Pharmacy Management Drug Policy

SUBJECT: Synagis® (Palivizumab): Respiratory Syncytial Virus (RSV) Prophylaxis
POLICY NUMBER: PHARMACY-51
EFFECTIVE DATE: 11/02
LAST REVIEW DATE: 08/26/2019

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial, Medicaid, and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Respiratory syncytial virus (RSV) is the leading cause of lower respiratory illness in children. The risk of serious RSV illness is highest among children with prematurity, chronic lung disease, congenital heart disease, multiple congenital anomalies and certain immunodeficiencies. In the United States, RSV infection accounts for more than 90,000 pediatric hospitalizations and 4,500 deaths annually.

Prophylaxis to prevent RSV infection in infants and children at increased risk for severe disease is available using Synagis (palivizumab):

- Synagis is an intramuscularly administered monoclonal antibody preparation. It is administered in a dose of 15 mg/kg once a month during the RSV season (usually considered beginning around November and terminating around the beginning of April). Number of doses varies based on risk factors, gestational age and age at the start of season.

In recent years, the national median duration of RSV season has been 17 weeks or less. For most children in the appropriate high risk categories, five monthly doses of Synagis will result in substantially more than 20 weeks of protective serum antibody concentrations for most of the RSV season, even with variation in season onset and conclusion.

POLICY:

Based upon our criteria and review of the peer-reviewed literature, RSV prophylaxis using Synagis administered in accordance with FDA and American Academy of Pediatrics (AAP) guidelines, has been medically proven to be effective and therefore, **medically appropriate** for the following indications:

Start and Duration of therapy *varies by regional and seasonal rates of infection. CDC reporting of antigen detection levels for specific regions will be monitored throughout the season. (Current levels can be found at http://www.cdc.gov/surveillance/nrevss/rsv/state.html)*

Prevention of RSV disease for the duration of one RSV season with ***maximum of 5 monthly doses*** *of Synagis is recommended in those who meet one of the following criteria, except where noted otherwise*

1. **Infants born prematurely:**
   Infants with a gestational age of 28 weeks 6 days or less who are less than twelve months old at the start of RSV season
   - The number of doses approved will be based on start date of the initial dose. Doses for months outside of the Synagis season will not be approved.
   - For infants born during the RSV season, fewer than 5 monthly doses will be needed.

OR

2. **Infants with immunodeficiencies:**
   Children less than 2 years of age at the start of RSV season with severe immunodeficiencies, such as, severe combined immunodeficiency or advanced acquired immunodeficiency syndrome (AIDS), and children less than 2 years of age, who have undergone lung transplant or hematopoietic stem cell transplant (BMT, peripheral blood, placental or cord blood).

OR

3. **Infants with pulmonary abnormalities or a neuromuscular disorder:**
   Children less than 12 months of age at the start of RSV season, with significant congenital abnormalities of the airway or severe neuromuscular disease which compromises handling of respiratory secretions. (such as, cerebral palsy, muscular dystrophy, neurological disease of the brain & spinal cord, ie Tay Sachs, spinal muscle atrophy)
   (Please note: insufficient data exist to determine the effectiveness of Synagis in infants with Down syndrome and currently no recommendation exists for routine prophylaxis in these patients. Please see exclusion list. Patients with active chronic lung disease or BPD please see #4)

OR

4. **Infants with Chronic Lung Disease (CLD)**
   During the first year of life for Infants and children less than 12 months old at the start of RSV season with a clinical diagnosis of chronic lung disease of prematurity or formerly designated as bronchopulmonary dysplasia (BPD). CLD of prematurity is defined as gestational age <32 weeks, 0 days and a requirement for >21% oxygen for at least the first 28 days after birth.

   Second year of life:
   Pavilizumab prophylaxis will only be approved during the second year of life for infants (≤ 24 months at the start of the season) who meet the definition of CLD of prematurity and continue to require medical treatment for their CLD within 6 months of RSV season.
   Medical Treatment is defined as at least one of the following:
   - Supplemental oxygen
   - Chronic Systemic Corticosteroid therapy
   - Diuretics to treat pulmonary disease

OR

5. **Infants with congenital heart disease (CHD)**
   Infants and children less than 12 months old at the start of RSV season considered by a cardiologist to have hemodynamically significant CHD (acyanotic [e.g. ventricular septal defect, etc.] or cyanotic [right to left shunt]). Including:
   - Infants with acyanotic heart disease who are receiving medication to control congestive heart failure (CHF) and will require cardiac surgical procedures
   - Infants with “moderate to severe” pulmonary hypertension
   - Infants with cyanotic heart disease in consultation with a pediatric cardiologist

The following conditions were noted to be considered hemodynamically *insignificant* in the 2012 AAP Red Book update, and would not typically be considered approvable CHD diagnoses:

- Hemodynamically insignificant heart disease (secundum atrial septal defect, small ventricular septal defect, pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and patent ductus arteriosus.
- infants with lesion adequately corrected by surgery unless they continue to require medication for congestive heart failure
- infants with mild cardiomyopathy who are not receiving medical therapy.
- Children in the second year of life

Note: For infants and children younger than 24 months who are receiving prophylaxis and continue to require prophylaxis after a surgical procedure, a post-operative dose of palivizumab should be considered after cardiac bypass or at the conclusion of extracorporeal membrane oxygenation

Children younger than 2 years who undergo cardiac transplantation during the RSV season may be considered for prophylaxis

OR

6. <u>Cystic Fibrosis</u>

During the first year of life for Infants and children less than 12 months old at the start of RSV season with a diagnosis of cystic fibrosis and clinical evidence of nutritional compromise OR a diagnosis of chronic lung disease 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.

