palivizumab (Synagis®)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO051

Description

Palivizumab (Synagis) is a humanized monoclonal antibody directed against the fusion protein of respiratory syncytial virus (RSV).

Length of Authorization

- Initial: Five months
- Renewal: N/A

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
palivizumab (Synagis)	100 mg/1mL	Respiratory syncytial virus (RSV) prophylaxis	15 mg/kg (1 dose) per 28 days
	50 mg/0.5mL		

Initial Evaluation

I. **Palivizumab (Synagis)** may be considered medically necessary when the following criteria below are met:
   A. Therapy is given during the current RSV season, **AND**
   B. Member is being managed by, or in consultation with, a pulmonologist or cardiologist; **AND**
   C. Member is less than 24 months of age; **AND**
   D. A diagnosis of one of the following:
      1. **Preterm Infants WITHOUT congenital morbidities** (e.g. chronic lung disease of prematurity; or congenital heart disease); **AND**
         i. Member was born before 29 weeks, 0 days of gestation; **OR**
      2. **Preterm Infants WITH Chronic Lung Disease (CLD)**; **AND**
         i. Member was born before 32 weeks, 0 days of gestation; **AND**
         ii. Member required respiratory support (supplement with greater than 21% oxygen) for at least the first 28 days after birth; **AND**
         iii. Continues to require medical support (e.g., chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of second RSV season; **OR**
      3. **Infants and Children with Hemodynamically Significant Congenital Heart Disease (CHD)**; **AND**
         i. Member has moderate to severe pulmonary hypertension; **OR**
         ii. Member has cyanotic heart disease; **OR**

iii. Member has acyanotic heart disease; **AND**
   a. Member is receiving medication to control congestive heart failure; **AND**
   b. Member will require cardiac surgical procedures; **OR**

4. **Children undergoing cardiac transplantation during RSV season**; **OR**
5. **Infants with Anatomic Pulmonary Abnormalities or Neuromuscular disorder**; **AND**
   i. Member has an impaired ability to clear secretions from the upper airway; **OR**
6. **Immunocompromised Children**; **AND**
   i. Member is profoundly immunocompromised (e.g. undergoing chemotherapy, HIV, SCID, DiGeorge, IgA deficiency, Hypergammaglobulinemia etc.); **OR**
7. **Children with Cystic Fibrosis, Primary Ciliary Dyskinesia, or other rare lung disease**; **AND**
   i. Member has clinical evidence of chronic lung disease (CLD); **OR**
   ii. Member has clinical evidence of nutritional compromise; **OR**
   iii. Member had a hospitalization for pulmonary exacerbation in the first year of life; **OR**
   iv. Member has abnormalities on chest radiography/chest computed tomography that persist when stable; **OR**
   v. Member has a weight for length less than the 10th percentile

II. Palivizumab (Synagis) is considered <u>not medically necessary</u> when criteria above are not met and/or when used for:
   A. Infants or children who were born after 32 weeks
   B. Infants and children with hemodynamically insignificant heart disease such as:
      1. Secundum atrial septal defect
      2. Small ventricular septal defect
      3. Pulmonic stenosis
      4. Uncomplicated aortic stenosis
      5. Mild coarctation of the aorta
      6. Patent ductus arteriosus
   C. Infants with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure
   D. Infants with mild cardiomyopathy who are not receiving medical therapy for the condition
   E. Children in the second year (≥24 months) of life
   F. Children with Down syndrome without other comorbid conditions listed in the Initial Evaluation (section I) portion of this policy.

III. Palivizumab (Synagis) is considered investigational when used for all other conditions, including but not limited to:
   A. For the treatment of RSV

Supporting Evidence

I. For current RSV trends, refer to: http://www.cdc.gov/surveillance/nrevss/rsv/index.html. The CDC utilizes the past year's surveillance season data to predict the timing of the next year's outbreak.

II. Palivizumab (Synagis) is a respiratory syncytial virus (RSV) F protein inhibitor monoclonal antibody indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients. The FDA approved palivizumab (Synagis) in 1998 for pediatric patients with a history of premature birth (<35 weeks of gestation), children with bonchopulmonary dysplasis (BPD), and those with hemodyanamically significant congenital heart disease (CHD).

III. The American Academy of Pediatrics (AAP) committee on infectious diseases (COID) has undertaken a systematic review of all recent, and older, peer-reviewed literature relating to the burden of respiratory syncytial virus (RSV) disease in infants and children, specifically focusing on publications that delineate children at greatest risk of serious RSV disease and studies that define pharmacokinetics, safety, and efficacy. Detailed input regarding this guidance has been solicited from 21 committees, councils, sections, and advisory groups within the AAP, as well as organizations outside the AAP. The updated (reviewed every 3 years) recommendations by AAP are based on review of the quality of all available data, as well as real world clinical impact of palivizumab (Synagis) prophylaxis for the population subset in the United States.

