

Corporate Medical Policy

Respiratory Syncytial Virus Prophylaxis

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Description of Procedure or Service

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections in children. Several factors that put certain children at higher risk for contracting RSV have been identified and include the following: age less than 2 years old, prematurity, chronic lung disease (CLD) of prematurity (formerly known as bronchopulmonary dysplasia), congenital heart disease, immunodeficiencies, and multiple congenital anomalies. Immune prophylaxis against RSV is a preventive strategy to reduce the incidence of infection and its associated morbidity, including hospitalization, in high-risk infants.

RSV infections typically occur in the winter months, starting from late October to mid-January and ending from March to May. Considerable variation in the timing of community outbreaks is observed year to year. According to the U.S. Centers for Disease Control and Prevention (CDC), onset of the RSV season occurs when the median percentage of specimens testing positive for RSV is 10% higher over a 2-week period. During 1997-2006, an estimated 132,000-172,000 children aged younger than 5 years were hospitalized for RSV infection annually in the United States. While RSV is a near ubiquitous infection, infants with underlying medical issues, especially a history of prematurity with associated lung problems, are at risk of developing serious complications from bronchiolitis secondary to RSV.

CLD of prematurity is a general term for long-term respiratory problems in premature infants. CLD results from lung injury to newborns who, consequently, must use a mechanical ventilator and supplemental oxygen for breathing. With injury, the lung tissues become inflamed and scarring can result. Some of the causes of the lung injury include the following: prematurity, low amounts of surfactant, oxygen use, mechanical ventilation. Risk factors for developing CLD include: birth at less than 34 weeks' gestation, birth weight less than 2,000 grams (4 pounds 6.5 ounces), hyaline membrane disease, pulmonary interstitial emphysema (PIE), patent ductus arteriosus (PDA), Caucasian, male infants, maternal womb infection (chorioamnionitis), and family history of asthma.

This medical policy does not address therapies to treat RSV infection.

In June 1998, biologic Synagis® (palivizumab; MedImmune, Inc, Gaithersburg, MD) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the biologics licensing application for use in the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at high risk of RSV disease. In July 2004, the FDA approved a liquid formulation of Synagis®, supplied as a sterile solution ready for injection, thus providing improved convenience for administration. This formulation is used in the physician office or home setting. There are no therapeutic equivalents to this drug.

Other RSV preventive agents, including vaccines, have been under development. A recombinant RSV fusion protein nanoparticle vaccine has been shown to induce an immune response in a phase 2 trial.

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Respiratory Syncytial Virus Prophylaxis

Policy

BCBSNC will provide coverage for Respiratory Syncytial Virus Prophylaxis when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

RSV Prophylaxis may require prior review.

When RSV Prophylaxis is covered

Monthly administration of immune prophylaxis for respiratory syncytial virus with palivizumab during the RSV season may be considered **medically necessary** in the following infants and children in accordance with guidelines-based recommendations (American Academy of Pediatrics [2014]):

1. In the first year of life, i.e., younger than 12 months at the start of the RSV season or born during the RSV season:
 - a. Infants born before 29 weeks, 0 days gestation;
 - b. Preterm infants with CLD of prematurity, defined as birth at less than 32 weeks, 0 days gestation and a requirement for more than 21% oxygen for at least the first 28 days after birth;
 - c. Certain infants with hemodynamically significant heart disease (e.g., infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures; infants with moderate to severe pulmonary hypertension; infants with lesions adequately corrected by surgery who continue to require medication for heart failure;
 - i. Decisions regarding palivizumab prophylaxis for infants with cyanotic heart defects in the first year of life may be made in consultation with a pediatric cardiologist.
 - d. Children with pulmonary abnormality or neuromuscular disease that impairs the ability to clear secretions from the upper airways (e.g., ineffective cough, recurrent gastroesophageal tract reflux, pulmonary malformations, tracheoesophageal fistula, upper airway conditions, or conditions requiring tracheostomy);
 - e. Children with cystic fibrosis who have at least one of the following conditions:
 - i. Clinical evidence of CLD; and/or
 - ii. Nutritional compromise.
2. In the second year of life, i.e., younger than 24 months at the start of the RSV season:
 - a. Children who were born at less than 32 weeks, 0 days gestation and required at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid, or diuretic therapy) during the 6-month period before the start of the second RSV season.
 - b. Children with cystic fibrosis who have either:
 - i. Manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable); or