Second year of life:

Pavilizumab prophylaxis will only be approved during the second year of life for infants (≤ 24 months at the start of the season) in patients with cystic fibrosis with 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 have a weight for length less than the 10th percentile.

<u>POLICY EXCLUSIONS</u>:

- Use in otherwise healthy infants born at or after 29 weeks 0 days (28 weeks, 6 days) gestation. Prophylaxis will only be approved for children who meet the above criteria.
- Use for prevention of RSV outside of the RSV season in the region in which the patient resides
- Use for the TREATMENT of RSV disease. (If a child develops breakthrough infection while on immunoprophylaxis therapy, therapy should be discontinued))[31]
- Use in adults for any diagnosis
- Use in children greater than 2 years old or in adults with congenital heart disease or immunodeficiencies
- Use in patients with Down Syndrome who do not otherwise meet the above criteria
- Health-care care associated RSV.

POLICY GUIDELINES:

1. Prior authorization is contract dependent.
2. Synagis is paid under the medical benefit.
3. All indications other than those listed in the policy section above are not covered.
4. Prophylaxis against RSV should be initiated at the onset of the RSV season and terminated at the end of the RSV season. In most seasons in the Northeast, the start of the season occurs mid November, and ends mid March to April 1. For those children meeting criteria for 5 monthly doses, the last dose should be administered at the beginning of March, which will provide protection through April.
5. For all patients approved for prophylaxis, regardless of the month the first dose was administered, the recommendation is for a maximum of 5 total dosages for ALL geographic regions.
6. The number of doses approved will be based on start date of the initial dose. Doses for months outside of the Synagis season will not be approved. For infants born during the RSV season, fewer than 5 monthly doses will be needed.
7. Approval Time Periods:

Line of Business	Medical approval time period
Medicaid Managed Care (MMC)/Child Health Plus (CHP)	Maximum of 5 doses; doses must be given during the current RSV season (Nov. 1st to March 31st for the Northeast).
Commercial/Exchange	Maximum of 5 doses; doses must be given during the current RSV season (Nov. 1st to March 31st for the Northeast).
Medicare	Maximum of 5 doses; doses must be given during the current RSV season (Nov. 1st to March 31st for the Northeast).

CODES: Number Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

HCPCS:

90378 Synagis

UPDATES:

Date	Revision
08/19	Revision
10/18	Revision
10/17	Reviewed
9/16	Revised
10/15	Revised
9/15	Revised
8/14	Revised
10/13	Reviewed
9/12	Revised
9/11	Reviewed
9/10	Reviewed
10/09	Revised
9/09	Revised
9/08	Revised

REFERENCES:

1. Synagis® package insert. Gaithersburg, MD: MedImmune, Inc.; 04/2012
2. The Impact RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high risk infants. *Pediatrics.* 1998; 102(3):531-537.
3. American Academy of Pediatrics: Committee on Infectious Diseases and Committee on Fetus and Newborn. Prevention of respiratory syncytial virus infections: Indications for the use of palivizumab and update on the use of RSV-IGIV (RE9839). *Pediatrics.* 1998; 102(5):1211-1216.
4. American Academy of Pediatrics: Committee on Infectious Diseases and Committee on Fetus and Newborn. Policy Statement. Revised Indications for the Use of Palivizumab and Respiratory Syncytial Virus Immune Globulin Intravenous for the Prevention of Respiratory Syncytial Virus Infections. *Pediatrics.* 2003; 112 (6) 1442-1446.
5. American Academy of Pediatrics. Respiratory Syncytial Virus In: Red Book: *2006 Report of the Committee on Infectious Diseases.*27th edition American Academy of Pediatrics. 2006:560-566
6. The American Academy of Pediatrics Red Book Online. Section 3. Summaries of infectious diseases: Respiratory Syncytial Virus .Available at: http://aapredbook.aappublications.org/cgi/content/full/2003/1/3.105
7. MedImmune, Inc. Phase 3 study shows Synagis reduces RSV hospitalization in young children with congenital heart disease. Press Release. Boston, MA: MedImmune, Inc; October 18, 2003.