IV. Available clinical data and the AAP recommendations note that there is limited clinical benefit derived from palivizumab prophylaxis for otherwise healthy infants and children and therefore, should be limited to the patient population described in this policy. Furthermore, the package insert for palivizumab (Synagis) states: "Synagis is indicated for the prevention of serious lower respiratory tract disease caused by RSV in children at high risk of RSV disease." And in the absence of a specific definition of "high risk" by the US FDA, the AAP has provided guidenace for determinining the "high risk" population characetistics which have been used to create this policy.

V. Palivizumab (Synagis) was evaluated in two randomized, double-blind, placebo-controlled trials of prophylaxis against RSV infection in children at high risk of an RSV-related hospitalization.
   - Trial 1 was conducted during a single RSV season with 1502 children who were less than or equal to 24 months of age with bronchopulmonary dysplasia (BPD) or infants with premature birth (less than or equal to 36 weeks of gestation) who were less than or equal to 6 months of age at study entry.

i. Results of Trial 1: 4.8% (49/1002) participants were hospitalized in the palivizumab (Synagis) group compared to 10.6% (52/500) participants were hospitalized in the placebo group.

- Trial 2 was conducted over four consecutive RSV seasons with 1287 children less than or equal to 24 months of age with hemodynamically significant congenital heart disease.
    i. Results of Trial 2: 5.3% (34/639) participants were hospitalized in the palivizumab (Synagis) group compared to 9.7% (63/648) participants were hospitalized in the placebo group.

VI. A technical review by the American Academy of Pediatrics (AAP) was completed in 2014 and the recommendation was palivizumab (Synagis) for RSV prophylaxis "cannot be considered as high-value health care for any group of infants" because there is minimal benefit, in addition to its high cost. From that technical review, AAP published the following guidance in 2014: Palivizumab (Synagis) Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection.

- The AAP states available data for infants born at 29 weeks, 0 days' gestation or later do not identify a clear gestational age cutoff for which the benefits of prophylaxis are clear. For this reason, infants born at 29 weeks, 0 days' gestation or later are not universally recommended to receive palivizumab (Synagis) prophylaxis. Infants 29 weeks, 0 days' gestation or later may qualify to receive prophylaxis on the basis of congenital heart disease (CHD), chronic lung disease (CLD), or another condition.

VII. For preterm infants born before 32 weeks, 0 days of gestational age, palivizumab (Synagis) prophylaxis is recommended if the infant developed chronic lung disease (CLD) of prematurity. This typically involves use of supplemental Oxygen (O_2) therapy during the first 28 days after birth to mitigate hypoxia and cyanosis. While normal O_2 saturation in inspired room air (FiO_2) is 20%, infants with CLD require supplementation with > 21% O_2 concentration. The Oxygen need is determined by the patient's disease severity and can range from 21% to up to 100%. Per WHO recommendations for treatment of CLD, supplemental Oxygen therapy should be initiated with 30% oxygen or air (if blended oxygen is not available), rather than with 100% oxygen. The use of progressively higher concentrations of oxygen should only be considered for newborns undergoing oxygen therapy if their heart rate is less than 60 beats per minute after 30 seconds of adequate ventilation with 30% oxygen or air.

VIII. AAP guidelines recommend palivizumab (Synagis) for infants with hemodynamically significant CHD. In this setting, the best therapeutic benefit is likely for infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures and in infants with moderate to severe pulmonary hypertension. 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. According to recommendations from key experts in pediatric cardiology, infants with cyanotic heart defects (e.g. heart valve defects, Ebstein anomaly, hypoplastic left heart syndrome, Tetralogy of Fallot, Truncus arteriosus) are at

a much higher risk of complications from RSV as compared to those with acyanotic heart defects (e.g. congential septal defects, patent ductus arteriosus, pulmonary stenosis, aortic stenosis). Consequently, prophylaxis using palivizumab (Synagis) may have a significant, real world clinical and potentially life-saving impact for the infant population with cyanotic heart disease. AAP guidelines recommend that the decision to use palivizumab (Synagis) in cyanotic heart disease patients must be made by or in consultation with a pediatric cardiologist.

IX. During the second year of life, consideration of palivizumab prophylaxis is recommended only for infants who satisfy the definition of CLD of prematurity and continue to require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the second RSV season. For infants with CLD who do not continue to require medical support in the second year of life prophylaxis is not recommended.