Respiratory Syncytial Virus Prophylaxis

- ii. Weight for length less than the 10th percentile.
3. In the first or second year of life:
 - a. Children who will be profoundly immunocompromised (e.g., will undergo solid organ or hematopoietic stem-cell transplantation or receive chemotherapy) during the RSV season.
4. After surgical procedures that use cardiopulmonary bypass, for children who still require prophylaxis, a postoperative dose of palivizumab may be considered **medically necessary** after cardiac bypass or at the conclusion of extracorporeal membrane oxygenation for infants and children younger than 24 months.

When RSV Prophylaxis is not covered

Immunoprophylaxis for RSV is considered not medically necessary for:

- Infants and children with hemodynamically insignificant heart disease (e.g., secundum atria septal defect, small ventricular septal defect, pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and patent ductus arteriosus); or
- Infants with lesions adequately corrected by surgery, unless they continue to require medication for heart failure; or
- Infants with mild cardiomyopathy who are not receiving medical therapy for the condition; or
- Children with congenital heart disease in the second year of life.

Other indications for immune prophylaxis for RSV are considered investigational including, but not limited to, controlling outbreaks of health care-associated disease; or use in children with cystic fibrosis or Down syndrome without other risk factors; or in children over 2 years of age, unless criteria for medical necessity (outlined above) are satisfied.

Policy Guidelines

Dosing and Administration

Palivizumab is administered by intramuscular injection in a dose of 15 mg/kg of body weight per month. The anterolateral aspect of the thigh is the preferred injection site. Routine use of the gluteal muscle for the injection can cause sciatic nerve damage.

Clinicians may administer up to a maximum of 5 monthly doses of palivizumab (15 mg/kg per dose) during the RSV season to infants who qualify for prophylaxis. Qualifying infants born during the RSV season will require fewer doses. For example, infants born in January would receive their last dose in March.

Hospitalized infants who qualify for prophylaxis during the RSV season should receive the first dose of palivizumab 48 to 72 hours before discharge or promptly after discharge.

Breakthrough RSV

If any infant or young child receiving monthly palivizumab prophylaxis experiences a breakthrough RSV hospitalization, monthly prophylaxis should be discontinued because of the extremely low likelihood of a second RSV hospitalization in the same season (<0.5%).

Prevention of Health Care Associated RSV Disease

RSV is known to be transmitted in the hospital setting and to cause serious disease in high-risk infants. Among hospitalized infants, the major means to reduce RSV transmission is strict observance of infection control practices, including restriction of visitors to the neonatal intensive care unit during respiratory virus season and prompt initiation of precautions for RSV-infected infants. If an RSV outbreak occurs in a high-risk unit (e.g., pediatric or neonatal intensive care unit or stem cell transplantation unit), primary emphasis should be placed on proper infection control practices, especially hand hygiene. No data exist to support palivizumab use in controlling outbreaks of health care-associated disease, and palivizumab use is not recommended for this purpose.

Respiratory Syncytial Virus Prophylaxis

Interactions

Palivizumab does not interfere with response to other scheduled childhood vaccines.

Palivizumab may interfere with RSV diagnostic tests that are immunologically-based (e.g., some antigen detection-based assays).

Risk Minimization Techniques

Infants, especially high-risk infants, never should be exposed to tobacco smoke. In published studies, passive household exposure to tobacco smoke has not been associated with an increased risk of RSV hospitalization on a consistent basis. However, exposure to tobacco smoke is a known risk factor for many adverse health-related outcomes. Exposure to tobacco smoke can be controlled by the family of an infant at increased risk of RSV disease, and preventive measures will be less costly than palivizumab prophylaxis.

