09-J0000-28

Original Effective Date: 07/15/01

Reviewed: 04/09/25

Subject: Palivizumab (Synagis®)

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Respiratory syncytial virus (RSV) is a viral respiratory infection characterized by an upper respiratory prodrome, increased respiratory effort, and wheezing in children less than two years of age. Several different types of laboratory tests are available for diagnosis of RSV infection. Many clinical laboratories currently use antigen detection tests or molecular diagnostic testing, such as reverse transcriptase-polymerase chain reaction (RT-PCR).

The incidence of RSV infection typically follows a seasonal pattern with most of the United States affected between November and March, with considerable regional and local variability. The duration of the RSV season remains five consecutive months for all geographic areas in the United States. Recent regional trends in the United States can be found at the Centers for Disease Control and Prevention (CDC) National Respiratory and Enteric Virus Surveillance System (NREVSS).

Palivizumab (Synagis) was approved by the U.S. Food and Drug Administration (FDA) June 1998 for the prevention of serious lower respiratory tract disease caused by RSV in children at high risk of RSV disease. Conditions that increase the risk of severe RSV disease in young children include preterm birth, chronic lung disease of prematurity, and hemodynamically significant heart disease. Palivizumab exhibits neutralizing and fusion-inhibitory activity against RSV to interfere with the ability of RSV to replicate and infect cells.

The American Academy of Pediatrics (AAP) has provided guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for RSV infection. In 2014, the AAP updated their recommendations based on new data about which children are at highest risk of RSV hospitalization. Currently, the AAP recommends that palivizumab prophylaxis be limited to infants born before 29 weeks gestation and to infants with certain chronic illnesses (e.g., congenital heart disease, chronic lung disease).

Palivizumab prophylaxis may be administered to infants at the start of RSV season. Variation in the onset and offset of the RSV season in different regions of Florida may affect the timing of palivizumab administration. In NREVSS, the onset week in an area is defined as the first of two consecutive weeks when the weekly percentage of all specimens testing positive for RSV antigen in all reporting laboratories in the area is greater than or equal to 10%. The offset is the end of the last two consecutive weeks when the weekly percentage positive is less than 10%.

Current guidance from the AAP states:

"Despite varying onset and offset dates of the RSV season in different regions of Florida, a maximum of 5 monthly doses of palivizumab will be adequate for qualifying infants for most RSV seasons in Florida. Even if the first of 5 monthly doses is administered in July, protective serum concentrations of palivizumab will be present for most infants and young children for at least 6 months and likely into February. More than 5 monthly doses are not recommended, despite the detection of a small number of cases of RSV infection outside this time window. A small number of sporadic RSV hospitalizations occur before or after the main season in many areas of the United States, but maximum benefit from prophylaxis is derived during the peak of the season and not when the incidence of RSV hospitalization is low."

POSITION STATEMENT:

NOTE: Medical necessity criteria apply equally to all geographical locations in Florida and the United States. Because five (5) monthly doses of palivizumab (Synagis) will provide more than six (6) months of adequate serum concentrations for most infants, administration should be limited to peak respiratory syncytial virus (RSV) seasons in the continental United States.

In NREVSS, the onset week in an area is defined as the first of two consecutive weeks when the weekly percentage of all specimens testing positive for RSV antigen in all reporting laboratories in the area is greater than or equal to 10%. The offset is the end of the last two consecutive weeks when the weekly percentage positive is less than 10%.

Initiation of palivizumab (Synagis) **meets the definition of medical necessity** for prophylaxis of respiratory syncytial virus (RSV) during RSV season for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Prematurity
    a. Member was born before 29 weeks, 0 days' gestation
    b. Member is younger than 12 months of age at the start of RSV season (see Other)
    c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season
    d. Dose does not exceed 15 mg/kg/month
2. Chronic Lung Disease of Prematurity
    a. Member was born before 32 weeks, 0 days' gestation
    b. Member required greater than 21% oxygen for the first 28 days after birth

c. Member is younger than 12 months of age at the start of RSV season (see Other)

d. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season

e. Dose does not exceed 15 mg/kg/month

3. Congenital Heart Disease

   a. Member is 12 months of age or younger at the start of RSV season (see Other)

   b. Member's congenital heart disease is hemodynamically significant

   c. Member meets **ANY** of the following:

      i. Member is diagnosed with acyanotic heart disease **AND** receives medication to control congestive heart failure **AND** will require (or previously required) cardiac surgical procedures