8. Committee on Infectious Diseases and Committee on Fetus and Newborn, "Respiratory Syncytial Virus Immune Globulin Intravenous: Indications for Use", (RE9718), Pediatrics, 1997 Apr, 99(4): 645-650.
9. Sondheimer HM, Cabalka AK, Feltes TF et al. (The Cardiac Synagis Study Group). Palivizumab (PV) prevents hospitalization due to respiratory syncytial virus (RSV) in young children with serious congenital heart disease (CHD). *Pediatr Cardiol.* 2002; 23(6): 664(Abstract #4).
10. Committee on Infectious Diseases and Committee on Fetus and Newborn, "Prevention of Respiratory Syncytial Virus Infections: Indications for the Use of Palivizumab and Update on the Use of RSV-IVIG", (S98-39), Pediatrics, 1998 Nov, 102(5): 1211-16.
11. Estrada B, "A New Approach to RSV Prophylaxis", Infect Med, 1998, 15(10): 682.
12. Impact-RSV Study Group "Palivizumab, A Humanized Respiratory Syncytial Virus Monoclonal Antibody, Reduces Hospitalization form Respiratory Syncytial Virus infection in High-risk Infants", Pediatrics, 1998 Sept, 102(3): 531-
13. Subramanian KN, et al, "Safety, Tolerance and Pharmacokinetics of a Humanized Monoclonal Antibody to Respiratory Syncytial Virus in Premature Infants and Infants with Bronchopulmonary Dysplasia", Medi-493 Study Group, Pediatr Infec Dis J, 1998 Feb, 17(2): 110-115.
14. Consensus Statement for the Use of Synagis from Divisions of Neonatology, Pulmonary, Infectious Diseases and General Pediatrics at the Children's Hospital at Strong Memorial Hospital, 11/98.
15. Boeckh M, Berrey MM, Bowden RA, et al. Phase 1 evaluation of the respiratory syncytial virus-specific monoclonal antibody palivizumab in recipients of hematopoietic stem cell transplants. *J Infect Dis.* 2001;184:350-354.
16. Dykewicz CA. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: Focus on community respiratory virus infections. *Biol Blood Marrow Transplant.* 2001;7:19S-22S.
17. Lieberman JM, Dingivan CA. Cystic fibrosis respiratory syncytial virus (RSV) registry: year 1 results. *Pediatr Pulmonol.* 1999 Sept;Supplement 19:277. Presented at: 13th Annual North American Cystic Fibrosis Conference. Seattle, WA, October 7-10, 1999 (Abstract #400).
18. Meissner HC, Anderson LJ, PickeringLK. Annual variation in respiratory syncytial virus season and decisions regarding immunoprophylaxis with paluvizumab. Pediatrics 2004;114:1082-1084
19. Malfoot A, Adam G, Ciofu O, et al. immunization in the current management of cystic fibrosis patients. jCyst Fibros. 2005;4:77-87
20. Journal of American Medical Association Brief Report: Respiratory Syncytial Virus Activity---United States, 2005-2006 JAMA, January 24, 2007;297(4):356-357
21. American Academy of Pediatrics. Respiratory syncytial virus. In: Red Book: 2006 Report of the Committee on Infectious Diseases, 27th ed, Pickering, LK (Ed), American Academy of Pediatrics, Elk Grove Village, IL 2006. p.560.
22. Hand, IL, Noble, L, Geiss, D, Shotkin, A. Respiratory syncytial virus immunoprophylaxis in an urban population: A comparison of delivery strategies and outcomes. Pediatr Infect Dis J 2008; 27:175.

23. Tulloh, R, Marsh, M, Blackburn, M, et al. Recommendations for the use of palivizumab as prophylaxis against respiratory syncytial virus in infants with congenital cardiac disease. Cardiol Young 2003; 13:420.
24. Medimmune website at: www.medimmune.com/pipeline/index.asp
25. American Academy of Pediatrics. Respiratory Syncytial Virus. In: Pickering LK, ed. *Red Book: 2009 Report of the Committee on Infectious Diseases.* 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009:560-569. Available at: http://aapredbook.aappublications.org/cgi/content/full/2009/1/3.110. Accessed August 18,2011
26. American Academy of Pediatrics, **Policy Statement—Modified Recommendations for Use of Palivizumab for Prevention of Respiratory Syncytial Virus Infections** PEDIATRICS Vol. 124 No. 6 December 2009, pp. 1694-1701
27. CDC website- RSV " Prophylaxis and High Risk Groups" accessed September 5, 2012 http://www.cdc.gov/rsv/clinical/prophylaxis.html
28. The American Academy of Pediatrics Red Book Online .2012, 29th edition Section 3. Summaries of infectious diseases: Respiratory Syncytial Virus p626-629.Available at: http://aapredbook.aappublications.org/content/1/SEC131/SEC249.body
29. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hopsitalization for Respiratory Syncytial Virus Infection. Pediatrics 2014; 134(6): 415-420
30. Technical Report: Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hopsitalization for Respiratory Syncytial Virus Infection. Pediatrics 2014; 134:e620-e638
31. Khalid A, Toaimah F, Almatar D, et al. Monoclonal Antibody Treatment of RSV Bronchiolitis in Young Infants: A Randomized Trial. Pediatrics 2019; 144 (1).