at high risk of RSV disease. Synagis is indicated for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients: with chronic lung disease of prematurity, formerly termed bronchopulmonary dysplasia (BPD), that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of RSV season; infants with a history of premature birth (≤ 35 weeks gestational age) and who are 6 months of age or younger at the beginning of RSV season; and children with hemodynamically significant congenital heart disease (CHD) and who are 24 months of age or younger at the beginning of RSV season.

The safety and efficacy of Synagis have not been established for treatment of RSV disease.

References

1. Groothuis JR, Simoes EA, Levin MJ, et al. Prophylactic administration of respiratory syncytial virus immune globulin to high-risk infants and young children. n *Engl J Med*. 1993;329(21):1524-30.
2. Wegzyn C, Toh, LK, Notario G, et al. Safety and Effectiveness of Palivizumab in Children at High Risk of Serious Disease Due to Respiratory Syncytial Virus Infection: A Systematic Review. *Infect Dis Ther*. 2014 Dec; 3(2): 133–158.
3. Centers for Disease Control and Prevention. Respiratory Syncytial Virus Activity - United States, July 2012-January 2014. MMWR. December 5, 2014 / 63(48);1133-1136.
4. Hall CB, Weinberg GA, Iwane MK, et al. The Burden of Respiratory Syncytial Virus Infection in Young Children. n *Eng J Med*. 2009;360(6):588-98.
5. Simoes E, Groothuis JR, Carbonell-Estrany X, et al. Palivizumab prophylaxis, respiratory syncytial virus, and subsequent recurrent wheezing. J Pediatr. 2007;151(1):34-42, 42.e1.
6. Robinson KA, Odelola OA, Saldanha IJ. Palivizumab for prophylaxis against respiratory syncytial virus infection in children with cystic fibrosis. Cochrane Database Syst Rev. 2016 Jul 20;7(7):CD007743. doi: 10.1002/14651858.CD007743.pub6. PMID: 27439110; PMCID: PMC6457857. Synagis [prescribing information]. Gaithersburg, MD: Medimmune, LLC. November 2021.
7. AAP updates guidance on use of palivizumab for RSV prophylaxis (Policy Statement). AAP News 2014; 35:8 1.
8. AAP updates guidance on use of palivizumab for RSV prophylaxis (Technical Report) AAP News 2014; 35:8 1.
9. Panozzo CA, Stockman LJ, Curns AT, et al. Use of respiratory syncytial virus surveillance data to optimize the timing of immunoprophylaxis. *Pediatrics*. 2010 Jul;126(1):e116-23.
10. Blanken MO, Rovers MM, Molenaar JM, et al. Respiratory syncytial virus and recurrent wheeze in healthy preterm infants. n *Engl J Med*. 2013 May 9;368(19):1791-9.
11. Andabaka T, Nickerson JW, Rojas-Reyes MX, et al. Monoclonal antibody for reducing the risk of respiratory syncytial virus infection in children. Cochrane Database Syst Rev. 2013 Apr 30;4:CD006602.
12. Perrin JM, Meissner HC, and Ralston SL. Updated AAP Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of RSV Hospitalization [webinar]. July 28, 2014.
13. Centers for Disease Control and Prevention. Respiratory Syncytial Virus Seasonality - United States 2014-2017. MMWR. January 19, 2018 / 67(2);71–76.
14. Midgley CM, Haynes AK, Baumgardner JL, et al. Determining the Seasonality of Respiratory Syncytial Virus in the United States: The Impact of Increased Molecular Testing. *J Infect Dis*. 2017;216(3):345-355.
15. Policy Statement: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. Pediatrics. 2014;134(2):415–420. Available at: https://pediatrics.aappublications.org/content/134/2/415. Reaffirmed February 2019.
16. Hamid S, Winn A, Parikh R, et al. Seasonality of Respiratory Syncytial Virus - United States, 2017-2023. MMWR Morb Mortal Wkly Rep. 2023;72(14):355-361. Published 2023 Apr 7. doi:10.15585/mmwr.mm7214a1.

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17. Mary T. Caserta, Sean T. O'Leary, Flor M. Munoz, Shawn L. Ralston, COMMITTEE ON INFECTIOUS DISEASES; Palivizumab Prophylaxis in Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. Pediatrics July 2023; 152 (1): e2023061803. 10.1542/peds.2023-061803.
18. Beyfortus [prescribing information]. Swiftwater, PA: Sanofi Pasteur, Inc. August 2024.
19. Jones JM, Fleming-Dutra KE, Prill MM, et al. 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 Morb Mortal Wkly Rep. 2023;72(34):920-925. Published 2023 Aug 25. doi:10.15585/mmwr.mm7234a4.
20. AAP Recommendations for the Prevention of RSV Disease in Infants and Children. Red Book Online. July 8, 2025.
21. Moline HL, Tannis A, Toepfer AP, et al. Early Estimate of Nirsevimab Effectiveness for Prevention of Respiratory Syncytial Virus-Associated Hospitalization Among Infants Entering Their First Respiratory Syncytial Virus Season - New Vaccine Surveillance Network, October 2023-February 2024. MMWR Morb Mortal Wkly Rep. 2024;73(9):209-214. Published 2024 Mar 7. doi:10.15585/mmwr.mm7309a4.
22. Patton ME, Moline HL, Whitaker M, et al. Interim Evaluation of Respiratory Syncytial Virus Hospitalization Rates Among Infants and Young Children After Introduction of Respiratory Syncytial Virus Prevention Products - United States, October 2024-February 2025. MMWR Morb Mortal Wkly Rep. 2025;74(16):273-281. Published 2025 May 8. doi:10.15585/mmwr.mm7416a1.
23. Enflonsia [prescribing information]. Rahway, NJ: Merck Sharp & Dohme LLC. June 2025.
24. Garegnani L, Roson Rodriguez P, Escobar Liquitay CM, Esteban I, Franco JV. Palivizumab for preventing severe respiratory syncytial virus (RSV) infection in children. Cochrane Database Syst Rev. 2025;7(7):CD013757. Published 2025 Jul 23. doi:10.1002/14651858.CD013757.pub3.
25. American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for the Prevention of RSV Disease in Infants and Children: Policy Statement. Pediatrics. 2025; doi: 10.1542/peds.2025-073923.

Policy History/Revision Information

Date	Summary of Changes

11/01/2025	**Coverage Rationale**
	• Revised coverage criteria; replaced criterion requiring "the patient has not previously received treatment with Beyfortus (nirsevimab-alip) during or entering the current RSV 'season'" with "the patient has not previously received treatment with Beyfortus (nirsevimab-alip) *or Enflonsia (clesrovimab-cfor)* during or entering the current RSV 'season'"
	Additional Information
	• Revised language pertaining to seasonality of RSV to indicate:
	  ○ Because the timing of the onset, peak, and decline of RSV activity might vary geographically, providers can adjust administration schedules based on local epidemiology
	  ○ RSV seasonality in tropical climates (including southern Florida, Guam, Hawaii, Puerto Rico, U.S.-affiliated Pacific Islands, and U.S. Virgin Islands) might differ from that of most of the continental United States or be unpredictable
	  ○ In Alaska, RSV seasonality is less predictable, and the duration of RSV activity is often longer than the national average duration
	Supporting Information
	• Updated *Background*, *Clinical Evidence*, and *References* sections to reflect the most current information
	• Archived previous policy version 2024D0005AB

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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