For all infants, particularly those who are preterm, the environment should be optimized to prevent RSV and other viral respiratory infections by offering breast milk feeds, immunizing household contacts with influenza vaccine, practicing hand and cough hygiene, and by avoiding tobacco or other smoke exposure, and by not attending large group child care during the first winter season, whenever possible.

The policy statements are in agreement with the 2014 American Academy of Pediatrics (AAP) Guidelines.

Initiation and Termination of Immunoprophylaxis

Initiation of immunoprophylaxis in November and continuation for a total of 5 monthly doses will provide protection into April and is recommended for most areas of the United States. If prophylaxis is initiated in October, the fifth and final dose should be administered in February.

In the temperate climates of North America, peak RSV activity typically occurs between November and March, whereas in equatorial countries, RSV seasonality patterns vary and may occur throughout the year. The annual occurrence of the RSV season is predictable, but the severity of the season, the time of onset, the peak of activity, and the end of the season cannot be predicted precisely. Substantial variation in timing of community outbreaks of RSV disease from year to year exists in the same community and between communities in the same year, even in the same region. These variations occur within the overall pattern of RSV outbreaks, usually beginning in November or December, peaking in January or February, and ending by the end of March or sometime in April. Communities in the southern United States, particularly in Florida, tend to experience the earliest onset of RSV activity. In recent years, the national duration of the RSV season has been 21 weeks. Please note that the latest information regarding geographic seasonal variation can be found on the CDC website at <http://www.cdc.gov/rsv/index.html>.

Results from clinical trials indicate that palivizumab trough serum concentrations more than 30 days after the fifth dose will be well above the protective concentration for most infants. Five monthly doses of palivizumab will provide more than 20 weeks of protective serum antibody concentration. In the continental United States, a total of 5 monthly doses for infants and young children with congenital heart disease or chronic lung disease of prematurity or preterm birth before 32 weeks' gestation (31 weeks, 6 days) will provide an optimal balance of benefit and cost, even with variation in season onset and end.

Data from the CDC have identified variations in the onset and offset of the RSV season in Florida that affect the timing of palivizumab administration. Northwest Florida has an onset in mid-November, which is consistent with other areas of the United States. In north central and southwest Florida, the onset of RSV season typically is late September to early October. The RSV season in southeast Florida (Miami-Dade County) typically has its onset in July. Despite varied onsets, the RSV season is of equal duration in the different regions of Florida. Children who receive palivizumab prophylaxis for the entire RSV season should receive palivizumab only during the 5 months following the onset of RSV season specific to their region (maximum of 5 doses).

Respiratory Syncytial Virus Prophylaxis

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 90378

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Article: "Prevention of Respiratory Syncytial Virus Infections: Indications for the Use of Palivizumab and Update on the Use of RSV-IVIG", American Academy of Pediatrics, 1998; Committee on Infectious Diseases, 1998-1999.

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Clearinghouse Update - Technologica - BCBS Association - BCBS Association - September 1998, page 5.

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October 1998 update, page 1705-1706.

Vice President - Healthcare Management - 1/99.

Medical Policy Advisory Group - 3/99

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Specialty Matched Consultant Advisory Panel - 5/2001

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BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 10/09/03.

American Academy of Pediatrics. (2003, December). Revised indications for the use of palivizumab and RSV IVIG for the prevention of respiratory syncytial virus infections. Retrieved on 12/23/2003 from <http://www.aap.org/policy/t020305.html>.

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Respiratory Syncytial Virus Prophylaxis

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American Academy of Pediatrics. Committee on Infectious Diseases. Policy statement- modified recommendations for use of palivizumab for prevention of respiratory syncytial virus infections. Pediatrics 2009 Sept 7 [Epub ahead of print]. Accessible at: <http://pediatrics.aappublications.org/cgi/reprint/peds.2009-2345v1?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=palivizumab&andexactfulltext=&and&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT>

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 10/08/10

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 10/04/11

Specialty Matched Consultant Advisory Panel – 2/29/12

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 9/13/12

Medical Director review 11/2012

Specialty Matched Consultant Advisory Panel – 2/20/13

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 8/8/13

Specialty Matched Consultant Advisory Panel – 2/25/14

Specialty Matched Consultant Advisory Panel – 2/2015

Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. Pediatrics. Aug 2014;134(2):415-420.