      ii. Member is diagnosed with moderate to severe pulmonary hypertension

      iii. Member is diagnosed with a cyanotic heart defect **AND** palivizumab prophylaxis is prescribed or supervised by a pediatric cardiologist

   d. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season

   e. Dose does not exceed 15 mg/kg/month

4. Cardiac Transplantation

   a. Member is younger than 2 years of age at the start of RSV season (see Other)

   b. Member underwent cardiac transplantation during the RSV season (see Other)

   c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season

   d. Dose does not exceed 15 mg/kg/month

5. Anatomic Pulmonary Abnormality

   a. Member is 12 months of age or younger at the start of RSV season (see Other)

   b. Member's ability to clear secretions from the upper airway is impaired because of ineffective cough

   c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season

   d. Dose does not exceed 15 mg/kg/month

6. Neuromuscular Disorder

   a. Member is 12 months of age or younger at the start of RSV season (see Other)

   b. Member's ability to clear secretions from the upper airway is impaired because of ineffective cough

   c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season

   d. Dose does not exceed 15 mg/kg/month

7. Immunocompromised
    a. Member is younger than 24 months of age at the start of RSV season (see Other)
    b. Member is profoundly immunocompromised (e.g., solid organ or hematopoietic stem cell transplantation, receiving chemotherapy, immunocompromised)
    c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season
    d. Dose does not exceed 15 mg/kg/month
8. Cystic Fibrosis
    a. Member is 12 months of age or younger at the start of RSV season (see Other)
    b. Member meets either of the following:
        i. Member required greater than 21% oxygen for the first 28 days after birth
        ii. Member displays clinical evidence of nutritional compromise
    c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season
    d. Dose does not exceed 15 mg/kg/month
9. American Indian
    a. Member is 12 months of age or younger at the start of RSV season (see Other)
    b. Member is a Navajo or White Mountain Apache American Indian
    c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season
    d. Dose does not exceed 15 mg/kg/month

Duration of approval: 5 consecutive months or until the end of RSV season (see Other), whichever is sooner

Continuation of palivizumab (Synagis) **meets the definition of medical necessity** for prophylaxis of respiratory syncytial virus (RSV) during RSV season for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Chronic Lung Disease of Prematurity
    a. Member was born before 32 weeks, 0 days' gestation
    b. Member required greater than 21% oxygen for the first 28 days after birth
    c. Member is between 12 and 24 months of age at the start of RSV season (see Other)
    d. Member required medical support (i.e., chronic corticosteroid therapy, bronchodilator therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the most recent RSV season (see Other)
    e. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season
    f. Dose does not exceed 15 mg/kg/month

2. Cystic Fibrosis
    a. Member is between 12 and 24 months of age at the start of RSV season (see Other)
    b. Member meets either of the following:
        i. Member has manifestations of severe lung disease (i.e., previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable)
        ii. Member's weight for length is less than the 10th percentile
    c. Member has not previously received nirsevimab-alip (Beyfortus) for prevention of RSV for the current RSV season
    d. Dose does not exceed 15 mg/kg/month

Duration of approval: 5 consecutive months or until the end of RSV season (see Other), whichever is sooner

A replacement dose of palivizumab (Synagis) **meets the definition of medical necessity** for prophylaxis of respiratory syncytial virus (RSV) during RSV season for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Cardiac Bypass
    a. Member is younger than 24 months of age
    b. Member is approved for palivizumab prophylaxis (initiation or continuation) by Florida Blue
    c. Member is post-cardiac bypass
    d. Member received at least one dose of palivizumab before undergoing cardiac bypass
    e. Member has not received palivizumab since undergoing cardiac bypass
    f. Member will continue to require palivizumab prophylaxis post-cardiac bypass
    g. Dose does not exceed 15 mg/kg

2. Extracorporeal Membrane Oxygenation (ECMO)
    a. Member is younger than 24 months of age
    b. Member is approved for palivizumab prophylaxis (initiation or continuation) by Florida Blue
    c. Member is post-ECMO
    d. Member received at least one dose of palivizumab before undergoing ECMO
    e. Member has not received palivizumab since undergoing ECMO
    f. Member will continue to require palivizumab prophylaxis post-ECMO
    g. Dose does not exceed 15 mg/kg

Duration of approval: 1 dose

Palivizumab (Synagis) is **not considered a medical necessity** for all other indications, including:

1. 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)
2. Infants with heart conditions adequately corrected by surgery that no longer require medication for congestive heart failure
3. Infants with mild cardiomyopathy who are not receiving medical therapy for the condition
4. Children with passive exposure to tobacco smoke unless they meet other criteria as documented in the position statement
5. Treatment of active RSV infection
6. Down syndrome unless qualifying heart disease, chronic lung disease, or prematurity
7. Controlling outbreaks of health care-associated disease
8. Primary asthma prevention or to reduce subsequent episodes of wheezing
9. Children in the second year of life (except for those who meet palivizumab medical necessity criteria for the following conditions as outlined in the position statement above: cardiac bypass, cardiac transplantation, chronic lung disease (continuation only), cystic fibrosis (continuation only), extracorporeal membrane oxygenation (ECMO), or immunocompromised)
10. Use in adults

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 15 mg per kg of body weight, administered intramuscularly prior to commencement of the RSV season and remaining doses administered monthly throughout the RSV season
- Children undergoing cardio-pulmonary bypass should receive an additional dose as soon as possible after the cardio-pulmonary bypass procedure (even if sooner than a month from the previous dose); thereafter, doses should be administered monthly as scheduled

Dose Adjustments

None

Drug Availability

- 50 mg/0.5 mL and 100 mg/1 mL single-dose liquid solution vials

PRECAUTIONS:

Boxed Warning

None

Contraindications

- Previous significant hypersensitivity reaction

Precautions/Warnings

- Anaphylaxis and anaphylactic shock (including fatal cases), and other severe acute hypersensitivity reactions have been reported; permanently discontinue and administer appropriate medications if such reactions occur
- Give with caution to children with thrombocytopenia or any coagulation disorder
- Palivizumab may interfere with immunological-based RSV diagnostic tests such as some antigen detection-based assays

BILLING/CODING INFORMATION:

The following codes may be used to describe:

CPT Coding:

90378	Respiratory syncytial virus, monoclonal antibody, recombinant, for intramuscular use, 50 mg, each
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular

ICD-10 Diagnosis Codes That Support Medical Necessity:

Z29.11	Encounter for prophylactic immunotherapy for respiratory syncytial virus (RSV)

REIMBURSEMENT INFORMATION:

The appropriate administration code is reported in addition to the immune globulin.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantages Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Antibody: a protein produced by the immune system.

Lower respiratory tract disease: infection of the lungs, such as pneumonia.

RELATED GUIDELINES:

None applicable.

OTHER:

A small number of sporadic RSV hospitalizations occur before or after the main season in many areas of the US (e.g., Central Florida, South Florida); however, maximum benefit from prophylaxis is derived during the peaks of the season and not when the incidence of RSV hospitalization is low. Additionally, administration of more than five monthly doses is not recommended within the continental United States.

The CDC National Respiratory and Enteric Virus Surveillance System (NREVSS) monitors the onset and end of RSV season. In NREVSS, the onset week in an area is defined as the first of two consecutive weeks when the weekly percentage of all specimens testing positive for RSV antigen in all reporting laboratories in the area is greater than or equal to 10%. The offset is the end of the last two consecutive weeks when the weekly percentage positive exceeds 10%.

These reports can be accessed here: http://www.cdc.gov/surveillance/nrevss/rsv/state.html

The start and end of Florida's 2021-2022 RSV season will be based on current RSV activity within Florida. Current RSV activity within Florida can be found here (Note: The full report contains the percent of specimens testing positive): http://www.floridahealth.gov/diseases-and-conditions/respiratory-syncytial-virus/index.html

Florida's RSV seasons by region (based on a 2008 recommendation from Florida's Department of Health – RSV Epidemiology Workgroup) are outlined in Table 1 below.

Table 1

Florida RSV Season by Region						
Region	**Counties**				**Season Start**	**Season End**
North	Alachua Baker Bradford Clay Columbia	Dixie Duval Gilchrist Hamilton Lafayette	Levy Madison Nassau Putnam St. John's	Suwannee Taylor Union	September	March
Northwest	Bay Calhoun Escambia Franklin	Gadsden Gulf Holmes Jackson	Jefferson Leon Liberty Okaloosa	Santa Rosa Wakulla Walton Washington	October	April

Central	Brevard Citrus Flagler Hernando	Hillsborough Lake Marion Orange	Osceola Pasco Pinellas Seminole	Sumter Volusia	August	March
Southwest	Charlotte Collier DeSoto	Glades Hardee Hendry	Highlands Lee Manatee	Polk Sarasota	September	April
Southeast	Broward Indian River	Martin Dade	Monroe Palm Beach	St. Lucie Okeechobee	January	December

REFERENCES:

1. American Academy of Pediatrics, Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Policy statement: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014; 134:415-20.
2. American Academy of Pediatrics, Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Technical report: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014; 134:e620-e638.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: www.clinicalpharmacilogy-ip.com. Accessed 5/28/21.
4. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 5/28/21.
5. MedImmune. Synagis (palivizumab) injection, solution. 1998 [cited 5/2/21]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=8e35c4c8-bf56-458f-a73c-8f5733829788/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/09/25.