X. Although the National Perinatal Association 2018 Respiratory Syncytial Virus (RSV) Prevention Clinical Practice Guideline: An Evidence-Based Interdisciplinary Collaboration published additional guidance and new information as it relates to RSV, after reviewing the new information, the AAP still recommended their guidelines from 2014 as the new evidence did not change the cost-benefit analysis that was done.

XI. Oregon Health Authority (OHA) has expanded the eligibility of palivizumab (Synagis) for Respiratory Syncytial Virus (RSV) prophylaxis from less than 12 months to less than 24 months of age for high-risk children. The OHA expansion is start for the 2022 – 2023 RSV season or the state of Oregon emergency declaration, whichever is longer. The recommended number of doses or length of treatment has not changed and should follow updates and recommendations from the American Academy of Pediatrics (AAP) and Oregon's Weekly RSV Surveillance Report to determine whether extending the number of doses is necessary.

Investigational or Not Medically Necessary Uses

I. The listed diagnoses are included in the AAP 2017 RSV Guidance as not medically necessary for immunoprophylaxis with palivizumab (Synagis)
   - A. Infants or children who were born after 32 weeks
   - B. Infants and children with hemodynamically insignificant heart disease such as:
     - i. Secundum atrial septal defect
     - ii. Small ventricular septal defect
     - iii. Pulmonic stenosis
     - iv. Uncomplicated aortic stenosis
     - v. Mild coarctation of the aorta
     - vi. Patent ductus arteriosus
   - C. Infants with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure
   - D. Infants with mild cardiomyopathy who are not receiving medical therapy for the condition

E. Children in the second year (≥24 months) of life
F. Children with Down syndrome without other comorbid conditions listed in the Initial Evaluation (section I) portion of this policy.

II. Treatment of RSV
A. Safety and efficacy has not been established for the use of palicizumab (Synagis) for the treatment of RSV.

References

1. Synagis [Prescribing Information]. Gaithersburg, MD: MedImmune, LLC. March 2014.Wegzyn C, Toh LK, Biguenet S, 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.
2. American Academy of Pediatrics: Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. Available at: https://pediatrics.aappublications.org/content/134/2/415
3. American Academy of Pediatrics: RSV recommendations unchanged after review of new data. Available at: https://www.aappublications.org/news/2017/10/19/RSV101917
4. Policy Statement: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee. *Pediatrics.* August 2014; 134(2): e415-20. doi: 10.1542/peds.2014-1665. Reaffirmed February 2019. Available online at https://pediatrics.aappublications.org/content/134/2/415.full#sec-13.
5. Goldstein M, Phillips R, DeVincenzo J, et al. The National Perinatal Association 2018 Respiratory Syncytial Virus (RSV) Prevention Clinical Practice Guideline: An Evidence-Based Interdisciplinary Collaboration. October 2017.
6. Center for Disease Control and Prevention: Respiratory Syncytial Virus Infection (RSV). Available at: https://www.cdc.gov/rsv/clinical/index.html
7. Red Book® 2018. Committee on Infectious Diseases; American Academy of Pediatrics; David W. Kimberlin, MD, FAAP; Michael T. Brady, MD, FAAP; Mary Anne Jackson, MD, FAAP; Sarah S. Long, MD, FAAP. Section 3: Respiratory Syncytial Virus. Available at https://redbook.solutions.aap.org/Book.aspx?bookid=2205. Accessed December 4th, 2020.

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated policy to follow OHA age expansion from < 12 months to < 24 months for the 2022 – 2023 RSV season.	12/2022
Formatting edits and minor edits to wording used in efforts to provide more clarity of policy intent; Addition of indication of 'cyanotic heart disease' as per AAP guidelines; Updated Supporting Evidence section to include more information surrounding clinical benefits of palivizumab (Synagis) prophylaxis and clarification that this policy follows AAP recommendations based on quality of clinical evidence instead of FDA approved indications listed in package insert	12/2020
Transitioned criteria into policy with supporting evidence, and incorporated the updated AAP RSV prophylaxis guidelines that details the specific coverage recommendations for: chronic lung disease in patients less than 24 months, patients less than 12 months with hemodynamically significant chronic heart disease, cardiac transplantation in patients less than 24 months, anatomic pulmonary	09/2019

abnormalities/neuromuscular disorder in patients less than 12 months, immunocompromised children, children with rare lung disease. Additionally, incorporated the recommendations from the updated AAP RSV prophylaxis guidelines to detail what diagnoses are not medically necessary for RSV prophylaxis/Synagis.	