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 9/11/14

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 10/15/15

Specialty Matched Consultant Advisory Panel – 2/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 8/11/2016

Specialty Matched Consultant Advisory Panel – 2/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 8/10/2017

Specialty Matched Consultant Advisory Panel – 2/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.10, 8/9/2018

Specialty Matched Consultant Advisory Panel – 2/2019

Policy Implementation/Update Information

1/99	Original policy issued.
5/99	Reviewed, “Description of Procedure and Service” changed. Reformatted, Medical Term Definitions added.
8/99	Reviewed, Reformatted, Description of Procedure or Service changed, Medical Term Definitions added.
8/99	Medical Policy Advisory Group 8/12/99.

Respiratory Syncytial Virus Prophylaxis

- 9/99 Statement added to the policy - RSV Vaccine is considered investigational.
- 4/01 System change.
- 5/01 Specialty Matched Consultant Advisory Panel review (5/2001). Changed statements regarding the RSV season to indicate that they season may be extended due to the prevalence of RSV in the community.
- 5/02 Revised criteria under when it is not covered to include the statement that other indications for immune prophylaxis for respiratory syncytial virus are considered **investigational** including, but not limited to adults and children with congenital heart disease or immunodeficiencies, or cystic fibrosis, not otherwise addressed by the above criteria. Format changes. Typos corrected. Codes 90780 - 90782 added to Billing and Coding section.
- 5/03 Specialty Matched Consultant Advisory Panel review. Revised under "when it is not covered" section to remove indications for children with congenital heart disease. Term "cyanotic" removed from Medical Term Definitions. Codes IJ013, IJ014, IJ025, IV825, and IV900 deleted from Billing/Coding section. Typos corrected. Format changes.
- 8/12/04 Code S9562 added to Billing/Coding section.
- 12/23/04 Policy Description, When Covered, and Policy Guidelines sections revised. What is covered section updated to add that infants born between 32 weeks and 35 weeks of gestation and are younger than 6 months at the start of the RSV season should have at least 2 or more risk factors. Risk factors are listed as well. Policy number added to Key Words section. Title changed from "RSV-IVIG Palivizumab" to "Respiratory Syncytial Virus Prophylaxis". Benefits Application and Billing/ Coding sections reformatted for consistent policy language. References added. Notification 12/23/ 2004. Effective 03/03/2005.
- 3/03/05 Statement, "For pre-exposure prophylaxis...." statement removed from Benefits Application section.
- 5/05/05 Specialty Matched Consultant Advisory Panel review on April 22, 2005. No changes made to the policy coverage criteria. Definition of gestation changed to say, "the length of time from the first day of the last menstrual period until birth." Definition of premature birth changed to say, "infants born before the thirty-seventh week." Fourth paragraph phrase [less than or equal to 35 weeks gestational age] removed.
- 10/08/05 Updated section "Description of Procedure or Service" to clarify statement regarding applicable age limit. Sixth paragraph phrase indicating administration should continue beyond 6 or 12 months of age changed to read, "administration should continue throughout the season and not stop at the point a child reaches the applicable age limit in the policy below."
- 1/05/06 Deleted CPT codes 90780, 90781, 90782 from Billing/Coding section.
- 10/16/06 Medical Policy reformatted and changed to Evidence Based Guideline. HCPCS Code S9562 removed from Billing/Coding section and statement added to Benefits Application section to indicate that services rendered in the home require prior plan approval.
- 4/23/07 Routine biennial review. Specialty Matched Consultant Advisory Panel review March 15, 2007. No changes to guidelines. (adn)
- 4/27/09 Routine biennial review. Description section revised. Medical criteria sections reformatted into outline format. Indications added to the "Not Recommended" section. RSV prophylaxis is not recommended for patients undergoing stem-cell transplantation and for children over the age of 2 years. Also, use of RespiGam (RSV-IVIg) is contraindicated in infants and children with cyanotic congenital heart disease. Specialty Matched Consultant Advisory Panel review meeting 3/26/09.
- 3/16/10 Revised description section. Note: RespiGam® is no longer available. Guidelines updated to include the current (2009) guidelines from the American Academy of Pediatrics. Rationale section