GUIDELINE UPDATE INFORMATION:

07/15/01	Medical Coverage Guideline Reformatted.
11/15/01	Added info on RSV season.
10/15/03	Reviewed with changes to both "When Covered" and "When Non-Covered" sections.
12/04/03	Revised When Services are Not Covered to clearly define age criteria for children with congenital heart disease and immunodeficiencies.
06/15/04	Revised information on RSV season and moved from the When Services are Covered to the Informational section.
01/01/06	Annual HCPCS coding update: deleted expired codes 90780, 90781, 90782, 90784 added new codes 90765, 90766, and 90772.
08/15/06	Biennial review, reformatted, added HCPCS codes.
10/15/06	Expanded description of RSV season and added reference.

12/15/06	Revised by changing from medical “director” review to medical “necessity” review under Dosage and Administration. Added Medicare Part D statement under Program Exceptions.
09/15/07	Review and revision to guideline; consisting of changing the name since RespiGam® is no longer available, reformatted guideline, maintain current coverage and limitations, added note regarding RespiGam® not being available, added dosing for Synagis®, removed RespiGam® HCPCS code and CPT codes, removed Medicare Part D delegation, updated internet links and updated references.
01/01/08	Annual HCPCS coding update: changed description on CPT-4 code 90378.
04/15/08	Revision to guideline consisting of added the HCPCS code J1565 after RespiGam® in the note under Description, stating that this drug is no longer available.
09/15/08	Review and revision to guideline, consisting of adding statement under the “Dosage and Administration” section regarding a website to obtain epidemiology information regarding RSV season and updating references and links.
01/01/09	Annual HCPCS coding update: deleted code 90772; added code 96372; deleted code C9003.
03/15/09	Revision to guideline consisting of adding verbiage to allow south Florida counties to treat for a 9 month RSV season.
06/15/09	Revision to guideline; consisting of modifying southeast Florida RSV season and defining RSV season for the rest of Florida. Also modified risk factors for infants born between 32 and 35 weeks less than 6 months of age at the start of RSV season to be consistent with AAP guidelines.
08/01/09	Revision to guideline; consisting of changing position statement to be in line with AAP recommendations.
01/01/10	Annual HCPCS coding update: revised descriptor for code 90378.
07/15/10	Review and revision to guideline; consisting of updating RSV season and references.
10/01/10	Revision to guideline, consisting of formatting changes.
11/15/10	Revision to guideline; consisting of clarifying the end of RSV season.
07/01/11	Review and revision to guideline; consisting of updating the position statement and references.
07/01/12	Review and revision to guideline; consisting of updating description, position statement and references.
06/15/13	Review and revision to guideline; consisting of adding coverage for infants and children with severe immune deficiencies. Updated E/I by adding active RSV infection, children with tobacco smoke exposure and no other AAP identified risk factors, non-cyanotic heart disease, surgically corrected heart disease that no longer requires medication support, Updated the 2013-2014 season start and end dates.
06/15/14	Review and revision to guideline; consisting of generally defining regional seasons.
08/15/14	Revision to guideline; consisting of description, position statement, dosage/administration, precautions, program exceptions, other, references
09/15/14	Revision to guideline; consisting of update to position statement.
05/15/15	Revision: update to billing/coding and Other.
07/15/15	Review and revision to guidelines; consisting of updating references.

11/01/15	Revision: ICD-9 Codes deleted.
11/15/15	Revision to guidelines; consisting of updating ICD10 coding, revising position statement.
06/15/16	Review and revision to guideline; consisting of revising position statement, references.
10/01/16	Revision to guideline; consisting of updating ICD10 code
06/15/17	Review and revision to guideline; consisting of updating description and references.
2/15/18	Revision to guideline consisting of updating HCPCS coding
05/15/18	Review and revision to guideline; consisting of updating description, position statement, other, and references.
05/15/19	Review and revision to guideline; consisting of updating references.
05/15/20	Review and revision to guideline; consisting of updating references.
12/15/20	Revision to guideline; updated position statement
07/15/21	Review and revision to guideline; consisting of updating other section and references.
04/15/25	Review and revision to guideline; consisting of updating position statement and references.