Respiratory Syncytial Virus Prophylaxis

- added. References updated. Specialty Matched Consultant Advisory Panel review meeting 2/11/10. (adn)
- 3/30/10 Converted from Evidence Based Guideline to Medical Policy. Added the following statement: “RSV Prophylaxis may require prior review” to the Benefits Application section. Notification given 3/30/10 for effective date 7/1/10. (LR)
- 7/1/10 Removed HCPCS code J1565 as applicable code under “Policy Guidelines” section (code removed 5/4/10). J1565 was deleted per HCPCS Level II Expert 2010 edition. Removed medical policy number. Policy effective 7/1/10. (lr)
- 3/29/11 Description section updated. No change to medical necessity criteria in the When RSV Prophylaxis Is Covered/Not Covered sections. Specialty Matched Consultant Advisory Panel review 2/23/11. (adn)
- 3/30/12 “Subsequently, AstraZeneca suspended Motavizumab development and requested the FDA withdraw its biological license application” added to Description. Removed “up to a maximum of 5 monthly doses” from When RSV Prophylaxis is Covered 1. Removed “born before 35 weeks of gestation” and “during the first year of life up to a maximum of 5 monthly doses” from When RSV Prophylaxis is Covered 4. Deleted “congestive” from “congestive heart failure” in policy statements. Policy Guidelines section updated. Specialty Matched Consultant Advisory Panel review 2/29/12. (sk)
- 11/27/12 Reference added. Updated Description section. Added the following statement to Policy Guidelines: “Palivizumab may interfere with RSV diagnostic tests that are immunologically-based (e.g., some antigen detection-based assays)”. Medical Director review. No change to policy statement. (sk)
- 3/12/13 Specialty Matched Consultant Advisory Panel review 2/20/13. No change to policy statement. (sk)
- 10/29/13 Reference added. Senior Medical Director review. No change to Policy statement. (sk)
- 4/1/14 Specialty Matched Consultant Advisory Panel review 2/25/14. No change to policy statement. (sk)
- 5/26/15 Specialty Matched Consultant Advisory Panel review 2/25/15. (sk)
- 7/1/15 References added. Senior Medical Director review. Policy coverage and non coverage criteria, and Policy Guidelines updated per the 2014 American Academy of Pediatrics recommendations. Statement added that immunoprophylaxis for RSV is considered not medically necessary for children with congenital heart disease in the second year of life. Statement added that immunoprophylaxis for RSV is considered not medically necessary for use in children with Down syndrome, unless criteria for medical necessity are satisfied. Notification given 7/1/15 for effective date 9/1/15. (sk)
- 12/30/15 Reference added. (sk)
- 4/1/16 Specialty Matched Consultant Advisory Panel review– 2/24/2016. (sk)
- 9/30/16 Reference added. (sk)
- 3/31/17 Specialty Matched Consultant Advisory Panel review– 2/22/2017. (sk)
- 10/13/17 Reference added. (sk)
- 5/25/18 Specialty Matched Consultant Advisory Panel review– 2/28/2018. (sk)
- 10/26/18 Updated “When Not Covered” section to clarify use of RSV prophylaxis in children with Down syndrome without other risk factors as considered investigational. Minor updates made to Description section for clarity. Reference added. (krc)
- 3/12/19 Specialty Matched Consultant Advisory Panel review- 2/20/2019. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber

Respiratory Syncytial Virus Prophylaxis

certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.